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ORIGINAL ARTICLE

Prophylactic Effects of Rhamnetin Flavonoid on Indomethacin-Induced Gastric Ulceration by Modulating HSP 70/Bax, SOD/MDA and TNF-α/IL-10

Mohammed T. Mohammed, Talal Salem Al-Qaisi, Ahmed A. J. Jabbar, Mohammed M. H. M. Raouf, Parween AbdulSamad Ismail, Ramzi A. Mothana, Omer I. Fantoukh ... See all authors

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ABSTRACT

Rhamnetin is a naturally occurring flavonoid compound found in many wild plant species and indigenous fruits. Despite its numerous biological potentials, such as anti-inflammatory, antioxidant and antimicrobial effects, there is a lack of literature elucidating its gastroprotective action and anticipating molecular mechanism. Natural products can be a good alternative to overcome the side effects and relapses associated with anti-ulcer drugs. This study aims to elucidate rhamnetin's acute toxicity and gastroprotective effects using the indomethacin ulceration model. Animals were arbitrarily divided into five groups: a negative control group (A) and a positive control group (B), both treated with 1% carboxymethyl cellulose; a reference group (C) receiving 20 mg/kg omeprazole; and low-dose (D) and high-dose (E) rhamnetin groups receiving 30 and 60 mg/kg, respectively. After 1 h, rats in Groups B–E were subjected to indomethacin-induced ulceration. Toxicity evaluations indicated the safety of rhamnetin at doses of up to 400 mg/kg in rats, without any noticeable physiological alterations. Rhamnetin (30 and 60 mg/kg) administered orally 1 h before indomethacin-induced gastric ulcer ameliorated the stomach lesions and lowered the ulcer index area by 73.81% and 77.87%, respectively. Rhamnetin supplementation ameliorated histopathological alterations and restored gastric barriers, including gastric pH and mucin secretion. Moreover, rhamnetin-treated rats exhibited increased anti-apoptotic heat shock protein 70 and decreased Bax protein in stomach tissues. These findings were in line with lowered accumulated MDA, increased superoxide dismutase, catalase and prostaglandin E2 levels, reduced serum inflammatory mediators (TNF-α and interleukin-6) and elevated interleukin-10 cytokines. The outcomes indicate rhamnetin's cicatrising and gastroprotective effects against indomethacin-mediated ulceration, possibly due to its modulatory actions on oxidative stress, inflammation and apoptotic pathways.