Studies of the role of the methanol fraction of the ethanol layer of the chloroform-ethanol leaf extract of *Dacryodes edulis* on diclofenac-induced gastric ulcer in rats

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**ABSTRACT**

**Background and Aim:** The leaves of *Dacryodes edulis* are used in traditional medicine for the treatment of gastric ulcer among other ailments in Nigeria. The aqueous extract, chloroform and ethanol layers of the chloroform-ethanol leaf extract of *D. edulis* were investigated for their qualitative and quantitative phytochemical compositions. Based on the outcomes of the preliminary investigations, the most promising of the three (ethanol layer) was further fractionated and the effects of the most desirable fraction (methanol fraction) on ulcer index, gastric juice volume, gastric juice pH and histopathology of diclofenac-ulcerated Wistar rats were determined. **Methods:** The qualitative and quantitative phytochemical compositions and acute toxicities of the aqueous extract, chloroform and ethanol layers as well as the effects of the methanol fraction of the ethanol layer of the chloroform-ethanol leaf extract of *D. edulis* on ulcer index, gastric juice volume, gastric juice pH and histopathology of diclofenac-ulcerated Wistar rats were determined using standard methods. **Results:** The qualitative and quantitative phytochemical analyses of the aqueous extract, chloroform and ethanol layers showed the presence and amounts of the following: alkaloids, flavonoids, tannins, saponins and steroids. Each of the aqueous extract, chloroform and ethanol layers was found to be safe at 5000 mg/kg body weight (b.w). At the tested doses (100, 200 and 400 mg/kg b.w), the methanol fraction caused significant (p < 0.05) and dose-dependent decreases in the ulcer indices and gastric juice volumes as well as increases in the gastric juice pH of the rats in the test groups compared with those of the rats in the ulcer-untreated group. Results of the histopathological evaluation supported the gastroprotective effects of the fraction. Results of the fraction were comparable with those of the standard anti-ulcer drug, ranitidine at the dose of 150 mg/kg b.w. **Conclusion:** Experimental findings indicate that the leaves of *D. edulis* possess remarkable anti-ulcer effect probably due to their phytochemical constituents.

**KEYWORDS:** *Dacryodes edulis*, Phytochemical compositions, Ulcer index, Gastric juice volume, Gastric juice pH, Histopathology and Diclofenac

**1. INTRODUCTION**

Plants have been the basis of many traditional medicine systems throughout the world for thousands of years and still remain as the main sources for the development of innovative drugs[1]. Herbal medicine is an alternative form of therapy and has become the mainstream throughout the world. The development of herbal products is dependent on local botanical flora[2]. Interest in botanical medicine has increased over the years, not only by the physicians, but also by the public in general who seem to prefer products containing natural extracts than those based on synthetic substances[3]. Medicinal plants are distributed worldwide and many abound in tropical countries. Nigeria has a rich variety of medicinal plants distributed in the different geoeological regions of the country. Millions of people in developing countries, for instance Nigeria, use herbal medicines because they are locally available and are prescribed by traditional medicine practitioners who are a part of their community[4,5].

The term peptic ulcers include ulcers of the digestive tract in the stomach (stomach or gastric ulcer) and the duodenum (duodenal ulcer). A peptic ulcer is a sore on the lining of the stomach or duodenum, the beginning of the small intestine. Less commonly, a peptic ulcer may develop just above the stomach in the oesophagus, the tube that connects the mouth to the stomach[6]. The formation of peptic ulcers depends on the presence of acid and peptic activity in
the gastric juice plus a breakdown in mucosal defence. Peptic ulcer
which includes gastric and duodenal ulcers is the most prevalent
gastrointestinal disorder and requires a well targeted therapeutic
strategy. The pathophysiology of peptic ulcer involves an imbalance
between the offensive factors (acid, pepsin and Helicobacter pylori)
and the defensive factors (mucin, prostaglandin, bicarbonate, nitric
oxide and growth factors). The most common sites for ulcers are the
stomach and the first few centimetres of the duodenum[7]. Gastric
ulcer is often a chronic disease; it may persist for 10-20 years and is
characterised by repeated episodes of healing and re-exacerbation.
Peptic ulcer affects a large proportion of the world’s population and
is induced by several factors including stress, smoking, nutritional
deficiencies and ingestion of non steroidal anti-inflammatory drugs[8].
Many natural products and modern synthetic drugs have been used
to treat gastric ulcer but so far, a complete cure has not been
discovered and hence, the reveille for the development of safe
indigenous inexpensive new anti-ulcer drugs and the search for novel
molecules in natural products (plants) such as D. edulis.

