Evaluation of Antiulcer Activity of Ginger, Clove and Castor Oils Against Aspirin Induced Gastric Ulcers in Rats

Eman Mohamed El-Metwally

Department of Home Economic, Women's College, Ain Shams University, Cairo, Egypt

Abstract: The objective of this study was to evaluate the antiulcer effects of ginger, clove and castor oils in aspirin-induced gastric ulcer model rats. Thirty six male albino rats were classified into normal control group and five aspirin induced gastric ulcer groups which divided into non treated control (+ve) and treated groups that were drug, ginger oil, clove oil and castor oil groups. The results revealed that, the treatment with these oils can protect from aspirin induced gastric ulceration. The mechanism of its gastro protective activity may be attributed to significant reduction in volume of gastric juice, total acidity of gastric juice, gastric ulcer index, serum total oxidative capacity TOC, serum interleukin-1 IL-1, serum tumor necrosis factor-alpha TNFα, gastric cyclooxygenase COX-2 activity and gastric total nitric oxide concentration TNO along with significant elevation in serum total antioxidant capacity TAC, blood hemoglobin, gastric prostaglandin PGE2 level and gastric cytochrome P 450 reductase activity compared with ulcerated control (+ve) group. Curative ratio percentage showed insignificant difference of oils treatment groups compared with RAN drug group. These obtained results are confirmed by the histopathological examination. The protection afforded by treatment of ginger, clove and castor oils was found to be effective. In conclusion, the ginger, clove and castor oils possess antiulcer potential due to its antioxidant and anti-inflammatory. The healing activity may be due to its cytoprotectivity effect coupled with anti-secretory activity.

Key words: Aspirin • Castor oil • Clove oil • Flavonoids • Gastric ulcer • Ginger oil

INTRODUCTION

Peptic ulcer disease encompassing gastric and duodenal ulcer is the most prevalent gastrointestinal disorder. The pathophysiology of ulcer involves an imbalance between offensive (acid, pepsin, H. pylori and non-steroidal anti-inflammatory agents) and defensive factors (mucin, prostaglandin, bicarbonate, nitric oxide and growth factors). Integrity of gastro duodenal mucosa is maintained through a homeostatic balance between these aggressive and defensive factors. Today, there are two main approaches for treating peptic ulcer. The first deals with reducing the production of gastric acid and the second re-enforcing gastric mucosal protection [1, 2]. Aspirin is a potent nonsteroidal anti-inflammatory drug (NSAID) that is used for the treatment of rheumatoid arthritis and related diseases as well as the prevention of cardiovascular thrombotic diseases. Gastric ulcer associated with the use of aspirin is a major problem. Many factors such as gastric acid and pepsin secretion, gastric microcirculation, prostaglandin E2 (PGE2) content [3] and proinflammatory cytokines interleukin (IL)-1 and tumor necrosis factor (TNF) play important roles in the genesis of gastric mucosal damage and its subsequent development [4,5]. It has been reported that increases in NO synthase (NOS) activity is involved in the gastrointestinal mucosal defense and also in the pathogenesis of mucosal damage [6, 7]. Flavonoids have anti-inflammatory activity and protect the gastric mucosa against a variety of ulcerogenic agents in different mammalian species. Plants containing flavonoids were found to be effective in preventing this kind of lesion, mainly because of their antioxidant properties. The antioxidant activity of flavonoids has attracted interest because of the strong evidence that oxidation processes are involved in the mechanisms of several gastric disorders, including ulcerogenesis [8, 9].
Ginger (*Zingiber officinale*) that has been used to treat many inflammatory conditions and associated pain. The major constituents of ginger phenolic compounds as shogaols and gingerols that have many interesting pharmacological effects, such as antioxidant, antitumor promoting and anti-inflammatory effects [10, 11]. Also, the phytochemical screening of ginger oil showed that alkaloids, carbohydrates, glycosides, proteins, saponines, steroids, flavonoids and terpenoids were present [12]. Magaji and Yaro [13] revealed the presence of tannins, resins, flavonoids, sterols, reducing sugars and phenols. Mallikarjuna *et al.* [14] reported ginger contains a very high level (3.85 mmol/100 g) of total antioxidants that effectively inhibit superoxide tube. 

