Evaluate the possible anti-peptic ulcer action of the water extract of Linum usitatissimum

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Abstract: The spasmolytic and indomethacin-induced ulcer protective effects of Linum usitatissimum seed in guinea pig ileum and mouse stomach, respectively, were investigated. The water extract of the whole seed, after being soaked for different periods, was employed to test it spasmolytic effect and its protective action against experimental ulcerogenesis. The extract was observed to show significant spasmolytic activity and protective effect against experimental ulcerogenesis ($p < 0.01$). Both effects were observed to increase with increase in the soaking period ($p < 0.01$). The present findings suggest that the seed of Linum usitatissimum could be a potential medicine in peptic ulcer therapy.

[Esmaeilzadeh M, Kazemzadeh F. **Evaluate the possible anti-peptic ulcer action of the water extract of Linum usitatissimum** . *Life Sci J* 2013;10(3s):509-511] (ISSN:1097-8135). http://www.lifesciencesite.com. 79

Keywords: Evaluate; anti-peptic ulcer action; water extract; Linum

Introduction

Peptic ulcer is a disease of multiple origin involving psychological and physical factors such as stress and chemicals (1). Antacids are the commonly prescribed drugs for peptic ulcer. Although these drugs are relatively cheap, they are not effective in severe cases. The majority of the Ethiopian population, thus, rely on traditional remedies such as barely and fenugreek infusion, and linseed water extract. The anti-ulcer activity of fenugreek was investigated earlier by Al-Mesal et. al (2).Linseed (or telba in Amharic) is a seed obtained from Linum usitatissimum L, a plant belonging to the family, Linaceae (3). The seed contains 30% to 40% of fixed oil, known as linseed oil, about 25% of mucilage and about 25% of protein, as well as other minor constituents, such as phenolic glucosides (4). Decoction of the seed is claimed to be effective in cough and urinary infection (5). The oil has been used as an emollient and purgative (4). The seed is traditionally employed in mumps, leprosy and scabies in Northern Ethiopia (3). Furthermore, the water extract of the whole seed, soaked overnight has long been used for gastrointestinal disorders such as peptic ulcer .In this study spasmolytic effect and ulcer index in experimental ulcer models were used to evaluate the possible anti-peptic ulcer action of the water extract of Linum usitatissimum whole seed in an attempt to get a clue (or its potential application.

Methods

Chemicals .Histamine was obtained from Sigma Chemical Company, St. Louis, MO. 6327, USA. Carbachol was obtained from BDH Chemicals Ltd., Prole, England, Indomethacin was obtained from Dumex Ltd., Denmark. Diethyl ether was obtained from BDH Chemicals Ltd.,Prole, England. Preparation of the plant material. Seeds of Linum usitatissimum were purchased from a super market, and one part of it was soaked in a ratio of one part of the seeds to six parts of water, and left for 24 and 48 hours. The colourless viscous consistency was then decanted and employed as 24 and 48 hour extract, respectively, in these experiments.

Effect of Linum usitatissimum seed 011 intestinal motility. An isolated guinea ileum (2-3cm long) was suspended in an organ bath (70 ml) containing oxygenated Tyrode's physiological solution at 3^0C, and allowed to equilibrate for one hour (6). Isotonic contractions with .different concentrations of histamine, the standard spasmogenic drug, were recorded using a kymograph (6). After washing out the preparation, 2 ml of the 24 hour extract of Linum usitatissimum whole seed was added, and contractile responses with same concentrations of histamine were recorded after 15 minutes of contact time. Similar procedure was employed for carbachol, another standard spasmogenic drug. The procedures were repeated with the 48 hour extract. Cumulative dose-response curves were then drawn.

Effect of Linum usitatissimum seed on experimental ulcerogenesis. Thirty albino mice were fasted for 18 hours but allowed free access to water. The animals were then divided into three groups (10 mice/group), and coded to avoid bias as much as possible. Two groups were gavaged with 24 and 48 hour extracts (0.3mI/g. # each), respectively, while the third group served as a control. One hour later, 30 mg/kg indomethacin (i.p.) was administered to all the groups according to the method described by Aguwa and Lawal(7). Seven hours after indomethacin administration, all the animals were anaesthetized with diethyl ether, and sacrificed as described by Aguwa and Lawal (7). The stomachs were then removed, opened along the greater curvature, rinsed with tap water, and examined for ulcers. The ulcers,

i.e., haemorrhagic areas of the mucosa that did not clear on rinsing, were counted with the aid of a hand lens (x4 magnification), and each was given a severity rating as follow: < 1 mm = 1; 1 -2 mm = 2; and > 2 mm = 3. The summation of the score was divided by a factor of 10, to derive the ulcer index for each animal as described by Aguwa and Lawal (7). The quantal ulcer response was also determined.

