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THE ACTION OF HISTAMINE ON THE HEARTS OF TWO LAMELLIBRANCH MOLLUSCS

By R. L. C. PILGRIM

From the Zoology Department, Canterbury University College, Christchurch, C. 1. New Zealand

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Although several isolated preparations, admirable for experimental purposes, have been described from Mollusca, particularly from the heart tissues, the action of histamine on them is almost completely unexamined. Jullien, Vincent, Vuillet & Bouchet (1939) found that at a concentration of 10^{-8} the drug caused a rise of tone, especially diastolic tone, leading to reduction in amplitude when applied to the isolated heart of *Helix pomatia*; at 10^{-5} severe arrhythmia occurred and the amplitude was reduced to *c.* one half. On other invertebrates the action of histamine varies; thus Wu (1939) found the effect inconstant on isolated preparations from earthworms, while von Euler, Chaves & Teodosio (1952) showed that histamine contracts the water-lung of *Holothuria* and relaxes the longitudinal muscle, the latter contracting in the presence of small doses of acetylcholine. Wu (1939) further described histamine as inhibiting the action of ACh, whereas Frommel, Aron, Herschberg, Piquet & Goldféder (1944) found histamine to sensitize leech muscle, *Helix* heart and frog rectus preparations to ACh, the sensitization being analogous to that produced by eserine; this latter observation falls into line with the opinion (Burn, 1950) that histamine may act as an anticholinesterase. Histamine or histamine-like substance has been detected by Ungar, Ungar & Parrot (1937) in a number of invertebrates, including *Mytilus edulis*.

The purpose of the present investigation was to examine the effect of histamine on isolated preparations of lamellibranch hearts; it has been shown (Pilgrim, 1954) that within the class Lamellibranchia different species react in widely differing respects, both quantitative and qualitative, to ACh, and from the series described in this earlier paper two species were selected largely on account of the great difference in their reactions to ACh, viz. *Amphidesma forsterianum* Finlay (very sensitive to ACh, usually arrested in diastole at high concentrations) and *Mytilus canaliculus* Martyn (much less sensitive, more commonly arrested at a high tone level).

METHODS

The preparations were set up as described by Pilgrim (1954). Histamine acid phosphate (B.D.H.) was used throughout; it was prepared daily in sea water at a concentration of 10^{-2} (w/v of the base itself) and convenient dilutions made from this so as to keep the amount added to the bath to no greater than 2·5 ml. It was found satisfactory to leave the preparations for from ½ to 1 hr between tests. A total of 220 experiments was made on forty-eight preparations.

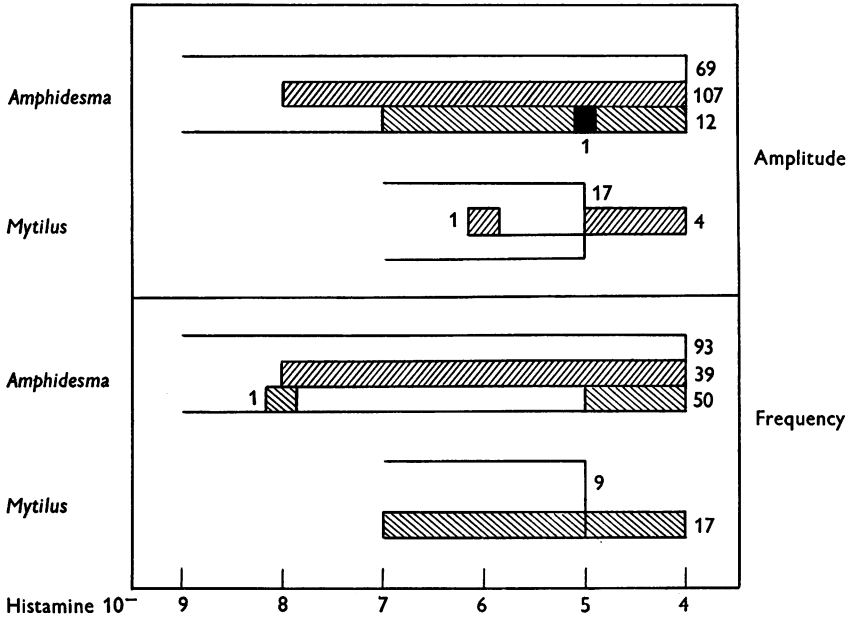

Fig. 1. Analysis of results in respect of amplitude and frequency changes caused by histamine. Open areas mean no effect; shaded areas, increase (▨) or decrease (▧); black area, systolic arrest. Figures refer to numbers of experiments in each case. Histamine concentration plotted logarithmically.