The basal diet was performed according to NRC [24]. The phytochemical screening of the crude extract revealed the presence of alkaloids, glycoside, steroids, carbohydrates, terpenoids, tannins, resins, phenolic compound and flavonoids [13, 15, 16]. Main active compound are eugenol and eugenyle acetate [17]. The antioxidant activity of commercial clove essential oil demonstrated scavenging activity [18]. It has potent antiviral, antimicrobial, antifungal, carminative, anesthetic [19, 20].

The phytochemical evaluation demonstrated that the castor oil (*Ricinus communis*) contains fatty oils, proteins, lectins and ricin. It also contains alpha tocopherol, linoleic acid, niacin, gamma tocopherol and quercitrin [21]. Furthermore, phytochemical screening of the castor extract revealed the presence of bioactive compounds tannin, saponine, alkaloid, phytate, oxalate, flavonoids, cyanogenic glycoside and phenols. The most abundant phytochemical present in the extract was tannin. The presence of biologically active chemicals of the oil plays an important role in determining its antimicrobial activity and anti-inflammatory [21, 22]. Considering the several side effects of modern medicine, indigenous drugs with fewer side effects should be looked for as a better alternative for the treatment of peptic ulcer. Recent studies found that different substances from medicinal plant sources not only afford gastro protection but also accelerate ulcer healing [1, 15]. Thus, the objective of this study was designed to evaluate the antiulcer effects of ginger, clove and castor oils in aspirin-induced gastric ulcer model rats.

**MATERIALS AND METHODS**

**Materials:** Thirty six male albino rats of Sprague Dawley strain were purchased from Laboratory Animal Colonies, Helwan, Egypt. The average weight was 140±10g. One gram vials of aspecic drug were obtained from Ameriya Company for Pharmaceutical and Chemical Industries, Cairo, Egypt. It was synthesized from salicylic acid, acetic anhydride and non corrosive 12- tungstophosphoric acid. One vial was dissolved in 10 ml distilled water and administered orally as a single dose every week of freshly prepared aspirin solution in dose 400 mg/kg body weight of rats to induce gastric ulcer according to Main and Whittle [23]. Ranitidine tablets were obtained from SEDICO Pharmaceutical Company, Giza, Egypt. Each tablet contains 150 mg of ranitidine hydrochloride that inhibits gastric ulcer. Ranitak drug was dissolved in distilled water in dose 30 mg/kg of rat using a stomach tube. The basal diet was performed according to NRC [24].

Ginger oil (*Zingiber officinale*), clove oil (*Syzygium aromaticum*) and castor oil (*Ricinus communis*) were obtained from Agricultural Research Center, Giza, Egypt. Each one of them was administered daily at dose 1ml/kg body weight of rats orally by stomach tube.

**Methods**

**Biological Study:** Rats were fed the basal diet for five days before starting the experiment for adaptation then the rats were allocated into six equal groups. Normal control group fed on the basal diet only while the other five groups were administered orally of freshly prepared aspecic solution to induce gastric ulcer then classified into non treated control (+ve) and treated groups that were drug group, 1 ml ginger oil, 1 ml clove oil and 1 ml castor oil treatment groups. Daily food intake and weekly body weight gain were calculated. Food efficiency ratio (FER) was determined according to the method of Chapman *et al.* [25]. At the end of the experiment period (6 weeks), rats were sacrificed after overnight fasting under ether anesthesia. Blood samples were taken from hepatic portal vein, small part was taken into heparinised tube and the remainder were left to clot by standing at room temperature for 15 minutes and then centrifuged at 3000 rpm for 20 minutes. Serum was carefully separated and transferred into clean quite fit plastic tubes and kept frozen at - 20°C until the time of analysis.

