

Silymarin and celecoxib attenuated the mycophenolate mofetil-induced myeloperoxidase activity and lipid peroxidation in the duodenum of rat

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Background and Aims: This study aimed to highlight the protective effect of Silymarin (SMN) and Celecoxib (CLX) on Mycophenolate Mofetil (MMF)-induced gastrointestinal (GI) disorders in rats.

Methods: Forty-two Wistar rats were assigned to 7 groups. The control animals received normal saline and the test animals treated with MMF (30 mg/kg, orally) and saline normal, MMF and SMN (25, 50 and 100 mg/kg, orally), MMF and Celecoxib (CLX, 50 mg/kg, orally), MMF and SMN plus CLX for 14 days. The Myeloperoxidase activity as a biomarker of neutrophil infiltration, nitric oxide content as an index of nitrosative stress and Malondialdehyde (MDA) production as an indicator of lipid peroxidation in the duodenal region of small intestine were determined. Histopathological examination also was conducted to show the impact of MMF administration and equally the protective effects of given compounds.

Results: The MMF-increased nitric oxide (NO) content, myeloperoxidase (MPO) activity, and malondialdehyde (MDA) level were reduced by SMN, CLX and SMN plus CLX administration, while the MMF-reduced level of total thiol molecules (TTM) increased significantly ($P < 0.05$) by given compounds. Concurrent administration of SMN and CLX resulted in a synergistic effect on the reduction of MDA level and MPO activity. Histopathological examinations including the villus height to crypt's depth ration, the MMF-induced villus atrophy and inflammatory cells infiltration were improved in SMN- and CLX-treated groups.

Conclusions: Our data suggested that the MMF-induced GI disorders may attribute to elevated NO, MDA levels and myeloperoxidase activity that result in pathological injuries. Moreover, the biochemical alterations and histopathologic injuries due to MMF administration were reduced by SMN alone or in combination with CLX indicating its protective effect.

Keywords: Gastrointestinal disorders; Mycophenolate mofetil; Protective effects; Silymarin; Synergistic effect