RESEARCH ARTICLE

Moringa (Moringa oleifera) Leaves' Extract and Linseed (Linum usitatissimum) Oil Ameliorate Piroxicam Induced Gastric Ulcers in Male Rats

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Abstract
Gastric ulcer is a standout amongst the most significant gastrointestinal disorders affecting human worldwide. An extraordinary interest should be given to find natural medications to treat this disease. Plant extracts are more favored because of their wide safety margins and less or no adverse health impacts. The present study was conducted to assess the antiulcer activities of hydroethanolic extract of moringa leaves (500mg/Kg BW) and linseed oil (0.3mL/ Kg BW) on piroxicam (30 mg/Kg BW) induced gastric ulcers in Wister albino rats. Forty five adult male albino rats were allocated into five equal (9 each) groups designated as negative control, piroxicam, ranitidine, moringa and linseed oil groups. The results revealed that administration of piroxicam in a single oral dose induced gastric ulcers in rats, decrease in body weights (187.50±10.51g) and increase in gastric juice (1.64±0.24mL) with altered hematological, biochemical and histological findings. Meanwhile, oral administration of ranitidine, Moringa oleifera and linseed oil ameliorated the ulcerogenic effect of piroxicam with curative ratios of 100, 97.5 and 100%, respectively. From the previous findings we concluded that hydroethanolic extract of moringa leaves and linseed oil were effective treatments of piroxicam induced gastric ulcer in rats. Antulcerogenic effect of moringa and linseed oil may be attributed to their anti-inflammatory and antioxidant properties.

Key words: Gastric ulcer, Linseed, Moringa, NSAIDs, Piroxicam

Introduction
Gastric ulcer is considered as one of the global health problems. It occurs as a result of a breakdown of the gastric mucosal defense particularly at the site where the mucosal epithelium is exposed to acid and pepsin [1] due to an imbalance between the aggressive and protecting factors. The most widely recognized causes of gastric ulcer are Helicobacter pylori infection and non-steroidal anti-inflammatory drugs (NSAIDs). Different less common causes as tobacco smoking, stress and liver cirrhosis may be involved [2]. The fundamental characteristic symptom of gastric ulceration is burning pain. Meanwhile, complications such as bleeding, perforation and blockage of the stomach may also occur in certain human cases with low percentage (15%) [3].

The NSAIDs are considered the most regularly recommended medications because of their high adequacy in the treatment of pain, fever, and inflammation. While, the most widely recognized unfavorable impact related to the utilization of NSAIDs in human and animals is gastrointestinal irritation [4]. Piroxicam is a NSAID of the oxicam class, which is used to mitigate the painful inflammatory conditions like arthritis. NSAIDs influence most mucosal resistance mechanisms chiefly by inhibition of cyclooxygenase and consequent concealment of mucosal prostaglandin synthesis [5].

Plant extracts are perceived as a source of natural antioxidants against oxidative stress and in this way, they can assume a significant role in the chemoprevention of many of diseases resulting from lipid peroxidation.
Moringa oleifera is a quickly developing evergreen deciduous, perpetual tree belongs to family Moringaceae. It is a native to the Indian sub-continent and naturalized in tropical and sub-tropical areas around the world. It has antioxidant, antimicrobial, anti-inflammatory, antipyretic, antidiabetic, antiulcer, antitumor antidiarreal and hypocholesteromic properties [6]. Linseed (Linum usitatissimum L.) is derived from the flax plant, of the family Linaceae, which is developed worldwide particularly, in Egypt. It can be used as a natural antioxidant and may have a role in the prevention of oxidative stress [7].

Hence, the present study was conducted to investigate the antiulcerogenic and curative effect of moringa (Moringa oleifera) leaves extract and linseed (Linum usitatissimum) on gastric ulcer induced by piroxicam in Wister albino rats.

Materials and Methods

Moringa (Moringa oleifera) leaves extract
Leaves of Moringa oleifera were obtained from Moringa Production Unit at the National Research Centre, Egypt. Hydroethanolic extract of Moringa oleifera leaves was prepared as described elsewhere [8]. In brief, one Kg of the dried leaves was ground into powder; the powder was soaked in 4 L of 3:1 (v:v) ethanol (70%): water for one week at room temperature then filtered using gauze and funnel. By using rotatory evaporators (buchi 124 rpm) at 60°C, 100 mbar pressure and 100 rpm, the lyophilized extract was obtained. The lyophilized extract (semisolid mass) was collected and stored in air tight container and kept in refrigerator at 4°C till use.

