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PROTECTIVE EFFECT OF GOAT MILK ON ALCOHOL-INDUCED PEPTIC ULCER IN BALB/C MICE

Elisha Paikray[1*], Saurabh Chawla[2] , Chandramohan Bathrachalam[3], Sarita Jena[4]

[1]*Asst. professor, Dept. of Pharmacology, Kalinga institute of medical sciences, KIIT university, Odisha
[2,3]National institute of science education and research, Jatni, Odisha
[4]Institute of life sciences, Bhubaneswar, Odisha

***Corresponding Author:** Elisha Paikray
*Asst. professor, Dept. of Pharmacology, Kalinga institute of medical sciences, KIIT university, Odisha

Introduction

Peptic ulcers are sores that develop in the lining of the stomach, lower esophagus, or small intestine. Predominantly, inflammation by Helicobacter pylori, regular intake of aspirin, ibuprofen, smoking, alcohol, radiation therapy, and stomach cancer are the factors (1, 17). In the general population, approximately 5-10% of the population is affected by peptic ulcer disease (PUD) and ulcer complications [1]. In the disease pathogenesis pathway, proinflammatory cytokines, oxidative stress, and apoptosis play essential roles [3–7]. Invasion of gastric tissues by neutrophils, marked with increased myeloperoxidase (MPO) activity, contributes to gastric mucosal damage [8]. In humans, the frequent consumption of alcohol is associated with the gastric mucosal lesion [2]. The use of antibiotics, proton pump inhibitors, prostaglandin analogues, and H2 receptor blockers has decreased the morbidity of PUD. However, attempts to discover new supportive therapy with lower cost and fewer side effects are necessary [12]. The experimental model of ethanol-induced gastric injury mimics several features of the human condition and thus provides a means for assessing peptic ulcer actions along with the implicated mechanisms for gastric protection [9-11].

Goat milk is rich in antioxidants [14] and tends to prevent and treat gastric ulcers (13). Goat milk is highly nutritious and contains higher levels of calcium, magnesium, and phosphorous than cow and human milk [15]. Moreover, goat milk is easier to digest than cow milk because of smaller fat molecules and slightly less lactose content [16]. It helps adults suffering from gastrointestinal disturbances and ulcers [16]. Goat milk has been a staple in human diets for centuries, establishing its historical safety. Additionally, it's noteworthy that Whole Goat Milk is recognized as Generally Recognized as Safe (GRAS) by the FDA.

Hence the milk is safe and non toxic which is an already established factThis pilot study aims to establish the protective effect of goat milk on an ethanol-induced ulcer in mice.

Material and method

Animals

The present study was approved by the Institutional Animal Ethics Committee (IAEC) at ILS (Institute of Life Sciences) as per CPCSEA guidelines, IAEC approval No. - ILS/IAEC-224AH/APR-21. We chose adult Balb/c mice, aged 6-8 weeks, from a pathogen-free colony for our

study. To avoid biases, we randomly grouped the mice. Balb/c mice were chosen as these are commonly used for disease models due to their well-known characteristics and physiology. Male Balb/c mice, 6-8 weeks old, bred and reared at the institutional Animal House facility, were used for the experiment. Animals were housed in polysulfone cages with autoclaved corncob bedding in a controlled environment with temperature and humidity ranging between 24 ± 3 °C and 40–70%. Water and feed were provided ad-libitum. Animals were randomly divided into 4 groups, with 8 animals in each group. They were acclimatized for a period of 3 days prior to the administration of any drug or compound.

Administration of Goat Milk:

Fresh authentic goat milk was procured locally and diluted at a ratio of 1:4 with distilled water prior to administration. The dose of milk administration was adopted as per Jeong-Hyun Yoo et al [1]. The chosen dose was 20 ml of goat milk per kg body weight of mice. Each group was fed once a day with either goat milk or an equal volume of distilled water for a period of 14 days. Animals were monitored for changes in behavior, feeding, drinking pattern, and body weight during the course of the study.

