Mechanism of A23187 induced histamine release

T. JOHANSEN (introduced by L.G. GARLAND)

Department of Pharmacology, Odense University, J.B. Winsløwsvej 19, DK-5000 Odense C, Denmark

Anaphylactic histamine release from guinea pig lung and disruption of rat mast cell due to antigen is dependent on temperature (Mongar & Schild, 1957; Högberg & Uvnäs, 1960), and on oxidative or glycolytic metabolism (Parrot, 1942; Moussatché & Prouvost-Danon, 1962). The amount of histamine released by the antigen-antibody reaction *in vitro* was dependent on mast cell ATP content and during the release there was an increased utilization of ATP (Johansen & Chakravarty, 1975). This was also the case for histamine release from rat mast cells induced by the ionophore A23187 (Johansen, 1977).

The purpose of this study was to compare the mechanism of A23187 induced histamine release with that of the anaphylactic histamine release. For A23187 induced histamine release, the effect of calcium concentration on the time course, the effect of temperature and the effect of heat inactivation has been studied. For both of the releasing agents, the effect of temperature on the rate of histamine release has been examined.

Pure populations of rat mast cells were isolated by differential centrifugation in concentrated human serum albumin. Histamine was determined by the fluorimetric method.

A 23187 induced histamine release was maximal in the presence of calcium (10^{-3} mol/l) and the release was completed after 10 minutes. However, when the cells were preincubated with A23187 histamine release induced by the same concentration of calcium was completed after 90 s, and with calcium (5×10^{-3} mol/l) the histamine release process lasted only 45 seconds. Anaphylactic histamine release was maximal at a calcium concentration of $1-2 \times 10^{-3}$ mol/l (Foreman & Mongar, 1972) and the release was completed within 30-40 s (Johansen & Chakravarty, 1975).

Maximal histamine release induced by A23187 was achieved between 33-39°C and the release declined above and below this temperature range. Essentially the same effect of temperature on anaphylactic histamine release from guinea pig lung and antigen induced mast cell disruption was reported by Mongar & Schild (1957) and Högberg & Uvnäs (1960).

Pretreatment at an elevated temperature (42.5°C for 30 min) did not inhibit A23187 induced histamine release at 37°C. However, preincubation at 43.1°C or 44.9°C caused a significant reduction and block of histamine release, respectively. A similar relationship has been demonstrated for anaphylactic histamine release (Mongar & Schild, 1957).

The rate of the initial part of A23187 induced or anaphylactic histamine release was enhanced when the incubation temperature was increased. The Arrhenius plots of incubation temperature against histamine release were identical and appeared to be biphasic with a break at 30°C. Calculation of the activation energies gave identical vallues about 45,000 cal $\times$ degree^{-1} $\times$ mol^{-1}.

These observations are consistent with the view that the same mechanism is involved in A23187 induced and anaphylactic histamine release. It may be speculated that an increase in the concentration of calcium in mast cell cytosol is the trigger of the release mechanism.

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