ABSTRACT

PHARMACOLOGICAL INVESTIGATION OF MANGIFERIN FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE (IBD)

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Keywords: Inflammatory Bowel Disease, Crohn’s Disease, Ulcerative colitis, Mangiferin, Antioxidant, Anti-inflammatory, Matrix Metalloproteinase, Reactive oxygen species, Trinitrobenzene sulfonic acid, Dextran sulfate sodium

Background: Inflammation, oxidative stress and altered mucosal barrier permeability are potential etiopathological or triggering factors for Inflammatory Bowel Disease (IBD).

Aims: In this study, the therapeutic potential of Mangiferin was investigated in vitro, in vivo in acute and chronic models of IBD and also attempts were made to understand mechanistic insights of Mangiferin in IBD using molecular docking techniques.

Material and Methods: Mangiferin was evaluated using in vitro assays such as DPPH, FRAP. Mangiferin was screened in three in vivo mice models: (1) Acute model for Crohn’s disease: Induced by intrarectal administration of TNBS (2) Acute model for Ulcerative colitis: DSS added to drinking water for 11 days followed by 3 days of normal drinking water. (3) Chronic relapsing model for Ulcerative colitis: Cyclical administration of DSS (7D DSS+ 7d water for 3 cycles). Mechanisms underlying the potential effects of Mangiferin were screened using in silico molecular docking studies.
Results and Discussion: In the current investigation we report the strong antioxidant activity of Mangiferin using in vitro DPPH and FRAP assays. Also Mangiferin was found to be useful in acute and chronic in vivo models of colitis induced by TNBS and DSS. Mangiferin treatment ameliorated the clinical parameters (body weight loss, stool consistency, occult blood), reduced microscopic damage (re-established mucosal architecture, abridged neutrophil infiltration), restored epithelial barrier integrity (diminished goblet cell loss), restored oxidative stress (GSH, CAT, SOD, MDA) and crucial inflammatory pathways (MPO, TNF–α, IL–1β, MMP–9) implicated in the pathogenesis of IBD. Also our docking studies using GLIDE software revealed for the first time TNF–α and MMP–9 as therapeutic targets for Mangiferin.

Conclusion: Mangiferin reduces colonic damage in various experimental models of colitis, assuages the oxidative and inflammatory events partly through influencing the TNF–α and MMP–9 activity and therefore might have therapeutic usefulness in the management of IBD.
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