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Inhibition of leukotriene B_4 production in human neutrophils by 2-styrylchromones

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2-Styrylchromones are a small group of naturally occurring chromones, vinylogues of flavones (2-phenylchromones). Natural and synthetic 2-styrylchromones have been tested in different biological systems, showing activities with potential therapeutic applications. Certain flavones are potent inhibitors of the production of eicosanoids, a group of powerful proinflammatory signalling molecules. However, the anti-inflammatory potential of 2-styrylchromones, concerning their possible interference in this pathway, has not been explored so far. Lipoxygenases (LOXs) are a group of enzymes involved in the arachidonic acid metabolism. From the LOXs existent in the mammalian tissues, 5-lipoxygenase (5-LOX), which is mainly found in cells of myeloid origin, is the most implicated in inflammatory and allergical disorders. 5-LOX produces 5-hydroxyeicosatetraenoic acid (5-HETE) and various leukotrienes (LTA_4-LTE_4), being 5-HETE and LTB_4 potent chemoattractant mediators of inflammation. Thereby, the aim of the present work was to study the putative inhibitory effect of 2-styrylchromones on the production of LTB_4 by human neutrophils. The obtained results show that some of the tested compounds are strong inhibitors of the LTB_4 production, which makes them promising subjects of study for their possible application in the treatment of inflammatory processes.

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INHIBITION OF LEUKOTRIENE B_4 PRODUCTION IN HUMAN NEUTROPHILS BY 2-STYRYLCHROMONES

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Introduction

2-Styrylchromones are a small group of naturally occurring chromones, vinylogues of flavones (2-phenylchromones). Natural and synthetic 2-styrylchromones have been tested in different biological systems, showing activities with potential therapeutic applications. Certain flavones are potent inhibitors of the production of eicosanoids, a group of powerful pro-inflammatory signalling molecules[1,2]. However, the anti-inflammatory potential of 2-styrylchromones, concerning their possible interference in this pathway, has not been explored so far.

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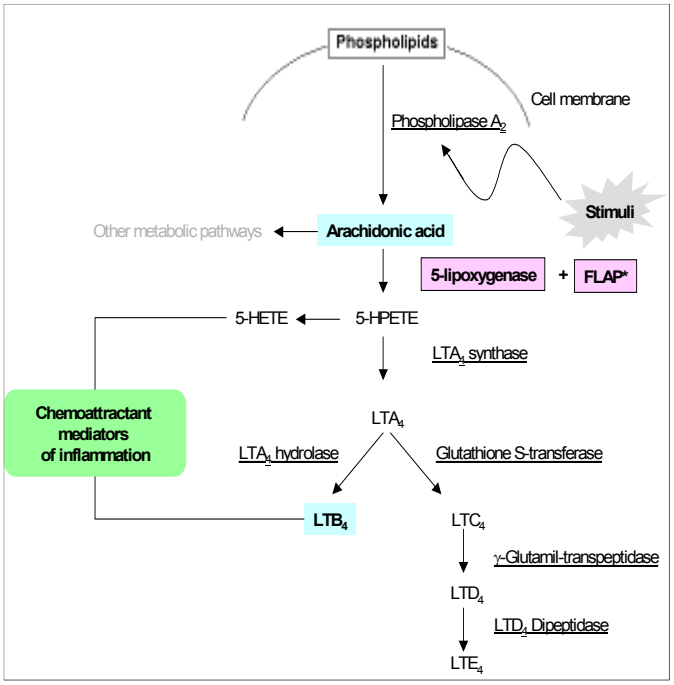
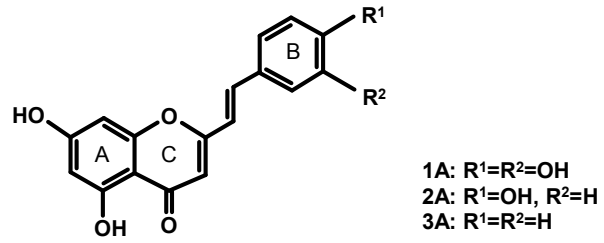


Fig. 1 – Arachidonic acid metabolic cascade (5-lipoxygenase pathway). *5-lipoxygenase activating protein

Methods

Human neutrophils were isolated from peripheral blood of healthy volunteers as previously described[3]. Neutrophil suspensions (2 x 10^6 cells/ml) were pre-incubated at 37 ºC for 10 min with the 2-styrylchromones (2 and 10 µM) or with the lipoxygenase inhibitor nordihydroguaiaretic acid (NDGA) (1 µM). The cells were subsequently incubated with the calcium ionophore A23187 (5 µM) at 37 ºC for 5 min. The samples were then centrifuged at 13,000 x g for 1 min, and the supernatants were stored at -70ºC until analysis. The amount of LTB_4 in the samples was measured using a commercial EIA kit (Cayman).

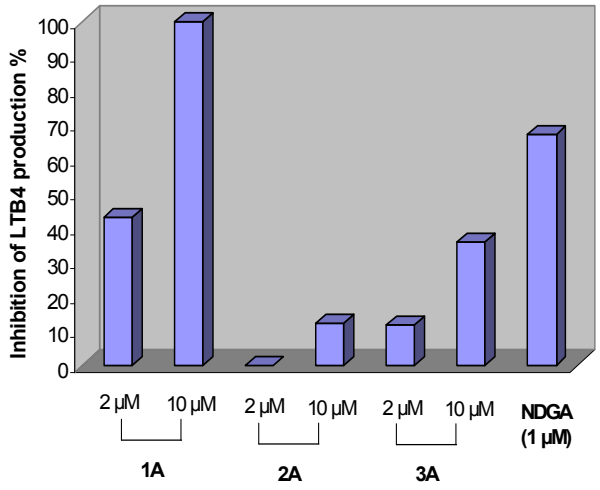


1A: R^1=R^2=OH
2A: R^1=OH, R^2=H
3A: R^1=R^2=H

Fig. 2 – Chemical structures of the tested 2-styrylchromones

Results

Inhibition of A23187 induced production of LTB_4 in human neutrophils



Conclusion

The influence of 2-styrylchromones in the 5-LOX pathway of the arachidonic acid metabolic cascade was investigated for the first time in the present work. The inhibitory effect upon the LTB_4 production shown by the tested compounds is a good indicator of their anti-inflammatory properties. Since the experiment was performed in human neutrophils, the results obtained open the perspective of a future usefulness of 2-styrylchromones in the prevention or treatment of human inflammatory diseases.

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