Linseed (Linum usitatissimum) oil
It was obtained from the squeezing and extraction of Linseed in the National Research Center, Dokki, Giza, Egypt. The extraction was done according to Dugani [7].

Experimental animals’ husbandry and management
This study was conducted on forty five male Wister albino rats weighing 180-200 g, obtained from the Laboratory Animal Farm, Faculty of Veterinary Medicine, Zagazig University. Rats were housed in cages (9 rats /cage) and were kept for 2 weeks at room temperature (25-28 °C) and humidity of 65-70% with 12 hours light and dark cycle before experimentation.

Drugs and Chemicals
Piroxicam was obtained from Phizer Chemical Company, Egypt; while Ranitidine was obtained from Medical Union Pharmaceuticals Egypt Company, Egypt. Kits used for determination of Glutathione peroxidase, Cat No EGPX-100 (Bioassay Systems, USA), Superoxide Dismutase, Cat No SD 2521 (Biodiagnostic, Egypt), Catalase, Cat No CA-2517 (Biodiagnostic, Egypt), Malondialdehyde, Cat No MD 2529 (Biodiagnostic, Egypt) and Tumor Necrosis Factor- alpha, Cat No. KRC 3011 (Thermofisher Scientific, USA) were utilized.

Antiulcer activity and experimental design:
The experiment was conducted according to rules set by the Animal Welfare and Research Ethics Committee, Faculty of Veterinary Medicine, Zagazig University, Egypt.

Induction of ulcer
After 24 hours of fasting, piroxicam (30 mg/Kg BW) was administrated as a single oral dose via stomach tube to all groups except the control one [9] as follow:

1st group: (Control group): rats were left untreated, they were given orally 1mL/100 g BW of normal saline daily for 3 successive weeks.

2nd group: (Piroxicam group): rats received piroxicam (30 mg / Kg BW) as single oral dose after 24 h of fasting.

3rd group (Ranitidine group): it was administered single oral dose of piroxicam (30 mg/ Kg BW). In the second day, 2 rats were sacrificed to ensure presence of ulcers then in 3rd day, they were given ranitidine (standard drug) (150 mg/ Kg BW) as single oral dose daily for 3 successive weeks [10].

4th group (moringa group): it was received single oral dose of piroxicam (30 mg/ Kg BW). In the second day, 2 rats were sacrificed then in 3rd day they were given hydroethanolic extract of Moringa oleifera (500 mg/Kg BW)
as single oral dose daily for 3 successive weeks [11].

5th group (Linseed oil group): each rat was given single oral dose of piroxicam. (30 mg/Kg BW). In the second day, 2 rats were sacrificed then in 3rd day, they were received linseed oil (0.3 mL/kg) as single oral dose daily for 3 successive weeks [12].

Body weights of rats were recorded at the beginning and at the end of experiment [13].

Collection of samples

The animals were fasted for 24 h, humanly euthized then two blood samples were taken. The first blood sample was collected on EDTA for haematological findings. The other sample was allowed to clot and the serum was separated by centrifugation at 3000 rpm/20 min for measurement of antioxidant enzymes, lipid peroxidation marker and pro-inflammatory cytokines.

Estimation of the volume of gastric juice and gastric juice decrease percentage

Stomach of animals was cut along greater curvature, gastric contents were collected in small tubes, centrifuged at 3000 rpm/5 min then the supernatant was separated and expressed as mL/100 g [14].