**Determination of Gastric Secretion:** Stomachs from each rat were legated around both openings and injected by 3 ml distilled water. The gastric juice was collected in a test tube and centrifuged at 3000 rpm for 10 minutes. The gastric juice volume was measured by graduated cylinder [26]. The total acid content of the gastric juice was determined by titrating it with 0.01 N NaOH, using phenolphthalein as indicator and was expressed as mEq/l [4, 27]. The acidity of gastric juice was calculated as total.
acid content/gastric juice volume in mEq/l [28]. The gastric juice decrease percentage was calculated for each group according to Parmar and Desai [29] as following:

The gastric juice decrease percentage = \[
\frac{\text{volume of gastric juice of control positive} - \text{volume of gastric juice of treated group}}{\text{volume of gastric juice of control positive}} \times 100\%
\]

The decrease in total acidity of gastric juice percentage was calculated for each treated group according to Paiva et al. [30] as following:

\[
\text{Decrease in total acidity percentage} = \frac{\text{total acidity of gastric juice of control positive group} - \text{total acidity of gastric juice of treated group}}{\text{total acidity of gastric juice of control positive group}} \times 100\%.
\]

**Determination of Gastric Ulceration:** The stomachs were opened longitudinally, washed with saline and examined under dissecting microscope for gastric ulcer. The length of gastric ulcer was measured for each group to determine the ulcer index (UI) and the curative ratio according to Parmar and Desai [29]. The ulcerative index was calculated by severity of gastric mucosal lesions 1mm or less, 1-2 mm and more than 2 mm and graded as 1, 2 and 3 score, respectively. Then the UI was calculated by using the formula:

\[
\text{UI} = 1 \times (\text{number of lesions of grade 1}) + 2 \times (\text{number of lesions of grade 2}) + 3 \times (\text{number of lesions of grade 3})
\]

Then the overall score was divided by a factor 10, which was designated as ulcer index.

The curative ratio was calculated for each group as following:

\[
\text{Curative ratio} = \frac{\text{length of gastric ulcer in control positive group} - \text{length of gastric ulcer in treated group}}{\text{length of gastric ulcer in control positive group}} \times 100\%
\]

**Determination of Serum Parameters:** Total antioxidants capacity (TAC), Total oxidative capacity (TOC), Interleukin-1 (IL-1), Tumor necrosis factor-alpha (TNF-α), were determined according to Cao et al. [31], Flohe and Gunzler [32], Grassi et al. [33] and Beutler et al. [34], respectively.

**Determination of Blood Hemoglobin:** Blood hemoglobin was estimated according to Drabkin [35].

**Determination of Gastric Mucosa:** Gastric mucosal of cyclooxygenase (Cox–) activity, prostaglandin E₂ (PGE₂) level, cytochrome P₄₅₀ reductase (Cyto P₄₅₀) activity and total nitric oxide (TNO) concentration were determined according to Hemler and Lands [36], Hamberg and Samuelsson [37], Mc-Lean and Day [38] and Griess et al. [39] respectively.

**Histopathological Examination:** Gastric tissue samples were taken from different rats in each group immediately after sacrificed. The tissues were washed with the normal saline solution to remove blood, fixed in 10% neutral formalin as fixative and sent to Cancer Institute for histopathological examination according to Bancroft et al. [40].

**Statistical Analysis:** The obtained data were statistically analyzed using computerized SPSS (Statistic Program Sigma stat, Statistical Soft-Ware, SAS Institute, Cary, NC). Effects of different treatments were analyzed by one way ANOVA (Analysis of variance) test using Duncan’s multiple range test and p<0.05 was used to indicate significance between different groups [41].

**RESULTS**

The statistical data in Table 1 show that, control (+ve) rat group showed a significant decrease in final body weight, body weight gain %, food intake and food efficiency ratio while drug, ginger oil, clove oil or castor oil rat groups showed insignificant difference in food intake and FER compared with control (-ve) group. Treatment with drug, ginger, clove and castor oil showed significant increase in final weight, weight gain %, food intake and FER compared with control (+ve) rat group.

