

RESPONSE OF SKIN TO AMMONIUM PERSULPHATE

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Abstract. In order to investigate the histamine liberating actions of ammonium persulphate, skin slices from three species (guinea pig, rat and monkey) were incubated in vitro with concentrations of ammonium persulphate ranging from 1 to 1 000 $\mu\text{g/ml}$. None of these concentrations released significant amounts of histamine in guinea pig or monkey skin. In the rat the highest concentration (1 000 $\mu\text{g/ml}$) released 20-24% of the histamine content of the skin, but the intensity of this response to cooling indicates a non-specific "toxic" action on mast cells. By contrast a known chemical histamine liberator, compound 48/80, released significant amounts of histamine from skin at much lower concentrations in all three species. Ammonium persulphate is clearly not a potent histamine liberator. Ammonium persulphate dermatitis is presumably a result of increased sensitivity of skin mast cells, due to immunological or other factors, in susceptible individuals.

Key words: Histamine; Dermatitis; Ammonium persulphate

Ammonium persulphate causes skin irritation in some individuals. It has been incriminated as the cause of dermatitis and urticarial reactions in bakers handling flour containing ammonium persulphate and in hair dressers using this agent in a bleach. Calnan & Shuster (1) obtained indirect evidence from experiments using a histamine depleting agent and anti-histamine that the whealing response to ammonium persulphate was due to histamine release. Ammonium salts characteristically act as histamine liberators and of those tested the sulphate proved the most potent (2). We have therefore examined the histamine liberating properties of ammonium persulphate in skin of several species and have compared its action with that of a known chemical histamine liberator, compound 48/80.

MATERIALS AND METHODS

Skin was obtained from the following: Guinea pigs (Dunkin-Hartley) wt. 400-450 g; Rats (CFY) wt. 300-400 g; Monkeys (Rhesus) 2-3 years old.

Reagents: Ammonium persulphate (Hopkin and Williams Ltd.); Compound 48/80 (Burroughs Wellcome Ltd.).

Histamine release experiments were carried out by the method of Greaves, Fairley & Yamamoto (3). 500 μm thick abdominal skin slices were obtained by means of a hand microtome. Triplicate samples (1-3 slices per sample) were incubated in Tyrode solution (pH 7.6) with a range of concentrations of ammonium persulphate or compound 48/80 for 15-30 minutes at 37°C, the reaction being terminated by cooling. Histamine was measured by bioassay. Released histamine was expressed as a percentage of the total histamine per sample. The total histamine was calculated from the sum of released and residual histamine, the latter being determined by boiling for 10 minutes and cooling the residual skin slices, followed by histamine bioassay. All values are corrected for 'spontaneous' histamine release by subtracting the value for the negative control release.

Bioassay

Histamine bioassay was carried out using an atropinized terminal guinea pig ileum preparation, using a matching assay technique in which the unknown solutions are 'bracketed' with responses to a series of standards. The identity of histamine was confirmed by using the specific antagonist mepyramine. At the concentrations used, ammonium persulphate did not interfere with the response of the guinea pig ileum to histamine during bioassay.

RESULTS

The results are summarized in Table I.

Guinea pig

In five experiments, concentrations of ammonium persulphate ranging from 1 to 100 $\mu\text{g/ml}$ failed to produce specific histamine release. By contrast, compound 48/80 10 $\mu\text{g/ml}$ caused a release ranging from 6 to 13% and 100 $\mu\text{g/ml}$ caused a release ranging from 29 to 46%. In a single experiment in which skin was incubated with 1 000 $\mu\text{g/ml}$ of ammonium persulphate, no histamine release was detected.

Table 1. Histamine release (%) from skin resulting from incubation with ammonium persulphate (AP) and compound 48/80

Each value in the concentration range 1–100 $\mu\text{g/ml}$ for guinea pig and rat skin represents the mean \pm S.D. of 5 experiments. Each value at 1000 $\mu\text{g/ml}$ represents the mean \pm S.D. of 3 experiments. Each value for the monkey is the result of a single experiment.

	1 ^a		10 ^a		100 ^a		1000 ^a	
	48/80	AP	48/80	AP	48/80	AP	48/80	AP
Guinea pig	0	0	10.1 \pm 1.4	0	37.3 \pm 3.8	0	ND	0
Rat	0	0.2 \pm 0.6	6.6 \pm 1.0	0.5 \pm 0.9	22.0 \pm 1.3	2.0 \pm 1.4	ND	20.6 \pm 1.6
Monkey	0	0	8.0	0	41.0	0	ND	0

^a Concentration ($\mu\text{g/ml}$); ND: not done.

Rat

The effect of ammonium persulphate 1–100 $\mu\text{g/ml}$ was studied. In five experiments no release was obtained with concentrations up to 100 $\mu\text{g/ml}$, although compound 48/80 10 $\mu\text{g/ml}$ released 5–9% and 100 $\mu\text{g/ml}$ caused a release ranging from 19 to 26%.

In a further three experiments the concentration of ammonium persulphate was increased to 1000 $\mu\text{g/ml}$. With this concentration, releases ranging from 20 to 24% were obtained. Release by this concentration was not temperature dependent, since release was not reduced by lowering the incubation temperature from 37° to 0°C.

Monkey

In a single experiment no release was obtained in the presence of up to 100 $\mu\text{g/ml}$ ammonium persulphate. By contrast 100 $\mu\text{g/ml}$ of compound 48/80 produced 41% histamine release and 10 $\mu\text{g/ml}$ caused 8% release. No histamine release was obtained in the presence of 1000 $\mu\text{g/ml}$ of ammonium persulphate.

COMMENT

The cause of the inflammatory reaction in skin as a response to contact with ammonium persulphate is not known yet.

In vitro studies with guinea pig lung fragments incubated with several salts of ammonium ion including the sulphate have shown it to be a histamine liberator (2). Calnan & Shuster (1) suggested that the clinical responses to ammonium persulphate could be attributed to its supposed ability to liberate histamine by a direct action on mast cells. However, the present results do not support this theory,

since the study of histamine release from skin of three species, including primate, has failed to demonstrate any significant histamine liberating properties of ammonium persulphate. The response to 1000 $\mu\text{g/ml}$ ammonium persulphate on rat skin was probably a non-specific toxic reaction, since it was not temperature dependent. Calnan & Shuster discounted the possibility of an immune mechanism on the basis of negative passive transfer tests. However, it is rather difficult to interpret their results, as they did not use conjugates of ammonium persulphate as antigen. Patients whose skin reacts to contact with ammonium persulphate may have skin mast cells which are abnormally susceptible to this agent. Whether this susceptibility is immunologically based or is a property inherent in the mast cell itself remains unknown.

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