RESULTS

The results are shown in the figure in which the extreme limits of reactions are incorporated.

Amplitude. This was clearly increased in *Amphidesma* in histamine at 10^{-4}, and in approximately half the preparations in 10^{-6}, while occasional reactions were obtained down to 10^{-8}. The increase in amplitude was due to a rise in systolic tone, but a slight rise in diastolic tone also occurred in 10^{-4} to 10^{-7}; in a few instances diastolic tone was raised to a greater extent than was systolic tone resulting in a reduction in amplitude, and in one case in temporary systolic arrest. The preparations of *Mytilus* were unaffected in respect to amplitude until the concentration of the drug reached 10^{-5}, when amplitude

was increased; in 3×10^{-5} and 10^{-4} the increase was sometimes partly obscured by alternate large and small beats or by a quite irregular rhythm.

Frequency. In *Amphidesma* this was unaffected in many preparations at all concentrations tested, but a distinct trend was evident in the remainder: in histamine 10^{-5} thirty-six experiments resulted in no change in frequency, fourteen showed a decrease and fifteen an increase; in higher concentrations the majority decreased in frequency, while in lower concentrations the tendency was for no change or an increase in frequency. Where they occurred, frequency decreases were distinct (*c.* 30%) and increases slight (*c.* 2–4%).

In *Mytilus* frequency decrease was found at higher concentrations as in *Amphidesma*, but in lower concentrations there was no sign of any increase.

DISCUSSION

The sensitivity of these preparations towards histamine differs from that towards ACh in being less marked; *Amphidesma* was shown (Pilgrim, 1954) to reduce amplitude and frequency in ACh at 6×10^{-11} but it is more than a thousand times less sensitive to histamine in this respect. *Mytilus* is a hundred times less sensitive in respect to frequency reduction and does not show amplitude reduction in histamine. The range of concentrations of histamine in which reactions occurred is much more similar in the two species than was the range of concentrations of ACh studied earlier (Pilgrim, 1954). Furthermore, the nature of the reactions is different from that obtained with ACh. *Amphidesma* preparations react to histamine with increase or decrease in both amplitude and frequency; in ACh both these properties reduced. *Mytilus* preparations in histamine show an increase in amplitude and reduction in frequency; in ACh there was found increase or decrease in both properties over the same range of concentrations. In histamine, some preparations of both species studied were insensitive to all concentrations of the drug used (except *Mytilus* at 10^{-4}).

The overall impression is that the reactions to histamine are not governed by a coherent behavioural pattern. The variability in amplitude reaction, however, can be simplified by considering instead the changes in tone levels: thus those preparations of *Amphidesma* which react to histamine mostly show a rise of systolic tone. The variation comes from the extent of changes in diastolic tone level which, when great, lead to a reduction in amplitude or in one instance to systolic arrest. It would be interesting to know if the variability shown by Wu in the reaction of earthworms to histamine could be similarly described.

It cannot be said that histamine is a substance which causes a distinct pattern of responses in these tissues. Many preparations do not react at any of the concentrations used and despite attempts to consider the results in

other ways, it must be said that the effects of this drug on amplitude and frequency are unco-ordinated and variable. It appears unlikely, therefore, that the substance is a natural agent in the transmission of stimuli in the heart tissues of lamellibranchs.

SUMMARY

1. Isolated ventricle-strip preparations from two species of New Zealand lamellibranch molluscs were submitted to the action of histamine in concentrations of 10^{-9} to 10^{-4}.

2. The reactions are more comparable between the two species than are those towards acetylcholine. Individual preparations varied, however, in their reaction; at any one concentration of histamine a preparation (either species) may be unaffected, or its amplitude increase or frequency decrease (*Mytilus*), or both amplitude and frequency increase or decrease (*Amphidesma*). The most marked tendency was for a decrease in frequency at high drug concentration and increase at low concentration.

3. It is concluded from these experiments that histamine may have no significance as a natural evocator of cardiac reaction in these animals.

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