The results in Table 2 indicate that aspirin administration caused significant increase in volume and total acidity of gastric juice associated with significant decrease in acidity of control (+ve) group. While, the treatment with RAN drug or ginger, clove, castor oils produced significant decrease in volume of gastric juice and total acidity and significant increase in acidity compared with control (+ve) group. The values of gastric ulcer index were significantly decreased in all treated rat groups compared with control (+ve) group. The treatment groups with ginger oil, clove oil or castor oil showed insignificant difference in curative ratio percentage compared with RAN drug group.
Table 1: Effect of ginger, clove and castor oils treatment on nutritional parameters against aspirin induced gastric ulcers in rats

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Initial weight (g)</th>
<th>Final weight (g)</th>
<th>Weight gain (%)</th>
<th>Food intake (g/d)</th>
<th>FER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal control group (-ve)</td>
<td>147.33±2.05</td>
<td>236.33±2.49</td>
<td>60.42±1.88</td>
<td>16.65±2.11</td>
<td>0.173±0.001</td>
</tr>
<tr>
<td></td>
<td>ASP. control group (+ve)</td>
<td>148.33±2.87</td>
<td>196.33±3.27</td>
<td>32.37±0.62</td>
<td>12.20±2.17</td>
<td>0.098±0.002</td>
</tr>
<tr>
<td></td>
<td>ASP+RAN drug group</td>
<td>150.33±5.18</td>
<td>218.00±2.16</td>
<td>45.17±5.23</td>
<td>15.90±2.11</td>
<td>0.164±0.003</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg ginger oil group</td>
<td>142.67±2.05</td>
<td>209.00±3.74</td>
<td>47.55±3.04</td>
<td>16.35±2.91</td>
<td>0.169±0.001</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg clove oil group</td>
<td>149.67±4.73</td>
<td>219.00±0.82</td>
<td>46.66±7.76</td>
<td>16.55±2.18</td>
<td>0.171±0.001</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg castor oil group</td>
<td>150.33±1.69</td>
<td>215.00±11.22</td>
<td>43.06±8.22</td>
<td>16.75±2.81a</td>
<td>0.174±0.003</td>
</tr>
</tbody>
</table>

Values with the same letters indicate insignificant difference and vice versa. 
ASP: aspirin, RAN: Ranitidine, FER: Food efficiency ratio

Table 2: Effect of ginger, clove and castor oils treatment on gastric juice analysis and gastric ulceration against aspirin induced gastric ulcers in rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Volume of gastric juice (1ml)</th>
<th>Decrease in volume of gastric juice%</th>
<th>Total acidity of gastric juice (meq/l)</th>
<th>Decrease in gastric total acidity%</th>
<th>Ulcer index (mm)</th>
<th>Curative ratio %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal control group (-ve)</td>
<td>1.03±0.17</td>
<td>-</td>
<td>5.09±0.47</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>ASP. control group (+ve)</td>
<td>7.13±0.17</td>
<td>-</td>
<td>2.53±1.16</td>
<td>-</td>
<td>25.67±1.69</td>
<td>10.87±2.99</td>
</tr>
<tr>
<td></td>
<td>ASP+RAN drug group</td>
<td>3.50±0.25</td>
<td>50.93±3.43</td>
<td>4.20±0.18</td>
<td>42.86±1.84</td>
<td>2.13±0.19</td>
<td>78.61±6.81</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg ginger oil group</td>
<td>4.20±0.23</td>
<td>41.12±3.43</td>
<td>3.60±0.25</td>
<td>58.45±4.86</td>
<td>2.47±0.66b</td>
<td>74.44±12.37</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg clove oil group</td>
<td>3.80±0.28</td>
<td>46.73±3.97</td>
<td>3.96±0.15</td>
<td>41.56±3.18</td>
<td>1.93±0.99</td>
<td>78.47±18.42</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg castor oil group</td>
<td>4.13±0.21</td>
<td>42.06±2.88</td>
<td>3.43±0.44</td>
<td>54.55±4.86</td>
<td>2.33±0.47b</td>
<td>76.81±7.42</td>
</tr>
</tbody>
</table>

Values with the same letters indicate insignificant difference and vice versa. 
ASP: aspirin, RAN: Ranitidine