Statistical analysis. All data were expressed as mean: t standard error of the mean (SEM). Statistical analysis of all the data was done and student t test was used to test for level of significance. $p < 0.01$ was considered significant in all the experiments .

Results

The contractile responses of both histamine (Figure 1) and carbachol (Figure 2) were found to decrease significantly by the water extract of Linum usitatissimum seed. There was a significant increment in the potency of the extract with increase in the soaking period as shown in Figures 1 and 2. Reproducible contractions were noted both by histamine and carbachol shortly after removal of the extract by washing the preparation.

The extract was also observed to reduce the ulcerogenic effect of indomethacin significantly as demonstrated by the decrease in ulcer index (Table 1). As can be seen in Table 1, a significant decrease in the ulcer index was observed for the extract obtained from seeds soaked over longer period of time. The quantal ulcer response also decreased with increase in the soaking period as shown in the same Table.

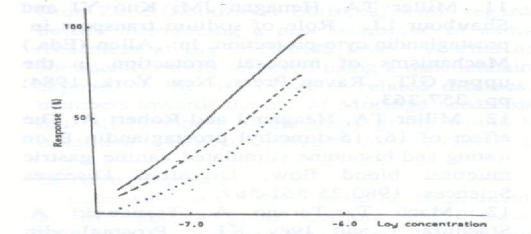

Figure 1: Effect of *Linum usitatissimum* seed on dose response curve of histamine on guinea pig ileum. N = 6. _____ control; ------- 24 hours extract; and ..... 48 hours extract.

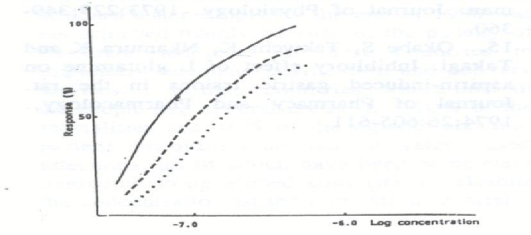

Figure 2: Effect of *Linum usitatissimum* seed on dose response curve of carbachol on guinea pig ileum. n = 6. _____ control; -------- 24 hours extract; and ..... 48 hours extract.

Discussion

The antagonizing effect of the extract on the contractile responses of the ileum to both histamine and carbachol may suggest that the extract either blocked both muscarinic and histaminic receptors or acted on non-specific receptors. The immediate reversal of the spasmolytic effect of the extract after its removal from the preparation explains that it may form a reversible complex with its receptor (s) if its action is receptor-mediated. The possibility of the mechanism of its antispasmodic action due to physical factor could as well be considered, as the increase in potency was observed with more consistency.

Ulcer induced by indomethacin was observed to be mediated systemically (8). That was why indomethacin was administered i.p. to the mice to induce ulcer in the present work. Its ulcerogenic effect has been proposed to be through its inhibiting action of prostaglandin synthetase (9). This enzyme inhibition could reduce the production of prostaglandins leading to: a) loosening of the gastric mucosal barrier and reduction in mucus secretion (10); b) inhibition of the formation of cAMP by the gastric mucosa resulting in increased hydrochloric acid secretion (11); and c) enhancement of the gasttf(; mucosal blood flow rendering the gastric mucosa more susceptible to noxious stimuli (12). Indomethacin also causes back diffusion of H ions and decreases cellular resistance to damage (13).

Table 1: Effect of linum usitatissimum water extract on indomethacin-induced ulcer.

	Quantal ulcer response	Uicer index
Control	10/10	3.24±0.41
24 h extract	09/10	1.20±0.30
48 h extract	07/10	0.48±0.23

Data = Mean ± SEM. n=10

The exact mechanism of action of the seed of Linum usitatissimum in protecting the mice against indomethacin-induced gastric ulcer is not known. Many investigators (9, 11,14,15) have suggested the possible mechanisms of anti-ulcer action of drugs used in peptic ulcer . The present plant material might have exerted its anti-ulcer action through one of the mechanisms described, such as increase in prostaglandin synthesis, increase in the production of cAMP by the gastric mucosa and formation of physical protection of the mucosa against noxious stimuli.

The significant anti-ulcer effect of the extract with increase in its soaking period could explain that the more the consistency the greater the potency. This was further supported by the lower quantal ulcer response with the more consistency of

the extract. As the seed extract reduced histamine and carbachol induced contraction of the ileum, it may have a negative influence on the gastric motility and gastric acid secretion to help in peptic ulcer therapy. Both the spasmolytic and ulcer protective effects of the seed observed in this study might have contributed to its traditionally claimed use in peptic ulcer .

The results obtained in the present study could, therefore, hint for the potential application of *Linum usitatissimum* seed in peptic ulcer therapy. Further studies, however, have to be undertaken with regard to its protective effect against ulcer of other origins, mechanism of action, pharmacokinetics and toxicity tests.

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