Gastric juice decrease % was determined according to Parmer and Desai [15] using the following equation.

\[
\text{Gastric juice decrease %} = \frac{\text{volume of gastric juice of +ve control} - \text{volume of gastric juice of treated group}}{\text{Volume of gastric juice of +ve control}} \times 100
\]

Recoding of ulcer score

It was calculated according to the 1 to 5 scoring system devised by Wilhelmi and Menasse-Gdynia [16] as follow: Score 1 (1 or 2 minute, sporadic, punctate lesion), score 2 (several small lesions), score 3 (one extensive lesion or multiple moderate sized lesions), score 4 (several large lesions) and score 5 (several large lesions with stomach perforation).

\[
\text{Ulcer index (U.I)} = \frac{\text{Means of ulcer score of animals similarly treated x percent of ulcerated animals in the group}}{100}
\]

Curative ratio was calculated according to Parmer and Desai [15] as following:

\[
\text{Curative ratio} = \frac{\text{U.I. of +ve control} - \text{U.I. of treated group}}{\text{U.I. of +ve control}} \times 100
\]

Haematological findings

Erythrogram was studied according to Feldman et al. [18]. However, leukogram was counted on Giemsa-stained blood films [18].

Biochemical analysis

Serum glutathione peroxidase (GPX) [19], super oxide dismutase (SOD) [20] and serum catalase (CAT) activities were assayed as mentioned before by Aebi [21]. Moreover, serum malondialdehyde (MDA) [22] and tumor necrosis factor-alpha (TNF-α) level were determined as described previously by Beutler et al. [23].

Histopathological examination:

Gastric specimens were preserved in 10% neutral buffered formalin solution, dehydrated in gradual ethanol (70-100%), cleared in xylene, and embedded in paraffin. Tissue sections (5μm thickness each) were prepared, stained with Hematoxylin and Eosin (H&E) then examined microscopically for pathological findings [24].

Statistical analysis

Data were analyzed and evaluated statistically using one-way analysis of variance (ANOVA). The results were expressed as mean ± SE. Significant difference between means was estimated at probability levels of less than 0.05 (p<0.05) [25].

Results

Effect of piroxicam, ranitidine, moringa and linseed oil on body weights of rats

Administration of piroxicam (30 mg/Kg BW) to male albino rats in a single oral dose, showed a significant decrease (p<0.05) in body weight (187±10.51 g), compared with the control group (249.75±1.65 g). Medication with ranitidine (150 mg/Kg BW) or moringa leaves extract (500 mg/Kg BW) or linseed oil (0.3 mL/Kg) in a single oral dose daily for 3 successive weeks revealed a significant increase in body weight (226.25±4.96, 227.0±5.82 and 234.5±6.29 g, respectively) compared with piroxicam group (187±10.51 g) (Table 1).
Table 1: Effect of oral administration of ranitidine, moringa and linseed oil in piroxicam induced gastric ulcer in rats (Mean±SE)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Body weight (g)</th>
<th>Gastric juice</th>
<th>Gastric ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>Volume (mL)</td>
</tr>
<tr>
<td>Control</td>
<td>197.00±5.61</td>
<td>249.75±1.65</td>
<td>1.00±0.18</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>194.75±9.63</td>
<td>187.50±10.51</td>
<td>1.64±0.24</td>
</tr>
<tr>
<td>Piroxicam + Ranitidine</td>
<td>194.50±12.7</td>
<td>226.25±4.96</td>
<td>1.40±0.30</td>
</tr>
<tr>
<td>Piroxicam + Moringa</td>
<td>200.00±5.40</td>
<td>227.00±4.96</td>
<td>0.70±0.12</td>
</tr>
<tr>
<td>Piroxicam + Linseed Oil</td>
<td>197.50±8.33</td>
<td>234.5±6.29</td>
<td>0.58±0.08</td>
</tr>
</tbody>
</table>

SE: Standard error of mean  
Means within the column having different superscripts letter are significantly different at p < 0.05.

Effect of piroxicam, ranitidine, moringa and linseed oil on volume of gastric juice of rats

Oral administration of piroxicam (30 mg/Kg BW) displayed a significant increase in volume of gastric juice (1.64±0.24 mL) when compared with the control group (1±0.18 mL). Medication with ranitidine (150 mg/Kg BW) resulted in non-significant decrease (p>0.05) in volume of gastric juice (1.40±0.30 mL), when compared with the piroxicam group (1.64±0.24 mL). While treatment with moringa leaves extract (500 mg /Kg BW) or linseed oil (0.3 mL/Kg) as single oral dose, daily for 3 successive weeks revealed a significant decrease in the volume of gastric dose, when compared with the piroxicam group (1.64±0.24 mL). While treatment with moringa leaves extract (500 mg /Kg BW) or linseed oil (0.3 mL/Kg) as single oral dose, daily for 3 successive weeks revealed a significant decrease in the volume of gastric juice (0.70 ±0.12 and 0.58±0.08 mL, respectively) compared with piroxicam group (Table 1). Gastric juice decrease percent was 14.6%, 57.3% and 64.6% in ranitidine, moringa leaves extract and linseed oil treated groups, respectively (Table 1).