Table 3: Effect of ginger, clove and castor oils treatment on serum levels of total antioxidative capacity, total oxidative capacity, Interleukin-1, tumor necrosis factor-alpha and blood hemoglobin against aspirin induced gastric ulcers in rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>TAC mmol/L</th>
<th>TOC mmol/L</th>
<th>IL-1 pg/ml</th>
<th>TNF-α pg/ml</th>
<th>Hb g/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal control group (-ve)</td>
<td>1.69±0.02</td>
<td>0.27±0.02</td>
<td>12.46±0.78</td>
<td>3.01±0.03</td>
<td>13.64±0.39</td>
</tr>
<tr>
<td></td>
<td>ASP. control group (+ve)</td>
<td>0.89±0.06</td>
<td>1.18±0.11</td>
<td>51.50±3.25</td>
<td>13.34±1.62</td>
<td>9.19±0.30</td>
</tr>
<tr>
<td></td>
<td>ASP+RAN drug group</td>
<td>1.37±0.08</td>
<td>0.45±0.07</td>
<td>24.06±12.2</td>
<td>5.68±0.44</td>
<td>13.29±0.92</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg ginger oil group</td>
<td>1.12±0.05</td>
<td>0.75±0.06</td>
<td>31.59±0.57</td>
<td>8.98±0.28</td>
<td>13.42±0.78</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg clove oil group</td>
<td>1.02±0.03</td>
<td>0.82±0.23</td>
<td>46.29±0.63</td>
<td>10.02±0.34</td>
<td>13.33±0.66</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg castor oil group</td>
<td>1.06±0.09</td>
<td>0.79±0.04</td>
<td>36.57±1.33</td>
<td>9.49±0.66</td>
<td>12.93±1.33</td>
</tr>
</tbody>
</table>

Values with the same letters indicate insignificant difference and vice versa. 
ASP: aspirin, RAN: Ranitidine, TAC: total antioxidative capacity, TOC: total oxidative capacity, IL-1: Interleukin-1, TNF-α: tumor necrosis factor-alpha, Hb: hemoglobin

Table 4: Effect of ginger, clove and castor oils treatment on gastric tissues of cyclooxygenase, prostaglandin E2, cytochrome P450 reductase and total nitric oxide against aspirin- induced gastric ulcers in rats

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Cox-2 ng/mg</th>
<th>PGE2 pg/mg</th>
<th>Cyto P450 reductase ng/mg</th>
<th>TNO pg/mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal control group (-ve)</td>
<td>4.91±0.25</td>
<td>502.83±13.19</td>
<td>1.87±0.04</td>
<td>35.39±4.07</td>
</tr>
<tr>
<td></td>
<td>ASP. control group (+ve)</td>
<td>17.25±0.97</td>
<td>298.23±1.27</td>
<td>0.69±0.06</td>
<td>70.38±9.59</td>
</tr>
<tr>
<td></td>
<td>ASP+RAN drug group</td>
<td>6.35±0.42</td>
<td>453.7±19.94</td>
<td>1.45±0.07</td>
<td>46.94±4.11</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg ginger oil group</td>
<td>8.16±0.22</td>
<td>425.23±9.49</td>
<td>1.11±0.02</td>
<td>52.51±0.89</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg clove oil group</td>
<td>13.94±0.69</td>
<td>384.57±5.12</td>
<td>0.87±0.06</td>
<td>60.99±3.05</td>
</tr>
<tr>
<td></td>
<td>ASP+ 1ml/kg castor oil group</td>
<td>13.87±0.25</td>
<td>378.17±3.77</td>
<td>0.79±0.02</td>
<td>54.30±5.77</td>
</tr>
</tbody>
</table>

Values with the same letters indicate insignificant difference and vice versa. 
ASP: aspirin, RAN: Ranitidine, Cox: cyclooxygenase, PG: prostaglandin, Cyto: cytochrome, TNO: total nitric oxide
As shown in Table 3, aspirin administration led to significant increases in serum total oxidative capacity, interleukin-1 and tumor necrosis factor-alpha levels while, there were significant decreases in serum total antioxidant capacity level and blood hemoglobin content. The treatment groups with drug and ginger, clove, castor oils showed significant decrease in total oxidative capacity, interleukin-1 and tumor necrosis factor-alpha while there were significant increase in total antioxidative capacity and hemoglobin compared to ulcerated positive control group.

