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Effect of St. John's Wort (*Hypericum perforatum* L.) on colonic inflammation and tissue damage in a rat model of TNBS-induced colitis

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Chronic inflammatory bowel diseases lack clear aetiology and effective treatments, highlighting the need for novel therapeutic approaches like St. John's Wort. This study investigated the effects of oral St. John's wort (SJW) administration on inflammation, immune responses in the rat colonic mucosa, and blood cytokine levels, using three different doses. One group was separated as a control. For colitis model, a single dose of 2,4,6-trinitrobenzene sulfonic acid (TNBS) was administered directly into the colon. Then, the rats were divided into eight groups: four groups observed for 3 days and four groups observed for 7 days. All groups received SJW exposure in different doses (none, 100, 500, or 1000 mg/kg/day). Serum levels of TNF-alpha, IFN-gamma, IL-4, IL-10 and IL-13 were assessed together with tissue macroscopic/microscopic evaluation and tissue total (anti)oxidant measurements. Macroscopic scoring showed healing rates of colonic mucosa reaching up to 52% in the acute term and 33% in the chronic term. Tissue oxidative stress index was higher both in acute and chronic term of the model, but TNF-alpha, IL-4 and IL-10 were especially prominent in the serum at the chronic term of the disease. They have been regulated by oral SJW treatment; microscopic findings and scoring also supported the beneficial effect SJW. Intracolonic intervention of TNBS induces chronic systemic inflammation, as evidenced by changes in serum cytokine levels. SJW, even when taken orally as a food supplement, can influence cytokine pathways, promote the ulcer healing. This indicates a potential reduction in drug requirements.

Keywords: Inflammatory bowel disease model, Cytokine modulation, Rational drug therapy, Oxidative stress biomarkers, Colonic inflammation, Rat model