D. edulis (Fig. 1) is a versatile plant in African ethnomedicine as its
various parts are employed to treat several diseases. Its bark has
long been used to cicatrise wound[9] and treat leprosy, dysentery,
anæmia, spitting blood, debility, stiffness, tonsillitis and skin
diseases[10]. The leaves are often crushed and the juice released to
cure generalised skin diseases such as scabies, ringworm, rashes
and wound while the stem or stem twigs are employed as chewing
sticks for oral hygiene[11]. When chewed with kolanut, its leaves
serve as anti-emetic while its leaf sap could be used for the treatment
of ear infections, fever, headache, malaria and cephalgy[12]. Recently,
Jiofack et al[13] reported that the leaves are made into plaster to treat
snakebite in southwest Cameroon. Besides, Ajibesin[14] had identified
phenolics such as ethylgallate and quercitrin in the plant leaves. The

leaves boiled singly or with lemon grass or pulp oil are employed in
the treatment of peptic ulcer[15]. In this study, we report the role of
the methanol fraction of the ethanol layer of the chloroform-ethanol
leaf extract of D. edulis on diclofenac-induced gastric ulcer in rats.

2. MATERIALS AND METHODS

2.1. Plant

Fresh leaves of D. edulis were plucked from their tree at Government
Reserved Area (GRA), Nsukka Local Government Area of Enugu
State, Nigeria. The leaves were identified by Mr. Alfred Ozioko of
Bioresource Development and Conservation Programme (BDCP)
Research Centre, Nsukka.

2.2. Extraction Procedure for the Aqueous Extract

The fresh leaves of D. edulis were washed with distilled water. The
leaves were spread on a clean mat in a well-ventilated room with
regular turning to enhance even drying and avoid decaying for 3
weeks. A known weight (600 g) of the pulverised leaves was
macerated in 5 volumes (w/v) of distilled water for 24 hours. The
mixture was thereafter, filtered using Whatman No 1 filter paper and
the filtrate concentrated and weighed.

2.3. Extraction Procedure for the Chloroform-Ethanol Extract

A known weight (1200 g) of the pulverised D. edulis leaves was
macerated in 5 volumes (w/v) of chloroform-ethanol (2:1) at room
temperature for 24 hours. The mixture was filtered with Whatman
No 1 filter paper. The filtrate of the macerate was vigorously shaken
with 20% distilled water to obtain two (2) layers. The upper layer (ethanol
layer) was separated from the lower layer (chloroform layer). The
ethanol and the chloroform layers were concentrated in a rotary
evaporator, air-dried, weighed and stored in the refrigerator.

2.4. Vacuum Liquid Chromatography (VLC) of the Ethanol Layer

Twenty-five grammes (25 g) of the ethanol layer was purified by
vacuum liquid chromatography using silica gel (230-400 mesh, 3.0 x
30 cm, 500 g) as the stationary phase and eluted with n-hexane (1500
ml), chloroform (3500 ml), ethyl acetate (2500 ml) and methanol (2500
ml) to obtain the n-hexane, chloroform, ethyl acetate and methanol
fractions respectively.

2.5. Phytochemical Analyses

Qualitative phytochemical analyses were carried out on the aqueous
extract, chloroform and ethanol layers of the chloroform-ethanol
extract according to the procedures outlined by[16] and[17]. Quantitative
phytochemical analyses were carried out to determine the
concentration of the following: alkaloids and flavonoids by the
methods of[18]; tannins by the method of[19]; steroids by the method
of[20] and saponins by the method of[21].