Antiulcerogenic activity of moringa and linseed oil

Piroxicam administration revealed a high incidence of ulceration (100%), large number of gastric mucosal lesions, mean ulcer scores of 2.5±0.3 and high ulcer index (2.5). On the other hand, treatment of peptic ulcers with ranitidine and linseed oil revealed zero incidence of gastric ulceration (Table 1). Furthermore, the curative ratio of ranitidine and linseed oil treated groups was 100% compared with piroxicam group (0%). While the groups medicated with moringa extract revealed a lower incidence of gastric ulceration (25%) and a decreased ulcer index (6.25) versus that of piroxicam group (250). Moreover, the curative ratio was 97.5% in moringa treated group compared with 100% in ranitidine and linseed oil treated group. A significant decrease was observed in mean ulcer score (0.25± 0.25) compared with piroxicam group (2.5±0.3) (Table 1).

Haematological findings

Administration of piroxicam produced a significant decrease in RBCs count, hemoglobin concentration and PCV (4.38±0.05×10⁶/mL, 10.43±0.13g/dL and 29.50±0.65%, respectively) compared with the control group (6.81±0.16×10⁶/μL, 15.70±0.26 g/dL and 46.25±1.11%, respectively). Treatment with ranitidine, moringa extract or linseed oil showed a significant increase in RBCs count (6.41±2.1, 5.55±0.13 and 4.97±0.16 ×10⁹/mL, respectively), hemoglobin concentration (14.05±0.18, 12.55±0.21 and 11.60±0.29 g/dL, respectively) and PCV % (44.2±1.11, 38.5±1.19 and 34.0±0.91 %, respectively) compared with piroxicam treated group (Table 2).
However, administration of piroxicam resulted in a significant increase in platelets counts (348.50±1.55×10³/µL) compared with the control group (246.75±4.11×10³/µL). Meanwhile, medication with ranitidine, moringa extract or linseed oil revealed a significant decrease in platelets count (265.5±3.23, 299.50±2.22 and 315.50±2.10×10³/µL, respectively) compared with the piroxicam group (Table 2).

Oral administration of piroxicam induced a significant increase in WBCs count (14.97±0.21×10³/µL) compared with the control group (9.24±0.29×10³/µL). While, medication with ranitidine, moringa extract or linseed oil revealed a significant decrease in total leukocytic count (10.04±0.29, 12.90±0.17 and 12.86±0.05×10³/µL, respectively) compared with piroxicam group (Table 2).

There were non-significant changes in lymphocytes count after administration of piroxicam, ranitidine, moringa extract or linseed oil (5.53±0.09, 5.68±0.16, 5.74±0.12 and 5.63±0.05×10³/µL, respectively, when compared with control group (50. 61±0.09×10³/µL) (Table 2).

Piroxicam evoked a significant increase in neutrophils, eosinophils and monocytes count (6.90±0.34, 1.70±0.02 and 0.85±0.02×10³/µL, respectively) compared with the control group (2.68±0.08, 0.67±0.03 and 0.29±0.02×10³/µL, respectively) but, treatment with ranitidine, moringa extract or linseed oil revealed a significant decrease in neutrophils count (2.82±0.26, 4.5±0.03 and 4.97±0.07×10³/µL, respectively), eosinophil count (0.96±0.01, 1.5±0.05 and 1.55±0.02×10³/µL, respectively) and monocytes count (0.33±0.05, 0.66±0.03, 0.72±0.02×10³/µL, respectively) when compared with piroxicam group (Table 2).

