

## **HARPAGOPHYTUM PROCUMBENS AQUEOUS EXTRACT INHIBITS HCT116 COLON CANCER CELL VIABILITY AND THE PRODUCTION OF INFLAMMATORY AND LIPOPEROXIDATION MARKERS IN ISOLATED RAT COLON CHALLENGED WITH LPS**

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Oxidative stress and depletion of antioxidants may play a key role in the pathogenesis of inflammatory bowel disease (IBD)-related intestinal damage (Koutroubakis et al., 2004). Antioxidant/anti-inflammatory herbal extract supplementation could represent an innovative approach to contrast IBD (Chung et al., 2007).

Extracts of the southern African plant, *Harpagophytum procumbens* (Hp), (Devil's claw), provide an herbal drug with a variety of traditional indications including chronic inflammation. It's known its use in the symptomatic treatment of painful osteoarthritis, relieving lower back pain, loss of appetite and dyspepsia (Brendler et al., 2006).

The aim of the present study was to explore the possible protective role of the aqueous extract of HP on mouse myoblast C2C12, human colorectal adenocarcinoma HCT116 cell lines and isolated rat colon specimens treated with lipopolysaccharide (LPS) by measuring the activities of different biomarkers of colon inflammation and lipid peroxidation such as ROS, serotonin (5-HT), prostaglandin (PG)E2 and 8-iso-prostaglandin (8-iso-PG)F2 $\alpha$ . In addition, we investigated the immune response modulatory effects of the plant, by measuring the gene expression of tumor necrosis factor (TNF)- $\alpha$ , a cytokine playing a key role in colon epithelium damage (Feghali and Wright, 1997).

In vitro study showed a different sensitivity between C2C12 and HCT116 cells, following *Harpagophytum* treatment; our findings could be related to a different response to the metabolic effects induced by the extract (Schopohl et al., 2016). We can speculate that the sensitivity of HCT116 to the cytotoxic effects of *Harpagophytum* could also depend on the low grade of differentiation (Ieta et al., 2008). The preliminary in vitro test was used as a valuable index of effective doses to define the concentration for colon tissue treatment.

In ex vivo experiments, *Harpagophytum* treatment (100-1000  $\mu$ g/mL) was able to significantly inhibit LPS-induced production of PGE2, 8-iso-PGF2 $\alpha$ , 5-HT and TNF $\alpha$ . The inhibitory effect was concentration-independent, while the efficacy was comparable with the reference drug, sulfasalazine (2 mg/mL). The inhibitory effects on the production of the tested pro-inflammatory mediators support a rationale use of the aqueous water extract by decoction of *Harpagophytum* in the management of the colon inflammation symptoms related to IBDs.

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