Induction of Acute Gastritis and Gastric Mucosal Damage:

The induction of gastric mucosal damage in Balb/c mice was done using the method described by Jeong-Hyun Yoo et al. Mice were deprived of food for 12 hours before the induction of gastric mucosal damage. One hour after administering the goat milk, the HCl and ethanol combination (98% ethanol containing 150 mM HCl used at the dose rate of 5 ml/kg of body weight) were orally fed using a 22 G oral gavage needle. After an hour, the animals were euthanized by cervical dislocation, and the stomach was opened along the greater curvature. The gastric fluid was collected, and the inner surface was cleared of residual matter with normal saline and examined for the severity of ulceration. The affected region was quantified, and the total area affected was expressed as a percentage.

Histopathology:

The stomach was fixed in 10% neutral buffered formalin for 48 hours, and paraffin-embedded tissue sections of 4μm were obtained using a rotary microtome (Leica, Germany). Hematoxylin and eosin staining were performed for histopathological visualization. The analysis of images of stained tissue sections was done using a light microscope (Meiji, Japan).

Results

Change in body weight and behavior of mice:

There was no significant difference in the change in body weight. All the mice exhibited normal behavior in terms of feed intake, water intake, and general behavior. There were no notable differences in body weight between the control and experimental mice during the study.

Severity of gross lesions:

In the control group, multifocal hemorrhagic lesions (irregular in shape) were observed throughout the gastric mucosa. However, the severity of lesions in mice treated with goat milk was not as profound. Only small patches of hyperemic mucosa were occasionally observed in a few mice treated with goat milk, whereas the control mice showed diffuse lesions. The gross lesions in the control group constituted about 40% of the total area of the gastric mucosa.

Histopathological findings:

Administration of ethanol caused severe epithelial mucosal damage, along with hemorrhages, destructive glandular structures, edema, and infiltration of inflammatory cells. In contrast, minimal mucosal damage was observed in mice treated with goat milk. The gastric epithelium in the goat milk-treated mice appeared organized with minimal damage to the normal architecture as seen during histopathological examination. However, mice treated only with distilled water showed severe gastritis with disruption of mucosal epithelium and glandular structures. There was a loss of

histoarchitecture of the gastric mucosa and submucosal layer with a high grade of inflammation and infiltration of inflammatory cells, primarily neutrophils.
This indicates that ethanol induced high-grade inflammation along with hemorrhagic lesions and erosion of epithelial cell architecture in animals. However, the severity of lesions was much less in animals pre-treated with goat milk, suggesting its gastroprotective effect.

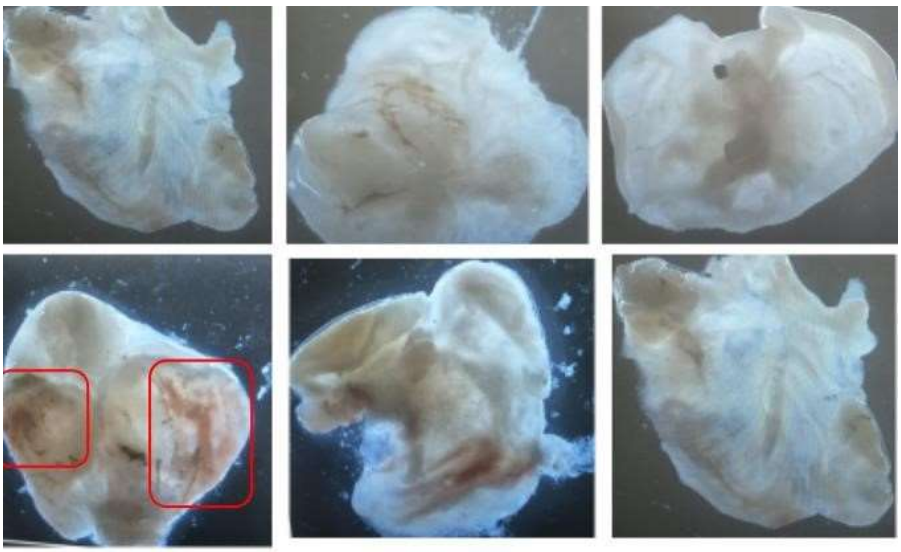

Fig 1: Severity of gross lesion

A. Representative images of gastric mucosa in mice pre-treated with goat milk. Oral pre-treatment of goat milk attenuated the severity of gross lesions
B. . Representative images of gastric mucosa in mice pre-treated with distilled water. Ethanol caused extensive hyperaemic and haemorrhagic lesions in gastric mucosa when treated alone with distilled water.

