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Anti-inflammatory effect of the ether extract and major fraction of *Physalis peruviana* calyces in acute TNBS-induced colitis

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Physalis peruviana L. (Cape gooseberry) is a member of the Solanaceae family widely used in traditional medicine for the treatment of malaria, asthma, hepatitis, dermatitis and rheumatoid arthritis. Extracts of this plant have showed relevant antioxidant and anti-inflammatory activities (Wu et al. 2006; Franco et al. 2007). The aim of this study was to investigate the anti-inflammatory effect of the petroleum ether extract and the corresponding major fraction of *P. peruviana* calyces on the acute model of ulcerative colitis induced by intrarectal instillation of 2,4,6-trinitrobenzenesulphonic acid (TNBS-40 mg/mL). Female Wistar rats, weighing 180-200 g, were randomly divided into groups. Control and TNBS groups received vehicle (saline 1 mL/Kg i.p.), treatment groups received petroleum ether extract (125 mg/kg/day i.p.) or the corresponding major fraction (10 mg/Kg i.p), 48, 24 and 1 h prior to instillation of TNBS and 24 h after. The inflammatory response was determined by quantifying the macroscopic and microscopic damage, myeloperoxidase activity (MPO) and tumor necrosis factor (TNF-α) levels in colon mucosa. Data were analyzed by ANOVA, $P<0.05$ was considered significant. Rats treated with TNBS developed severe colitis characterized by black necrotic zones, edema, deep ulcerations, hemorrhage and significant increase in weight/length ratio of rat colon, an indicator of inflammation. At the histological level was observed colonic mucosa ulceration, the architecture of the crypts was distorted and the lamina propria was thickened in peripheral areas of distorted crypts, as well as edema and infiltration of inflammatory cells. Enhancement in MPO activity and TNF-α levels was also observed. Treatment with the ether extract of *P. peruviana* calyces (125 mg/kg/day i.p.) did not show signs of toxicity *in vivo* and demonstrated a significant protective effect of intestinal damage induced by TNBS, reducing edema, extent of colonic tissue damage, ulceration and hyperemia. Based on these promissory results, this extract was fractionated by chromatographic procedures. The major fraction obtained from the ether extract of *P. peruviana* (10 mg/kg/day i.p.), constituted by the mixture of two new sucrose esters, attenuated the macroscopic damage to the colon, reduced significantly the weight/length ratio, and prevented the disturbances in morphology associated to TNBS treatment with significant reduction of inflammatory cells in the crypts, submucosa and muscular layer. Colonic injury induced by TNBS administration was characterized by an increase of TNF-α level in the inflamed colon (90.0 ± 8.3 compared to 13.1 ± 1.5 pg/mg tissue in the control group), and enhancement in MPO compared to the control (4.50 ± 0.34 and 1.03 ± 0.06 U/mg tissue, respectively) indicating an extensive neutrophil infiltration into inflammatory tissue. Intraperitoneal administration of TNBS-rats with the major fraction of *P. peruviana* significantly reduced the levels of TNF-α (66.4 ± 6.2 pg/mg of tissue, $p<0.05$ vs. TNBS group), but did not reduce the degree of leukocyte infiltration. In conclusion, the results of our study indicate that treatment of animals with the major fraction of *P. peruviana* reduced the inflammation and the colonic damage induced by rectal instillation of TNBS. This affirmation was supported by macroscopic, microscopic, and biochemical data. This is the first report showing a putative pharmacological effect of the extract and an enriched fraction from *P. peruviana* calyces in an experimental model of TNBS-induced ulcerative colitis.

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References:

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