The statistical data in Table 4 presented that, control (+ve) rat group showed significant increase in gastric cyclooxygenase (COX2) activity and total level nitric oxide compared to (-ve) control group, while showed significant decrease in gastric prostaglandin E2 and cytochrome P450 reductase activity compared to (-ve) control group. The treatment groups with drug, ginger oil, castor oil or clove oil showed a significant decrease in gastric cyclooxygenase (COX2) activity and total nitric oxide compared to (+ve) control group, while showed a significant increase in gastric prostaglandin E2 and cytochrome P450 reductase activity compared to (+ve) control group.

**Histopathological Results:** The obtained results are confirmed by the histopathological examination. Stomach of control (-ve) group showed normal histological gastric mucosa.
mucosa (Picture 1). While, stomach of control (+ve) rat group showed focal necrosis of gastric mucosa associated with mucosal and submucosal eosinophilic cells infiltration (Picture 2). Stomachs of drug, ginger, clove and castor oils treatment groups showed no histopathological changes (Picture 3-6, respectively).

**DISCUSSION**

In accordance with the obtained results, aspirin has been reported to reduce the gastric juice pH and increase the volume of gastric juice [4]. The anti-ulcerative effects of ginger, clove and castor oils were investigated in aspirin-induced gastric ulcer model rats. It is evident from the present results that all these oils have potent ulcer protective activity at 1ml/kg. There was significant decrease in ulcer index in these oils treated rats as ranitidine treated rats. Also, there was significant decrease in the volume of gastric content and total acidity in all oils treated rat groups as compared with ulcerated control rats. The curative ratio % in all oils treated groups showed insignificant difference compared to ranitidine group.

The data presented here provided scientific evidence that ginger, clove and castor oils may contain biologically active substances with potential anti-ulcer properties. This gastro protective effect may be due to the high flavonoids content of these oils. The obtained results are consistent with those of Khushtar et al. [28] who indicate that ginger oil has a protective action against gastric ulcers induced by aspirin in rats. The ginger oil has antisecretory activity, as observed by the decrease in total acidity and volume of gastric juice. Further, the ginger oil treatment offers cytoprotection by increasing mucus. Also, Magaji et al. [15] reported that clove extract showed good gastro protective anti-ulcerogenic activity and they attributed this effect to the anti-oxidative activity of flavonoids found in extract. Furthermore, Rachhadiya et al. [21] demonstrated that castor oil possess antiulcer activity against the ulceration caused by aspirin. Aspirin a well known NSAID which induces erosions and ulcers in gastroduodenal tract through different processes, such as inhibition of cyclooxygenase mediated prostaglandin synthesis, generation of reactive oxygen species (ROS) and induction of apoptosis. Inflammatory injury is associated in part with increased generation of ROS [42]. Moreover, Shyamal and Chandan [9] reported that aspirin significantly decreased SOD, CAT and GSH activities and increased of lipid oxidation MDA in aspirin- treated experimental group compared with control group.

The inhibition of TAC level and the elevation of TOC concentration in the present results during aspirin induced ulcer due to the increased generation of reactive free radicals, which can create an oxidative stress in the cells. The administration of RAN drug and using herbal oils inversed these results which protected from the free radical induced oxidative stress. This result supports that, these oils have potential antioxidant action on gastric ulcer rat model through phenolic compounds that capable of scavenging peroxyl radicals and have powerful antiulcer activities. These compounds contain an OH group linked with the aromatic ring and thus may possess potential antioxidant and antiulcer activities [9]. Inflammation and neutrophil infiltration are also important in the pathogenesis of the gastric damage induced by NSAIDs [43]. The inflammation induced in the gastric mucosa by aspirin is accompanied by increased TNF-α production [44, 45], which augments neutrophil-derived superoxide generation [46] and stimulates IL-1 production, leading to neutrophil accumulation [47, 48]. Over production of TNF-α increases the risk of gastric ulcer and cancer [49]. In the present study, the levels of TNF-α and IL-1 were increased by aspirin administration and the treatment with all using oils inhibited the increases in TNF-α and IL-1 levels. These results are in agreement with those obtained by Wang et al. [50] who reported that ginger powder inhibited the increases in TNF-α and IL-1 levels without ulcer formation progressing. Suppression of TNF-α and IL-1 production this may be attributed to the anti-inflammatory activity of these treatment oils. The inhibition of TNF-α and neutrophil infiltration will ultimately inhibit tissue destruction by reactive oxygen species [46].

