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Immunopharmacology and inflammation

Biochemical and histological evaluations of anti-inflammatory and antioxidant p-chloro-selenosteroid actions in acute murine models of inflammation

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ABSTRACT

This study investigated the potential *p*-chloro-selenosteroid (PCS) anti-inflammatory effect in different animal models of acute inflammation. In order to determine a time- and a dose-curve response of action, female adult Swiss mice (25–35 g) were divided in different groups and pretreated by the intragastric route (i.g.) with PCS (5–10 mg/kg) and after the specific times (5, 30 and 60 min) the ear inflammation was induced with croton oil (2.5%, 20 μl). The ear edema, myeloperoxidase (MPO) activity and histological analyses were performed. In a second experiment, the pleurisy model was used to determine the PCS protective effect (10 mg/kg, i.g., 30 min before induction) in the inflammatory and oxidative alterations induced by an intrapleural injection of a 1% carrageenan solution (0.1 ml) in exudate and lung samples. Dexamethasone (1 mg/kg, i.g.) was used as positive control for both models. Statistical analysis was performed through a One-Way ANOVA test followed by the Newman–Keuls' test. Pretreatment of 30 min with PCS, only at a dose of 10 mg/kg, decreased ear edema and the MPO activity as well as the histological alterations induced by croton oil. In the pleurisy model, PCS (10 mg/kg, i.g.; 30 min) reduced the leukocyte counts, histological alterations, MPO and adenosine deaminase activities, oxidative damage and the non-enzymatic antioxidant defense imbalance. PCS had a similar anti-inflammatory profile to dexamethasone; however, it showed a better antioxidant effect. PCS had anti-inflammatory and antioxidant actions in two well established inflammation models in mice.

1. Introduction

The inflammatory response is a complex and essential process involving selective and temporal migration of specific cell types to the affected site, vascular alterations, synthesis and release of several mediators (Medzhitov, 2008). These events are orchestrated by a plethora of mediators that act in sequence to give rise to the ever-changing inflammation pattern (Rankin, 2004). By design, inflammation is a finite process that presents the characteristic of self-healing as soon as the threat of infection decreases and is able to repair the tissue as a whole. Despite its protector role, the inflammation can become disadvantageous when it acts with excessive intensity and prolonged endurance (Nathan, 2006).

The pharmacological treatment to counteract the inflammatory disorders comprises non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids (Ong et al., 2007; Rhen and Cidlowski, 2005). Nevertheless, there are concerns about their effectiveness and safe usage, mainly in cases of management of long lasting pathologies. Therefore researches intending to develop novel approaches to treat inflammation have received special attention by the scientific community.

Considering that inflammation involves several distinct events, signaling pathways and mediators that feature the inflammatory process as a multifactorial and complex state, an optimal intervention would be effective to decrease and down-regulate as many targets as possible (Frantz, 2005). In view of a wide range of biological activities assigned to organoselenium compounds, the last decade has been marked by a true explosion of research into

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pharmacological properties of these compounds (Nogueira and Rocha, 2011; Nogueira et al., 2004). Among them the potential protective effect of organoselenium compounds in different animal models of inflammation (Bruning et al., 2015a; Luchese et al., 2012; Nogueira et al., 2003; Petronilho et al., 2015; Savegnago et al., 2007) has been reported, reinforcing the relevance of these molecules as a resource for therapeutic application.