**Biochemical Parameters**

Administration of piroxicam revealed a significant decrease in glutathione peroxidase (GPX), catalase (CAT) and superoxide dismutase (SOD) activities to be 26.70±1.32 U/L, 135.25±1.89 U/L and 0.75±0.04 U/mL, respectively compared with 60.63±0.78 U/L, 236.50±3.23 U/L and 2.72±0.08 U/m, respectively for the control group. Medication with ranitidine, moringa extract and linseed oil revealed a significant increase in the activity of GPX (51.13±1.12, 38.15±3.17 and 29.03±1.25 U/L, respectively; CAT (204.75±4.59, 165.5±3.43 and 149.75±3.35 U/L, respectively) and SOD (2.04±0.04, 1.24±0.02 and 0.88±0.01 U/mL, respectively) when compared with piroxicam group (Table 3).
Also, piroxicam administration resulted in a significant increase in MD and TNF-α concentration (27.03±1.66 nmol/mL and 91.05±0.58 pg/ mL, respectively) compared with the control group (4.80±0.22 nmol/mL and 25.28±0.58 pg/ mL, respectively). However, treatment with ranitidine, moringa extract and linseed oil revealed a significant decrease in MDA (7.35±0.22, 15.89±0.46 and 20.67±0.68 nmol/mL, respectively) and TNF-α concentrations (34.98±0.70, 38.15±2.30 and 47.28±1074 pg/ mL, respectively) when compared with piroxicam group (Table 3).

**Table 3: Effects of oral administration of ranitidine, moringa and linseed oil on piroxicam induced gastric ulcer in rats on antioxidant enzymes activities, oxidant status and TNF-alpha (Mean±SE)**

<table>
<thead>
<tr>
<th>Groups</th>
<th>GPX (U/L)</th>
<th>CAT (U/L)</th>
<th>SOD (U/mL)</th>
<th>MDA (nmol/mL)</th>
<th>TNF-alpha (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>60.63±0.78</td>
<td>236.50±3.23</td>
<td>2.72±0.28</td>
<td>4.80±0.22</td>
<td>25.28±0.58</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>26.70±1.32</td>
<td>135.25±1.89</td>
<td>0.75±0.04</td>
<td>27.03±1.66</td>
<td>91.05±0.58</td>
</tr>
<tr>
<td>Piroxicam+Ranitidine</td>
<td>51.13±1.12</td>
<td>204.75±4.59</td>
<td>2.04±0.04</td>
<td>7.35±0.22</td>
<td>34.98±0.70</td>
</tr>
<tr>
<td>Piroxicam+Moringa</td>
<td>38.15±3.17</td>
<td>165.50±3.43</td>
<td>1.24±0.02</td>
<td>15.89±0.46</td>
<td>38.15±2.30</td>
</tr>
<tr>
<td>Piroxicam+Linseed oil</td>
<td>29.03±1.25</td>
<td>149.75±3.35</td>
<td>0.88±0.01</td>
<td>20.67±0.68</td>
<td>47.28±1.74</td>
</tr>
</tbody>
</table>

SE: Standard error of mean
Means within the column having different superscripts letter are significantly different at p < 0.05.
CAT: catalase enzyme, SOD: superoxide dismutase, GPx: glutathione peroxidase, MDA malondialdehyde and TNF-α: Tumor necrosis factor-alpha

**Histopathological findings**
Grossly, the stomach of control rats appeared normal with folded gastric mucosa (Figure 1, slide 1). Numerous scattered superficial defects (erosions) or deep destructed mucosa with red borders (ulcers) of various sizes and shapes were seen in stomach of piroxicam group (Figure 1, slide 2). The mucosa of rats in ranitidine group was slightly hyperemic with little sticked mucus (Figure 1, slide 3). Mild thickened and hyperemic gastric mucosa without erosions or ulcers was the main changes in moringa and linseed oil groups (Figure 1, slides 4 and 5).

**Figure 1**: Macrograph of rats’ gastric mucosa. (1): Control (normal), (2): Piroxicam (ulcerated), (3): Ranitidine (apparently normal, mild hyperemia without ulceration), (4): Moringa (apparently normal, mild hyperemia with focal regeneration), and (5): Linseed oil (normal).
Microscopically, the stomach of control rats had normal coats (mucosa, submucosa, muscular and serosa). The glandular mucosa contained surface mucus cells, parietal cells area and chief cell area beside micro vessels in the superficial mucosa (Figure 2 slide 1). The glandular stomach of piroxicam group showed erosive changes, which represented by loss of superficial gland with minimal inflammatory reaction in the mucosa and hypermic mucosal blood vessels. The ulcerative mucosa revealed intense mucosal destruction containing necrotic debris and inflammatory cells (Figure 2 slide 2). Ranitidine group had apparently normal glandular mucosa with mild inflammatory cells in submucosa beside hyperemic blood vessels and regenerative attempts from the glandular portion in the middle third of mucosa particularly parietal cells (Figure 2 slide 2). Moringa treated rats showed restore of gastric coats mainly mucosa and complete regeneration of induced lesions with little inter-glandular edema and lymphocytes in mucosa and submucosa (Figure 2 slide 4). While, linseed oil group had the greatest ameliorative effect and represented by apparently normal gastric mucosa beside high regenerative activities of parietal and chief cells (Figure 2, slide 5).