Prostaglandins have protective effects against various gastric injury models. Aspirin has been shown to reduce the mucosal PGE2 content [50]. Prostaglandin, a key molecule that stimulates the complex array of ulcer healing mechanism, gets synthesized in the mucosal cells by cyclooxygenase (COX) enzymes. It stimulates the secretion of biocarbonate and mucus, maintains mucosal blood flow and regulates mucosal turn over and repair. Suppression of prostaglandins synthesis by aspirin may be led to increase the susceptibility of stomach to mucosal injury and gastroduodenal ulceration [51, 52]. The obtained data in the current investigation were in
parallel line with these previous data, aspirin significantly reduced gastric mucosal prostaglandin E2 (PGE2) level and gastric cyto P<sub>450</sub> reductase activity while elevated COX-2 activity compared to control. Treatment with oils significantly inversed these results when compared to aspirin treated rats. This finding was explained by Borrelli and Izzo [53] who reported that flavonoids may protect the gastric mucosa from damage by increasing the mucosal prostaglandin content and by inhibiting histamine secretion from mast cells by inhibition of histidine decarboxylase. Ginger appears to exert anti-inflammatory effects by suppressing COX-2 activity [54].

One of the mechanisms by which aspirin damages the gastric mucosa is the increased production of NO due to the over expression of inducible nitric oxide synthetase (iNOS) [55]. NO is a mediator not only of gastrointestinal mucosal defense, but also of its damage. It has been shown that different concentrations of NO have completely opposite effects in the same tissue. In general, the mucosal and endothelial NOS isoforms produce low amounts of NO. However, the high quantity of NO produced by iNOS damages the epithelium [56]. The excessive release of NO from gastric epithelial cells induced by aspirin has been reported to exert detrimental effects [57, 58]. Inhibiting aspirin induced increases in iNOS expression in the gastric mucosa leads to a reduction in gastric mucosal damage [55]. In the present study, the results of ginger, clove and castor oils treatment groups agree with Wang et al. [50], who reported ginger powder reduced iNOS activity and inhibited the production of gastric ulcers, even in the presence of aspirin. Both constituents of ginger showed protective effects against aspirin-induced gastric ulcers together with anti-inflammatory effects by reducing iNOS activity in the gastric mucosa and inflammatory cytokine (TNF and IL-1) expression. These effects of ginger powder seem to be derived from the actions of gingerol and shogaol, the main ingredients of ginger [50, 59, 60]. Another study by Mari et al. [7], who explained those anti-inflammatory compounds of flavonoids as Flavone, the isoflavones, the flavonols isorhamnetin, kaempferol, quercetin and the anthocyanin inhibited iNOS expression.

Histopathological studies on the gastric mucosa revealed that aspirin administration induced a mucosal ulceration, associated with significant increase in lipid peroxidation. This was manifested as lamina epithelial necrosis, blood vessels congestion and leukocyte infiltration [61, 62]; this effect on histological derangement was in accordance with our results. While, all treatment groups with oils showed protective effect against aspirin induced inflammatory infiltration and congestion at the ulcer sites. It prevented gastric mucosal lesions through its flavonoids content. Flavonoids could scavenge free radicals, inhibit lipid peroxidation and increase prostaglandins and mucosal content of the gastric mucosa; showing cyto-protective effects [63].

**CONCLUSION**

Ginger, clove and castor oils possess antioxidant, anti-inflammatory and immunosuppressive actions, which may be responsible for its antulcerogenic activity. The presence of phyto-constituents in these medicinal oil, particularly flavonoids might be responsible for these pharmacological actions. These phyto-constituents provide protection against gastric mucosal damage induced by aspirin. The healing activity may be due to its cyto-protective effect coupled with anti-secretory activity.

**REFERENCES**


