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Canthin-6-one ameliorates TNBS-induced colitis in rats by modulating inflammation and oxidative stress. An in vivo and in silico approach

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Abstract

Background and Purpose: Canthin-6-one (Cant) is an indole alkaloid found in different medicinal plants, reported to be gastroprotective, anti-inflammatory, anti-microbial, anti-diarrheal and anti-proliferative. We aimed to explore Cant in the management of ulcerative colitis (UC) using a trinitrobenzenesulfonic acid (TNBS)-induced rat model. Experimental Approach: Cant (1, 5 and 25 mg/kg) was administered by oral gavage to Wistar rats followed by induction of colitis with TNBS. Macroscopic and histopathological scores, myeloperoxidase (MPO), malondialdehyde (MDA) and reduced glutathione (GSH) were assessed in colon tissues. Pro- (TNF-α, IL-1β and IL-12p70) and anti-inflammatory (IL-10) cytokines, and vascular endothelial growth factor (VEGF) were also quantified. Mitogen-activated protein kinase 14 (MAPK14) and Toll-like receptor-8 (TLR8), as putative targets, were considered through in silico analysis. Key Results: Cant (5 and 25 mg/kg) reduced macroscopic and histological colon damage scores in TNBS-treated rats. MPO and MDA were reduced by up to 61.69% and 92.45%, respectively, compared to TNBS-treated rats alone. Glutathione concentration was reduced in rats administered with TNBS alone (50.00% of sham group), being restored to 72.73% (of sham group) under Cant treatment. TNF-α, IL-1β, IL-12p70 and VEGF were reduced, and anti-inflammatory IL-10 was increased following Cant administration compared to rats administered TNBS alone. Docking ligation results for MAPK14 (p38α) and TLR8 with Cant, confirmed that these proteins are feasible putative targets. Conclusions and Implications: Cant has an anti-inflammatory effect in the intestine by down-regulating immune molecular mediators and decreasing oxidative stress. Therefore, Cant could have therapeutic potential for the treatment of inflammatory bowel disease and related syndromes.

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