Boldine suppresses dextran sulfate sodium-induced mouse experimental colitis: NF-κB and IL-6/STAT3 as potential targets

ABSTRACT

Ulcerative colitis (UC) is a nonspecific inflammatory disorder characterized by oxidative and nitrosative stress, leucocyte infiltration, and upregulation of inflammatory mediators. Boldine is an alkaloid compound found in Boldo tree, with multiple pharmacological actions, mainly anti-inflammatory, antioxidant, antitumor, and immunomodulatory activities. Hence, the effect of boldine for its anti-inflammatory properties against dextran sulfate sodium (DSS)-induced UC in BALB/c mice was studied. Administration of boldine to DSS-induced mice protects colon damage by reduced disease activity index, spleen weight, and increased colon length. Also administration of boldine showed a reduction in the activity of myeloperoxidase (MPO) and CD 68+ expression. Boldine reduced the colon damage, with significant reductions in both the extent and the severity of the inflammation as well as in crypt damage and leukocyte infiltration in the mucosa. Analysis in vivo showed clear decrease in the production of tumor necrosis factor (TNF)-α, Interleukin (IL)-6, IL-17, and signal transducer and activator of transcription-(p-STAT3)(Y705) with nuclear factor (p65-NF-κB) production being reduced significantly. Moreover, p65-NF-κB activation was reduced in mouse macrophage RAW 264.7 cells in vitro. The data demonstrated that boldine may be beneficial in colitis through selective immunomodulatory effects, which may be mediated, at least in part, by inhibition of p65-NF-κB and STAT3 signaling pathways.

Keyword: NF-κB; STAT3; Boldine; Enzymic antioxidants; Ulcerative colitis