Accordingly, *p*-chloro-selenosteroid (PCS), a synthetic selenium-containing steroidal molecule, is a relative compound of both organoselenium and glucocorticoids classes (Ibrahim-Ouali, 2008; Rodrigues et al., 2010). Recently, PCS has been reported to have antinociceptive and anti-inflammatory actions in different animal models of nociception, through a mechanism that seems to be associated with dopaminergic and adenosinergic systems, without

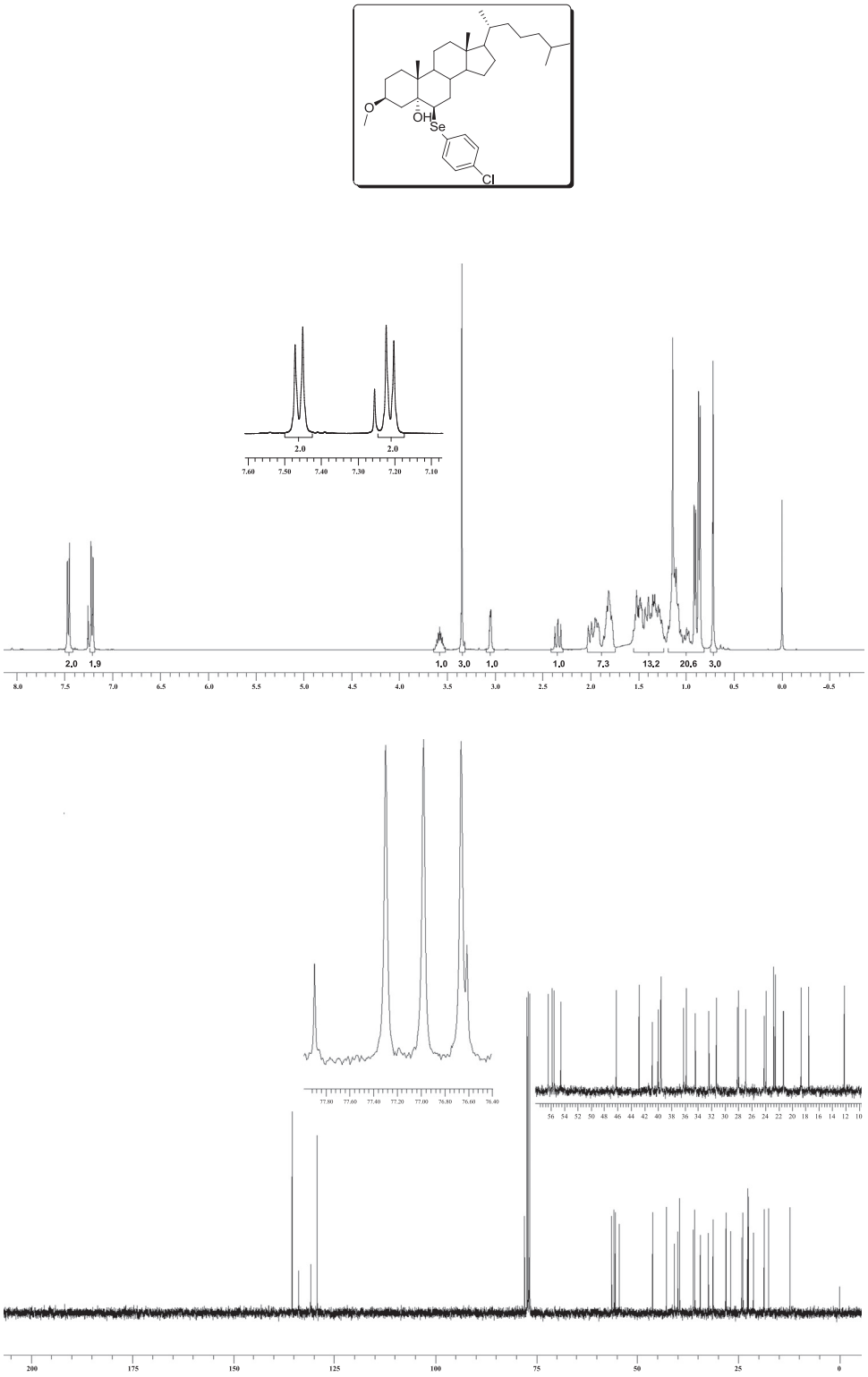

Fig. 1. Chemical structure, ^{1}H NMR and ^{13}C NMR spectra of PCS.