Figure 2: Photomicrograph of rats’ gastric mucosa: (1): Control rats showing normal layers (black arrow), sub mucosa (yellow arrow) and the muscular coat (star), with some goblet cells (open arrow) and mucus (closed arrow), the HCL secreting parietal cells (arrow head) and chief cells (curved arrow). H&E X 00 (A, B), or X 400 (C, D). (2): Piroxicam group showing erosion (A), necrosis (open arrow) with desquamated cells (arrow head), mild inflammation (yellow stars) beside congested vessels (curved arrow), the ulcerative lesion (thick arrows) (B, C, D) are represented by complete necrosis (black star) with necrotic sheets (circle) and inflammation (yellow stars). Inflammatory reaction (square), leukocytic infiltrations, predominantly eosinophils (open arrow), lymphocytes (curved arrow) and macrophages (arrow head) in addition to hyaline degeneration in the muscular layer (yellow arrow). H&E X 100. (3): Ranitidine group showing apparently normal with mild inflammation (star) and hyperemia (arrow head); focal regeneration (curved arrow); H&E X 100 (A, B); 400 (C, D). (4): Moringa group showing apparently normal layers (circle), hyperemia (arrow head) with focal regeneration (curved arrow) with increase parial and chief cells (red curved arrow); H&E X (A,B); 400 (C, D). (5): Linseed oil group showing normal layers with mild increased activity of the gastric glands (curved arrow) and mild inflammation (star) in addition to chief cells (arrow head) and cells hyperactivity (closed arrow); H&E X 100 (A,C); 400 (B, D).
Discussion

Gastric ulcer is one of the most important gastrointestinal disorders affecting humans worldwide. A special interest should be given to find natural medications to protect and treat this disease. Natural extracts from plants and herbs are more preferred because of wide safety margins and less or no adverse health effects. The obtained results in this study revealed a significant decrease in the body weights of rats at the end of the experiment in piroxicam group in comparison with ranitidine, moringa extract and linseed oil treated groups. The piroxicam administration results in indigestion, appetite loss and severe abdominal pain which is in line with that stated by El-Metwally [13]. Meanwhile, the significant increase in the body weights of rats in moringa and linseed oil treated groups could be attributed to androgenic properties of moringa leaves which possess anabolic action as the leaves contain considerable concentrations of crude protein, vitamins, calcium and iron [26], in addition to the ability of linseed oil to improve intestinal motility, enhance intestinal transient and increase weight [27].

The volume of gastric juice increased in piroxicam group in comparison with other treated groups. This result could be attributed to the ability of NSAIDs (piroxicam) to increase the gastric secretions due to COX-1 mediated prostaglandin depletion [28], piroxicam acidic nature [29] and hindrance of prostaglandin synthesis by inhibition of cyclooxygenase 1 and 2 which catalyze the arachidonic acid to prostaglandin G2, and also catalyze prostaglandin G2 to prostaglandin H2 [30]. While, the volume of gastric juice significantly decreased in moringa and linseed oil treated groups because moringa is very rich in phenolic compounds, which have gastro-protective properties through various mechanisms and anti-secretory properties that result in decrease in gastric acid volume [31]. Also, linseed oil had anti-secretory activities and has the ability to raise the pH of gastric juice by inhibiting the gastric secretion and total acidity [32].

