JOHNSTON, G. A. R. & CURTIS, D. R. (1972). *J. Pharm. Pharmac.*, **24**, 251.
KURIAKI, K., YAKUSHIJI, T., NORO, T., SHIMUZU, T. & SAJI, Sh. (1958). *Nature*, **181**, 1336–1337.
POTTER, L. T. & MURPHY, W. (1967). *Biochem. Pharmac.*, **16**, 1386–1387.
TABACHNICK, I. A. A. (1960). *Ibid.*, **3**, 166.
VOLLE, R. L. (1966). *Pharmac. Rev.*, **18**, 839–869.

Disodium cromoglycate and the dextran response in rats

Recently, Orr, Hall & others (1971) showed that low concentrations (1×10^{-5}M) of disodium cromoglycate (DSCG) inhibited the release of histamine from rat isolated mast cells induced by compound 48/80. However, Assem & Richter (1971) found that significant inhibition of histamine release by compound 48/80 from rat peritoneal mast cells was effected only with high concentrations (1×10^{-3}M) of DSCG. They also reported that DSCG (100 mg/kg) inhibited the intracutaneous response to dextran in rat skin. We have examined the effects of DSCG on the dextran response in different tissues of the rat.

Groups of five male Sprague-Dawley rats (250–300 g) were injected intraperitoneally with dextran (180 mg/kg, molecular weight 67 000) alone or containing DSCG (dissolved in the dextran solution), and the anaphylactoid response was assessed by a method similar to that of Parratt & West (1957) using an arbitrary scale at half-hourly intervals for 4 h. Other rats received intradermal injections (8/rat) of 0·1 ml Tyrode solution containing either dextran (200 μg) or histamine (36 μg) into the shaved skin of the back, the animals previously having been injected intravenously with azovan blue dye (30 mg/kg); some of the rats also received intravenous injections of DSCG immediately before the intradermal injections. 30 min later, the rats were killed and the amount of blue dye in each wheal was estimated after extraction and assay using the method of Harada, Takeuchi & others (1971).

To study histamine release from the peritoneal cavity, rats were injected intraperitoneally with 1 ml normal saline (0·9%) containing different amounts of DSCG. 30 s later they received an intraperitoneal injection of dextran (180 mg/kg) and heparin (1 mg/kg). 5 min later the animals were killed, the peritoneal fluid collected and centrifuged, and the supernatant was assayed for histamine on the atropinized guinea-pig ileum.

DSCG (5 mg/kg) significantly inhibited the anaphylactoid reaction produced by intraperitoneal dextran, but only after 2 h, the maximum response being at 4 h when the reaction was depressed by about 20%. Doses higher than 5 mg/kg produced less inhibition.

Intravenous DSCG (10 mg/kg) significantly reduced the increased vascular permeability produced by intradermal dextran (as determined by the amount of blue dye leaking into the tissues: dextran 22 $\pm$ 2·5 μg, dextran + DSCG 10 $\pm$ 7 μg), but this dose did not reduce the histamine response. Higher intravenous doses of DSCG produced no further reduction in the response. Intradermal DSCG (36 μg) was also effective in reducing the intradermal dextran response.

Dextran injected intraperitoneally released histamine (range 0·5–1·13 μg/ml) from the peritoneal cavity of rats and intraperitoneal DSCG inhibited this release over the range 2·5–2500 μg/kg (Fig. 1). Thus DSCG inhibits the dextran response in all three tests.

DSCG has been used successfully in the treatment of allergic asthma and as a means of identifying immunological systems that have a common pathway for mediator release. Thus DSCG inhibits degranulation of rat mast cells sensitized with reaginic antibodies on exposure to the antigen (Goose & Blair, 1969). It also prevents mediator release from passively sensitized human lung on exposure to

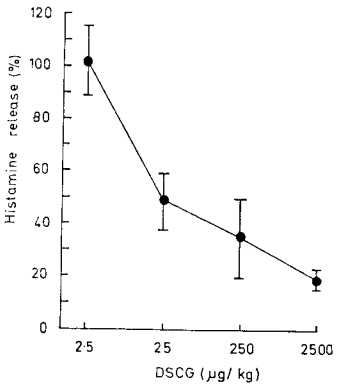

FIG. 1. The effect of DSCG (μg/kg) on the release of histamine from rat peritoneal cavity by dextran (180 mg/kg). Results are mean ± s.e. of at least 5 experiments.

antigen (Sheard & Blair, 1970). In addition, Orr, Gwilliam & Cox (1970) have shown that DSCG is a weak inhibitor of non-reaginic anaphylaxis. DSCG therefore inhibits the immunological release of histamine from mast cells. In view of this, the present results indicate that dextran-induced histamine release may be initiated by a means similar to that of the immunological release of histamine.

Kabat, Turino & others (1957) showed that dextran may be antigenic in man and found some individuals who had small amounts of an antibody before any known contact with dextran. In addition, Kabat (1957) reported that the precipitation reaction between dextran and human antidextran serum, like the dextran response in rats, can be inhibited by simple sugars. No antibody to dextran has yet been found in the rat, but Poyser & West (1968) have suggested that there may be an innate antibody in the rat sensitive to carbohydrate polymers such as dextran. The fact that DSCG inhibits the dextran response supports this hypothesis.

Department of Applied Biology,
North East London Polytechnic,
Longbridge Road,
Dagenham, Essex.

T. H. P. HANAHOE
A. HOLLIMAN
D. GORDON
W. WIECZOREK

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REFERENCES

ASSEM, E. S. K. & RICHTER, A. W. (1971). *Immunology*, **21**, 729–739.
GOOSE, J. & BLAIR, A. M. J. M. (1969). *Ibid.*, **16**, 749–760.
HARADA, M., TAKEUCHI, M., FUKAO, T. & KATAGIRI, K. (1971). *J. Pharm. Pharmac.*, **23**, 218–219.
KABAT, E. A. (1957). *J. Cell. Comp. Physiol.*, **50**, 79–102.
KABAT, E. A., TURINO, G. M., TARROW, A. B. & MAURER, P. H. (1957). *J. clin. Invest.*, **36**, 1160–1170.
ORR, T. S. C., GWILLIAM, J. & COX, J. S. G. (1970). *Immunology*, **19**, 469–479.
ORR, T. S. C., HALL, D. E., GWILLIAM, J. & COX, J. S. G. (1971). *Life Sci.*, **10**, 805–812
PARRATT, J. R. & WEST, G. B. (1957). *J. Physiol., Lond.*, **139**, 27–41.
POYSER, R. H. & WEST, G. B. (1968). *Brit. J. Pharmac.*, **32**, 219–226.
SHEARD, P. & BLAIR, A. M. J. N. (1970). *Int. Arch. Allergy*, **38**, 217–224.