Inhibition of the Oxidative Burst and Chlorinating Activity of Myeloperoxidase by Aminochalcones

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Excessive activation of neutrophils generates reactive oxygen species (ROS) and secretion of specific granular enzymes, such as myeloperoxidase (MPO), which is implicated in numerous inflammatory diseases. The ability of MPO to generate hypochlorous acid (HOCl, an important microbial killer) from hydrogen peroxide in the presence of chloride ions is a unique and definite activity for this enzyme. The purpose of this study was to evaluate the activity of aminochalcones on oxidative burst (PMA-stimulated neutrophils) and on chlorinating activity of MPO. The aminochalcones: 4'-aminochalcone (1); 4'-amino-4-fluorochalcone (2); 4'-amino-4-methylchalcone (3) e 4'-amino-4-hydroxychalcone (4) were synthesized by Claisen-Schmidt condensation at room temperature. Neutrophils were isolated from the blood of healthy donors by Ficoll–Paque density gradient centrifugation. The superoxide anion and total ROS production by stimulated neutrophils were measured by the lucigenin- and luminol-enhanced chemiluminescence assays (LumCL and LucCL, respectively). The chlorinating activity of MPO was determined by measuring the production of HOCl. The aminochalcones had a dose-dependent inhibition on the LumCL and LucCL assays, reaching 50% inhibition at ca. 2 µM. The cytotoxicity, evaluated by the trypan blue exclusion assay, showed that the compounds were not toxic to neutrophils at concentrations lower than 100 µM. The aminochalcones were identified as potent inhibitors of the chlorinating activity of MPO, with inhibitory concentration of 1 (IC_{50} = 0.265 ± 0.036 µM, 2 (IC_{50} = 0.250 ± 0.081 µM) and 3 (IC_{50} = 0.250 ± 0.012 µM), similar to F-tryptamine (IC_{50} = 0.192 ± 0.012 µM). Therefore, aminochalcones may have potential as pharmacological agents for inflammatory diseases.

Word Keys: neutrophils, chemiluminescence, myeloperoxidase, aminochalcones.
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