Adelmidrol, a palmitoylethanolamide analogue, as a new pharmacological treatment for the management of inflammatory bowel disease

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Oxidative stress, leukocyte infiltration and increased expression of intercellular adhesion molecule 1 (ICAM-1) in the colon are the most important factors in inflammatory bowel disease. The goal of the current study was to investigate the effects of adelmidrol, an analogue of the anti-inflammatory fatty acid amide signaling molecule palmitoylethanolamide, in mice subjected to experimental colitis. Additionally, in order to clarify if the protective action of adelmidrol is dependent on activation of peroxisome proliferator-activated receptors (PPARs), we investigated the effects of a PPAR-γ antagonist, GW9662, on adelmidrol action. Adelmidrol (10 mg/kg daily o.s.) was tested in a mouse experimental model of colitis induced by intracolonic administration of dinitrobenzene sulfonic acid. Nuclear factor-kB translocation, cyclooxygenase-2 and phospho-extracellular signal-regulated kinase as well as tumor necrosis factor-a and interleukin-1ß were significantly increased in colon tissues after dinitrobenzene sulfonic acid administration. Immunohistochemical staining for ICAM-1, P-selectin, nitrotyrosine and poly(ADP)ribose showed a positive staining in the inflamed colon. Treatment with adelmidrol decreased diarrhea, body weight loss and myeloperoxidase activity. Adelmidrol treatment, moreover, reduced nuclear factor-kB translocation, cyclooxygenase-2 and phospho-extracellular signal-regulated kinase expression, pro-inflammatory cytokine release, the incidence of nitrotyrosine and poly(ADP)ribose in the colon and decreased the up-regulation of ICAM-1 and P-selectin. Adelmidrol treatment produced a reduction of Bax and an intensification of Bcl-2 expression. This study clearly demonstrates that adelmidrol exerts important anti-inflammatory effects that are partly dependent on PPAR-?, suggesting that this molecule may represent a new pharmacological approach for inflammatory bowel disease treatment.