The ulcerative effect of piroxicam on gastric mucosa could be attributed to the gastrointestinal damage that depends on prostaglandin-independent mechanisms, such as uncoupling of oxidative phosphorylation, alterations of mucosal cell mechanisms such as neutrophil activation followed by enhanced endothelial adhesion [33]. Other pathogenic mechanisms are attributed to acid included interference with the process of restitution and ulcer healing, impairment of haemostasis, and indirectly stimulating mucosal injury by increasing the absorption of acidic NSAIDs [28].

The antiulcerogenic effect of moringa is attributed to its ability to decrease gastric motility and acid secretion [34], in addition to the gastro-protective effects of the phyto-components in leaves [35]. This result was in accordance with Almuzafar [36] who reported a significant anti-ulcer activity of moringa in rats in comparison to the control. This result was due to its direct effect on the mucus and prostaglandins secretion, thus protect the gastric mucosa. While the antiulcerogenic activity of linseed oil is due to its cyto-protective effect [7] and its high content of essential fatty acids (linoleic acid and α-linolenic acid), which regulate prostaglandins synthesis [37]. These results were in accordance with Ibrahim et al. [38] who reported that oral administration of linseed oil has a protective effect against gastric ulcer in rats.

There was a significant decrease in RBCs count, Hb and PCV % in piroxicam group as a result of hematological disorders due to congestion of the blood vessels [39], inhibition of cyclooxygenase enzymes and the effect of piroxicam on DNA affecting the protein synthesis [40].

Moringa caused a significant increase in RBCs count of rats as the moringa leaves contain β -carotene and vitamin B12, and the extract can stimulate erythropoiesis, increase the haemoglobin concentrations, packed cell volume and platelets counts [41].

Increased platelets count in piroxicam group may be due to the ability of piroxicam to cause a systemic bleeding by impairing thromboxane-dependent platelet aggregation and prolonging the bleeding time [42]. Moringa has hematopoietic properties; it is
beneficial to platelet count and red blood cell formation [43]. Furthermore, linseed oil showed antiplatelet activity by inhibiting ADP and epinephrine induced platelet aggregation due to phenolic compound and flavonoids, which have anticoagulant or anti-platelet aggregation activity [44].

In piroxicam treated group, the significant increase in WBC values might be due to enhanced bone marrow effect of piroxicam on leucopoiesis [45]. While, the increase in WBC count observed in moringa treated group may be due to immunological response of the body to the extract as an antigen [46]. Linseed oil exhibited inhibition of protein exudation vascular permeability, comparable to NSAIDs. The oil also inhibited the leukocyte migration.

It was found that piroxicam induced a remarkable decrease in the activities of GPX, SOD, CAT enzymes and a remarkable increase in MDA level. These findings were in agreement with Usoh et al. [47] who illustrated that piroxicam has the ability to induce stress resulting in damage to the cells (oxidative stress-mediated lipid peroxidation). The SOD and CAT may play an important role in detoxification of superoxide anion and hydrogen peroxide, respectively. The high level of liver antioxidant enzyme activities in piroxicam treated mice may be due to the presence of chemical compounds which reduce the oxidative stress by stimulating the antioxidant enzymes [48]. Concerning to treated samples by moringa and linseed oil, the activities of antioxidant enzymes (GPX, CAT, SOD) were high in comparison with piroxicam group, while, the lipid peroxidation marker (MDA) was low. These results could be attributed to decrease hepatic marker enzymes and lipid peroxidation with a simultaneous increase in the level of antioxidants [49] because moringa leaves contain phenolic acids that exhibit high antioxidant activities [50]. Linseed oil has antioxidant properties due to its content of some phenolic compound [51].

Concerning to serum level of TNF-α, which is a key mediator in inflammatory response as well as the initiation of apoptosis, piroxicam group showed a significant increase in TNF-α due to the ability of NSAIDs to produce TNF from blood monocytes, which is in consistent with Page et al. [52] who revealed that NSAIDs resulted in an increase in TNF and may exacerbate the proinflammatory environment.

The inhibitory effects of moringa extract on the proinflammatory cytokines may be mediated by oxidative stress either dependent or independent pathways [53]. Moringa has the ability to reduce the blood levels of proinflammatory cytokines, and inhibit the pathogenesis of vascular inflammation [43]. Linseed oil is a source of α-linolenic which modulates the immune system, predominantly with respect to macrophage cytolytic activity during eicosanoid production and TNF-α synthesis [54].

