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BOOK OF ABSTRACTS

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NOVEL 2-STYRYLCHROMONES WITH HIGH ANTI-INFLAMMATORY POTENTIAL THROUGH PREVENTION OF LTB_4 PRODUCTION BY HUMAN LEUKOCYTES, INHIBITION OF COX-1 ACTIVITY ÀND SCAVENGING OF ROS AND RNS

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Abstract

2-Styrylchromones (2-SC) are a chemical family of heterocyclic compounds, vinylogues of flavones (2-phenylchromones), whose occurrence in nature has been reported. Several natural and synthetic chromones have demonstrated to possess biological effects of potential therapeutic applications. However, the anti-inflammatory potential of 2-SC has not been explored so far.

Our aim was to evaluate the putative anti-inflammatory properties of several synthetic 2-SC (Fig. 1) by studding their influence on different mechanisms involved in the inflammatory process: the overgeneration of reactive oxygen species (ROS) and reactive nitrogen species (RNS), and the 5-lipoxygenase (5-LOX) and cyclooxygenase 1 and 2 (COX-1 and COX-2) pathways of the arachidonic acid metabolism.

Some of the studied 2-SC proved to be extremely efficient scavengers of the different ROS and RNS, showing, in some cases, IC_{50s} under 1 μM. The hydroxylation pattern of 2-SC, especially in the B-ring but also in the A ring, modulates the activity of these compounds, the 3',4'-catechol derivatives being the most effective scavengers. The styryl pattern also contributes to their outstanding antioxidant activity.

Some of the tested 2-SC were able to inhibit both COX-1 activity and leukotriene B_4 production which makes them dual inhibitors of the COX and 5-LOX pathways. The most effective compounds were those having structural moieties with proved antioxidant activity (3',4'-catechol and 4'-phenol substituted B-rings). The dual inhibitors may exhibit anti-inflammatory activity with a wider spectrum than that of classical non-steroidal anti-inflammatory drugs (NSAIDs) by inhibiting 5-LOX product-mediated inflammatory reactions, towards which NSAIDs are ineffective.

In conclusion, in the present study, several of the tested 2-SC were shown to be efficient scavengers or ROS and RNS, to prevent LTB_4 production by human leukocytes and to inhibit COX-1 activity. All together, these compounds may become a new therapeutic option in the treatment of inflammatory processes.

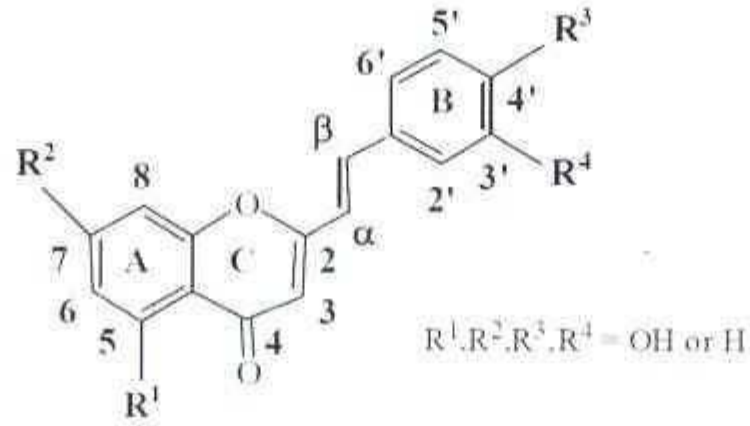

Figure 1. General structure of the tested 2-SC.

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