PROCEEDINGS OF THE
British Pharmacological Society

26th-27th March, 1975

WELSH NATIONAL SCHOOL OF MEDICINE CARDIFF

COMMUNICATIONS

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A possible mode of action of piperazine

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Histamine, a putative neuromuscular transmitter substance in nematodes, has been identified in the tissues of *Ascaris suum* (Miyagawi, 1961; Phillips, Sturman & West, 1975). In the following study, the effect of the anthelmintic drug, piperazine, on the histamine content of whole, mature, female worms has been determined using both fluorimetric and biological techniques.

The mean (± s.e. mean) histamine content of 20 control Ascaris (obtained from the intestines of freshly slaughtered pigs) after incubation for 24 h at 38°C in modified Baldwin Ringer solution (Baldwin & Moyle, 1947) was 104 ± 9 ng/g. When concentrations of piperazine (from 0.05% to 0.2%) were included in the incubation mixture, reductions of up to 16% in the histamine content were found. Partial paralysis of the parasites occurred at the highest concentration. When the concentration of piperazine was increased to 0.5%, the histamine content was raised slightly above the control value and total immobilization was noted.

The histamine content of *Ascaris suum* incubated in Ringer solution containing 10 μg/ml histamine increased to 368 ± 49 ng/g and it increased further to 560 ± 32 ng/g (a significant increase of 52%) when 0.05% piperazine was present. In the presence of 0.1% piperazine and histamine, the histamine content was raised over two and a half times although this value was not increased further when 0.2% piperazine was included in the incubation mixture. Paralysis of the parasites was always greater when histamine was present with the piperazine.

These results indicate that piperazine tends to lower the histamine content of *Ascaris suum* and in high concentrations it immobilizes the parasites. Low concentrations of piperazine, however, become more effective in producing muscular relaxation when histamine is included in the incubation mixture, and expulsion of the parasites from the host's intestine would then be assisted. As the histamine content of pig intestinal fluid is 3-10 μg/ml, the experimental conditions used reflect the normal environmental conditions of *Ascaris suum* as regards the histamine levels. The

mechanism of action by which the histamine content of the worm is increased by piperazine in the presence of histamine remains uncertain but increased absorption across the body wall and relaxation of the muscle around the mouth (thereby increasing ingestion) are possibilities.

We would like to thank the Dunmow Flitch Bacon Factory for providing facilities for collecting *Ascaris suum* samples. This work was carried out during the tenure of an A.R.C. grant (J.L.P.).

References

BALDWIN, E. & MOYLE, V. (1947). An isolated nerve-muscle preparation from *Ascaris lumbricoides*. *J. exp. Biol.*, 23, 277-291.

MIYAGAWI, Y. (1961). Histamine in *Ascaris lumbricoides* and the effect of some anthelmintics on it. *Jap. J. Parasitol.*, 10, 419-428.

PHILLIPS, J.L., STURMAN, G. & WEST, G.B. (1975). The presence of histamine in the tissues of *Ascaris suum*. *Comp. Gen. Pharmac.* In press.

Site of action of an anti-inflammatory fraction from normal human plasma

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A fraction isolated from normal human plasma contains a substance of low molecular weight, below 500, which shows anti-inflammatory activity in animal tests in which the emigration of circulating leucocytes is a major factor (Ford-Hutchinson, Smith, Elliott, Bolam, Walker, Lobo, Badcock, Colledge & Billimoria, 1975). We have now studied its effects on the release of complement-derived chemotactic factors and anaphylatoxin from rat serum.

Preparations of the plasma fraction which caused a significant reduction in the accumulation of leucocytes in sponges implanted subdermally in the intact rat were tested at the same time for their effects on the directed migration of isolated rat leucocytes using the Boyden chamber technique (Goetzl & Austen, 1972) and on the production of anaphylatoxin by the method of Kleine, Poppe & Vogt (1970). Antigen-antibody complex was used as the activator of the classical pathway of complement and zymosan and *E. coli* endotoxin as activators of the alternate pathway.

The results (Table 1) show that the plasma fraction inhibited the release of chemotactic factors and anaphylatoxin when complement was activated by zymosan or endotoxin but not by antigen-antibody. However, there was no interference with the actions of the released chemotactic factors and anaphylatoxin on either the rat peripheral leucocytes or the isolated guinea-pig ileum. It is suggested that the active substance in the plasma fraction inhibits the C3 activator system in rat serum (Götze & Müller-Eberhard, 1971). This effect may be of some significance because of the recent observation (Goldstein & Weissmann, 1974) that leucocyte lysosomes contain a material causing a non-immune activation of the complement system thus amplifying the inflammatory response through a positive feed-back loop mechanism.

This work was supported by grants from the National Research Development Corporation, the King's College Hospital and Medical School Research Committee, the Wates Foundation, and the Nuffield Foundation.

Table 1 Effects of plasma fraction on the release of chemotactic and anaphylatoxic activities from rat and guinea-pig serum.

Addition to serum	*Chemotaxis (no. of cells per high power field)*	*Anaphylatoxin (% change: activator = 100)*
Zymosan	14.7 ± 1.7 (9)	
Zymosan + PF	8.6 ± 0.6 (9)*	−40 ± 8 (5)*
Endotoxin	22.4 ± 0.7 (9)	
Endotoxin + PF	13.2 ± 0.7 (9)*	
Antigen-antibody	14.9 ± 1.1 (9)	
Antigen-antibody + PF	15.1 ± 0.4 (8)	+2 ± 3 (3)

Results given as mean ± s.d., number of separate experiments in brackets. PF, plasma fraction (0.1 ml); * $P < 0.001$, significant difference from the corresponding value with activator alone.