Regarding to histopathological examination of gastric mucosa, piroxicam administration resulted in 100% gastric ulceration, gastric mucosal redness with brown hemorrhagic erosions due to vasodilation and congestion of gastric blood vessels as well as increased level of HCL which adversely affected the haemorrhagic lesion. These results were in agreement with Najm [55] who illustrated that the widespread uses of aspirin and NSAIDs have a destructive effect on gastric mucosa.

The microscopic picture illustrated that, piroxicam induced superficial and deep erosions in the gastric mucosa, desquamation of luminal cells with leukocytic and inflammatory cell infiltration in the mucosa, submucosa and subserosa. Nearly similar result was reported by Musumba et al. [56] after induction of gastric ulcer by piroxicam (20 mg/Kg BW).

Treatment of gastric ulcer by moringa leaves extract significantly decreased the inflammatory effect of NSAIDs and improved the healing process with apparently normal gastric layers and mild hyperemia of the superficial capillaries with focal regenerative changes of the lining epithelium. This result was in accordance with Kazi et al. [57] who found that moringa extract had antiulcer effects on the gastric mucosa.

Also, treatment of gastric ulcer in rats by linseed oil revealed normal layers of stomach with mild increase in the activity of gastric glands and parietal mild inflammatory reaction in the submucosa in addition to chief cell and
cell hypersensitivity. This result was in line with Kaithwas and Majumdar [12] who used linseed oil (0.3 mL/Kg BW) orally, daily for 21 successive days to treat gastric ulcer in rats and found that linseed oil had antiulcer and healing properties.

**Conclusion**

The present study revealed that moringa (*Moringa oleifera*) leaves extract and linseed oil (*Linum usitatissimum*) had antiulcer activities. Linseed oil was highly effective in treatment of gastric ulcer than moringa. Hence, plant extracts (linseed oil and moringa) can act as a good remedy with wide safety margin for treatment of gastric ulcer.

**Conflict of interest**

The authors have no conflict of interest to declare.

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**References**


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الملخص العربي

تأثير خلاصة أوراق المورينجا وزيت بذرة الكتان على الفرح المعدية في ذكور الجرذان

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تعد قرحة المعدة من أبرز الاضطراابات المعدية التي تصيب مختلف الأشخاص حول العالم. لذلك، اتجهت الأنظار إلى البحث عن طرق علاجية بديلة لعلاج هذا المرض. تعتبر المستخلصات الطبيعية من النباتات أكثر فضيلة نظراً لقلة أو عدم وجود آثار جانبية ضارة بالصحة. لذلك أجريت هذه الدراسة لتقديم الآثار العلاجية لكل من مستخلص أوراق نبات المورينجا (0.5 مل/كمج) وزيت بذرة الكتان (0.3 مل/كمج) على الفرح المعدية بفعالية مع بعيرة البروكسيكيم (0.4 مل/كمج) في ذكور الجرذان. تم تخصيص عدة خمسة وأربعين من ذكور الجرذان البيضاء في خمس مجموعات متساوية (9 لكل منها) وهي المجموعة الضابطة وال مجموعة المعاكسة بعيرة البروكسيكيم والراتبتيين ومستخلص أوراق المورينجا وزيت بذرة الكتان. أظهرت النتائج أن تناول جرعة واحدة من البروكسيكيم عن طريق المريض يسبب قرحة المعدة في الفرخان مع انخفاض في أوزان الجسم (187، 185 ± 10.5) جرام وزيادة في مستويات الفرح المعدية (1.4 ± 0.24 مل) مع تغيرات في الدم والكيمياء الحيوية والنسجية. بينما المجموعات المعاكسة بالراتبتيين ومستخلص أوراق نبات المورينجا وزيت بذرة الكتان أظهرت تحسين محظوظ من تأثير التجريبي للبروكسيكيم بنسبة 100%، 97.5% و 100% على الترتيب. من النتائج السابقة توصلنا إلى أن مستخلص أوراق نبات المورينجا وزيت بذرة الكتان يعتبر علاجاً فعالاً لقرحة المعدة التي يسببها البروكسيكيم في الفرخان والوقاية منها، ويعزى هذا التأثير إلى وجود خصائص مضادة للالتهابات ومعضادات الأكسدة في كل من المورينجا وزيت بذرة الكتان.