



ORAL PRESENTATION

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# Platelet activating factor-induced mast cell degranulation is inhibited by rupatadine, and to a lower extent by levocetirizine and desloratadine, in a mast cell line (LAD-2)

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## Background

Platelet activating factor (PAF) is a lipid mediator that appears to be involved in the pathophysiology of several allergic reactions such as anaphylaxis and potentially urticaria and allergic rhinitis. The role of rupatadine, a drug with dual antihistamine and anti-PAF effect, in mast cell (MC) degranulation is not known. The objective of this study was to investigate the expression of PAF receptors and the effect of rupatadine on PAF-induced MC degranulation compared with other second generation antihistamines (desloratadine, levocetirizine) and a pure specific PAF inhibitor in a human mast cell line (LAD-2).

## Methodology

MC degranulation was evaluated by the  $\beta$ -hexosaminidase and histamine release while PAF receptor expression was evaluated by western blot. After stimulation with PAF in a dose-response and time course manner, the optimal PAF conditions to induce LAD-2 degranulation were identified (10  $\mu$ M and 30 minutes). The effects of rupatadine, desloratadine, and levocetirizine (from 1  $\mu$ M to 100  $\mu$ M) on PAF-induced LAD-2 degranulation were investigated. The inhibitory effect of CV6209 (specific anti-PAF) at 2  $\mu$ M was used as positive control in all experiments.

## Results

Protein expression of the PAF receptor was found in LAD-2 cells. Rupatadine (5 to 10  $\mu$ M,  $p < 0.005$ ) and levocetirizine (5  $\mu$ M,  $p < 0.01$ ) but not desloratadine inhibited

PAF-induced  $\beta$ -hexosaminidase release. Rupatadine (1 to 10  $\mu$ M,  $p < 0.01$ ), levocetirizine (1 to 25  $\mu$ M,  $p < 0.05$ ), and desloratadine (10  $\mu$ M,  $p < 0.05$ ) also inhibited PAF-induced histamine release.

## Conclusions

This study shows that the ant-H1 compounds rupatadine, and to a lower extent levocetirizine and desloratadine, have an anti-PAF effect in the mast cell line LAD-2, suggesting that rupatadine could be more effective than other antihistamine drugs in those allergic disorders where PAF may act as an important inflammatory mediator.

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