

Gastroprotective Effect of Formononetin against Ethanol-Induced Gastric Ulceration in Rats via Augmentation of Cytoprotective Markers and Curtailing Apoptotic Gene Expression

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Submitted: 24-04-2018

Revised: 08-06-2018

Published: 17-01-2019

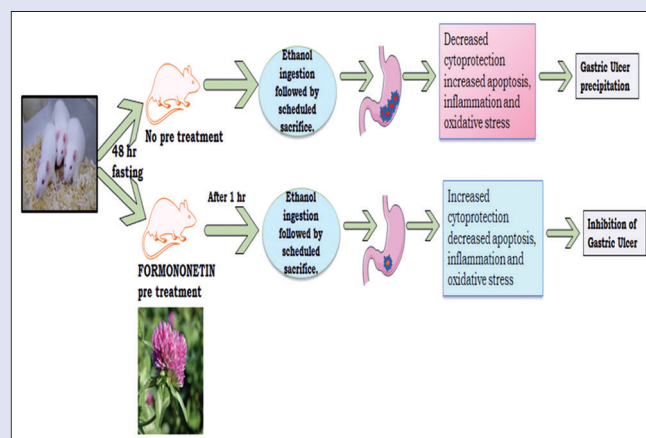
ABSTRACT

Background: Formononetin (FMN), one of the major isoflavones in red clover, has been shown to possess antioxidant, anti-inflammatory, antitumor, neuroprotective, and cytoprotective activities. However, there is no report on the gastroprotective effect of FMN against ethanol-induced gastric ulcer. **Objective:** Excessive alcohol consumption can lead to gastric ulcer, and the purpose of the present study was to examine the protective effect of FMN on mucosal lesions induced by ethanol. **Materials and Methods:** Fasted rats were orally administered with FMN at different doses, omeprazole (20 mg/kg), followed by intragastrical ingestion of ethanol (5 ml/kg) after 1 h and sacrificed after 1 h of exposure. Gross microscopic, macroscopic, and biochemical assays were scrutinized. **Results:** Compared with ethanol, FMN pretreatment showed a significant increase in the gastric levels of glutathione while decreased the malondialdehyde content remarkably. FMN pretreatment also bestowed the cytoprotective efficacy against ethanol-induced ulceration by reestablishing the decreased level of nitrite (NO). Furthermore, in histopathological sections, reduced pathological changes of gastric lesions were markedly observed in the FMN-pretreated groups compared with those in the ethanol group. **Conclusion:** These results indicate that FMN exerts gastroprotective effects through the antioxidative, anti-inflammatory, and antiapoptotic that are probably mediated by enhanced NO release, suggesting its therapeutic use to treat gastric ulceration by preserving mucosal glycoproteins and diminishing oxidative stress.

Key words: Apoptosis, cytoprotection, formononetin, gastric ulcer, oxidative stress

SUMMARY

- FMN is found to be highly potent against ethanol-induced gastric ulcer
- FMN decreased the oxidative stress and increased the cytoprotection through enhancement of nitrite levels
- The isoflavone is also found to decrease both inflammation and apoptosis in gastric tissue after ethanol ingestion
- Therefore, FMN exerts anti-inflammatory and cytoprotective effect along with acting as an antioxidant and depletion of apoptosis in gastric tissue.



Abbreviations used: NSAIDs: Nonsteroidal anti-inflammatory drugs; FMN: Formononetin; CMC: Carboxymethylcellulose; UI: Ulcer index; MDA: Malondialdehyde; GSH: Reduced glutathione; NO: Nitrite; TNF- α : Tumor necrosis factor-alpha; Hgb: Hemoglobin; T-RBC: Total red blood cells; Hct: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; TLC: Total leukocyte count

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DOI: 10.4103/pm.pm_205_18

Access this article online

Website: www.phcog.com

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INTRODUCTION

Persistent exposure of the gastric tract to a number of substances such as hydrochloric acid and digestive enzymes causes epithelial damage.^[1] Mucosal injury occurs when these noxious factors destroy an intact mucosal layer or when it gets impaired.^[2] Peptic ulcer, one of the most common and life-threatening diseases of the gastrointestinal tract, occurs due to imbalance between the offensive (e.g., acid, pepsin,

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Cite this article as: Alauddin, Chaturvedi S, Azmi L, Shukla I, Naseem Z, Rao CV, et al. Gastroprotective effect of formononetin against ethanol-induced gastric ulceration in rats via augmentation of cytoprotective markers and curtailing apoptotic gene expression. *Phcog Mag* 2018;14:S605-12.