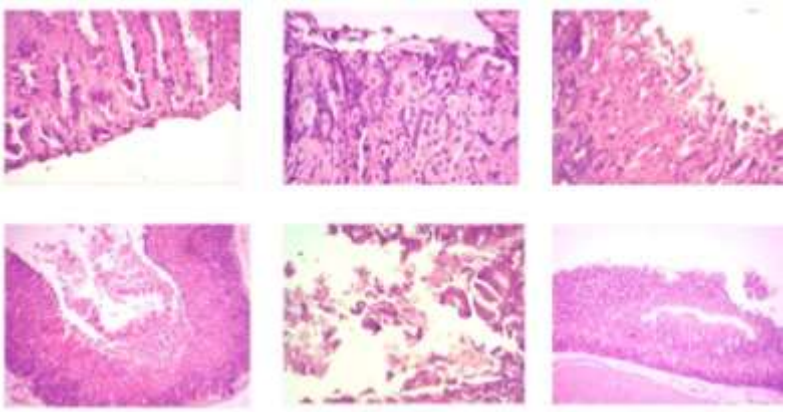

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Fig 2: Histology of Stomach

A. Normal gastric Mucosa with intact architecture. 2. Mild disruption of Gastric Mucosa with low grade infiltration of inflammatory cells. 3) Disruption of gastric mucosa with moderate inflammation and infiltration inflammatory cells.
B. Disruption of Gastric Mucosa with moderate inflammation and infiltration of inflammatory cells 2) Loss of histo-architecture of gastric mucosa and submucosal layer with high grade inflammation and infiltration of inflammatory cells.3) Disruption of Gastric Mucosa with moderate inflammation and infiltration of inflammatory cells

Discussion:

The gastric mucosa is constantly exposed to the secretion of strong endogenous acids, but several protective mechanisms work at various levels to maintain its integrity. Gastric ulcers can be induced by lifestyle changes such as alcohol consumption, stress, or the overuse of antiinflammatory drugs, and a significant proportion of the human population is affected by this disease at some point during their lifetime. Goat milk, which is highly nutritious and easily available, is believed to possess medicinal properties.

Goat milk offers antioxidant properties, nutrition, and better digestibility. Additionally, it contains lower lactose levels compared to cow milk, making it more suitable for individuals with lactose intolerance. Cow milk has been reported to inhibit gastric ulcers by reducing gastric damage, increasing prostaglandin synthesis, and enhancing the mucin content of the adherent mucosal layer. However, limited data are available on the gastroprotective effect of goat milk, which is often considered a more accessible alternative to cow milk. Therefore, we conducted a study to evaluate the effect of pre-treatment with goat milk on an ethanol-induced gastric ulcer model in Balb/c mice.

Our study did not show any significant changes in body weight or alterations in feed/water consumption, indicating that goat milk is safe and well-accepted in monogastric animals. On the other hand, our results demonstrated that goat milk can attenuate the effects of ethanolinduced gastritis in mice. Similar results have been reported with cow milk in studies conducted on mice by Yoo et al. in 2018. They showed that bovine milk can enhance the antioxidant defense system and reduce the severity of gastric lesions by modulating the expression of inflammation-related genes. The gross findings of our study were consistent with the histological observations, confirming that pre-treatment with goat milk can decrease the severity of alcohol-induced gastritis and inflammation. Therefore, the consumption of goat milk could be considered as a preventive measure for individuals at high risk of peptic ulcer disease (PUD).

However, this study has certain limitations. The underlying mechanism of action for the protective effect of goat milk needs further examination, and the efficacy of pre-treatment should be confirmed in other animal models, such as those using aspirin or H. pylori to induce gastric ulcerative disease. Further research is necessary to fully understand the mechanisms and potential applications of goat milk in gastroprotection.

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