HUMIC ACID HAS PROTECTIVE EFFECT ON GASTRIC ULCER BY ALLEVIATING INFLAMMATION IN RATS

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The new agents are needed in treatment of gastric ulcer that have less side effects, adequate efficacy, and no drug interactions. In this study, we aimed to investigate the potential protective effects of humic acid on experimental gastric ulcer. Wistar Albino male rats (n = 48) were randomly divided into 8 groups as follow; Control (without any applications), Humic acid (50 mg/kg), ethanol group (1 ml/rat), and indomethacin group (25 mg/kg). In the treatment groups, both gastric ulcer model and humic acid 50 mg/kg were applied. In addition, famotidine the anti-ulcer drug was used as positive control. All medications were administered by oral gavage. Levels of ADAM10 and ADAMTS12 in gastric mucosa were determined by ELISA method. Hematoxylin-Eosin (H&E) staining, iNOS, and PCNA immunohistochemical staining were performed for histopathological investigations. Apoptosis was demonstrated by using the TUNEL method. In addition, the levels of inflammatory cytokines (TNF-α, IL-6, IL-10) and caspase-3 gene were determined by qRT-PCR. ADAM10 and ADAMTS12 levels significantly increased in the treatment groups compared to the ulcer groups ($p<0.05$). The experimental groups showed mucosal erosion, bleeding, leukocyte infiltration and edema. Treatment with humic acid and famotidine was found to suppress iNOS activity, thereby decreasing proinflammatory activity and preventing damage to the gastric mucosa, while reducing the number of apoptotic cells. IL-6, IL-10, TNF-α and caspase-3 levels were significantly decreased in the treatment groups compared to damaged gastric mucosa. As a result, humic acid may be defined as a potential protective agent with its anti-inflammatory effect in gastric ulcer.

Key words: *Gastric mucosa injury, Humic acid, ADAM10, ADAMTS12, Inflammation, Famotidine*

ЗАХИСНИЙ ВПЛИВ ГУМІНОВОЇ КИСЛОТИ ПРИ ВИРАЗЦІ ШЛУНКУ У ЩУРІВ ШЛЯХОМ ЗМЕНШЕННЯ ЗАПАЛЕННЯ

Лікування виразки шлунку вимагає нових препаратів, що мають менше побічних дій, належну ефективність та не взаємодіють з іншими лікарськими препаратами. У цьому дослідженні ми вивчали потенційний захисний вплив гумінової кислоти при експериментальній виразці шлунку. Білі самці щурів лінії Wistar (n = 48) були рандомізовано поділені на вісім груп наступним чином: контроль (без будь-якого введення), гумінова кислота (50 мг/кг), група етанолу (1 мл/щур) та група індометацину (25 мг/кг). У групах, що отримували лікування, було застосовано і модель виразки шлунку, і гумінову кислоту (50 мг/кг). Крім того, фамотидин, противиразковий препарат, використовували в якості позитивного контролю. Всі препарати вводили за допомогою шлункового зонду. Рівні ADAM10 і ADAMTS12 в слизовій шлунку визначали методом ELISA. Для гістопатологічних досліджень використовували зафарбовування гематоксиліном-еозином (H&E) та іммуногістохімічне зафарбовування з використанням індуцибельної NO-синтази та ядерного антигена клітинної проліферації (PCNA). Апоптоз був продемонстрований за допомогою методу TUNEL. Крім того, рівні запальних цитокінів (TNF-α, IL-6, IL-10) і гену каспази-3 були визначені за використання кількісної ПЛР у реальному часі. Рівні ADAM10 і ADAMTS12 були значно вищими у групах, що отримували лікування, порівняно з групами з виразкою ($p < 0,05$). В експериментальних групах спостерігали ерозію слизової, кровотечу, інфільтрацію лейкоцитів і набряк. Було виявлено, що лікування за допомогою гумінової кислоти і фамотидину пригнічувало активність індуцибельної NO-синтази, знижуючи прозапальну активність і попереджаючи пошкодження слизової шлунку, одночасно зменшуючи кількість апоптичних клітин. Рівні IL-6, IL-10, TNF-α і каспази-3 були значно знижені у групах, що отримували лікування, порівняно з пошкодженою слизовою шлунку. Отже, гумінову кислоту можна вважати потенційним захисним агентом, який має протизапальну дію при виразці шлунку.

Ключові слова: пошкодження слизової шлунку, гумінова кислота, ADAM10, ADAMTS12, запалення, фамотидин.

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