2.6. Animals

Adult male Wistar rats of between 8 and 12 weeks old with an average
weight of 125 ± 25 g and albino mice weighing 30 ± 5 g were obtained
from the Animal house of the Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka. The rats were acclimatised for one week under a standard environmental condition with a 12 hour light and dark cycle and maintained on a regular feed and water ad libitum. There was adherence to the Principles of Laboratory Animal Care. The University Animal Research Ethical Committee approved the experimental protocol.

2.7. Chemicals and Reagents
The chemicals used for this study were of analytical grade. They included the following: diclofenac (Evans Medical Plc., Nigeria), ranitidine (Evans Medical Plc., Nigeria), absolute ethanol and chloroform, 45% (v/v) ethanol (BDH Chemicals Ltd., Poole, England), dilute tetraoxosulphate (vi) acid, 2% (v/v) hydrochloric acid, 1% (w/v) picric acid, methyl orange, 3% (v/v) tween 80, Dragendorff’s reagent, Mayer’s reagent, Wagner’s reagent, Millon’s reagent, Fehling’s solution, 5% (w/v) ferric chloride solution, aluminium chloride solution, lead subacetate solution, ammonium solution, Molisch’s reagent, 10% formalin, xylene, Lugol’s solution, 50% sodium thiosulphate, Scott’s solution (Sigma-Aldrich, Inc., St. Louis, USA).

2.8. Acute Toxicity Study
The acute toxicity and lethality (LD₅₀) of the aqueous extract, chloroform and ethanol layers of the chloroform-ethanol extract were determined using mice according to slightly modified method of[22].

2.9. Gastric Ulcer Index, Gastric Juice Volume and Gastric Juice pH
The methods described by[21] were employed in these studies.

2.10. Histopathological Evaluation
The histopathological evaluation of the stomach tissues of the rats was carried out according to the methods described by[23] and[24].

2.11. Statistical Analysis
The data obtained were subjected to one-way Analysis of Variance (ANOVA). Significant differences are observed at p < 0.05. The results are expressed as means ± standard errors of means (SEM). The analysis was done using the computer software known as Statistical Product and Service Solutions (SPSS), version 18.

3. RESULTS

3.1. Qualitative Phytochemical Compositions of the Aqueous Extract, Chloroform and Ethanol Layers of the Chloroform-Ethanol Leaf Extract of D. edulis
As shown in Table 1, the qualitative phytochemical analyses showed the presence of alkaloids, flavonoids, tannins, saponins, carbohydrates, proteins, steroids and fats and oil in each of the aqueous extract, chloroform and ethanol layers. Terpenoids were only present in the chloroform and ethanol layers. Resins, reducing sugars, glycosides and acidic compounds were not detected in any of them.

### Table 1: Qualitative phytochemical constituents of the aqueous extract, chloroform and ethanol layers of the chloroform-ethanol extract of the leaves of D. edulis

<table>
<thead>
<tr>
<th>Phytochemical constituents</th>
<th>Aqueous extract</th>
<th>Chloroform layer</th>
<th>Ethanol layer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloids</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Tannins</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Resins</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Saponins</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Reducing sugars</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Glycosides</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Proteins</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Steroids</td>
<td>+</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Terpenoids</td>
<td>ND</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Fats and oil</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Acidic compounds</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

+= present in low concentration ;++= present in moderately high concentration ;+++ = present in very high concentration ;ND = not detected

### Table 2: Concentrations of alkaloids, flavonoids, tannins, saponins and steroids in the aqueous extract, chloroform and ethanol layers of the chloroform-ethanol extract of the leaves of D. edulis

<table>
<thead>
<tr>
<th>Phytochemical constituents</th>
<th>Aqueous extract</th>
<th>Chloroform layer</th>
<th>Ethanol layer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloids (mg/100 g)</td>
<td>1.77 ± 0.26</td>
<td>3.19 ± 0.14</td>
<td>3.52 ± 0.49</td>
</tr>
<tr>
<td>Flavonoids (mg/100 g)</td>
<td>2.21 ± 0.41</td>
<td>5.25 ± 0.34</td>
<td>4.46 ± 0.53</td>
</tr>
<tr>
<td>Tannins (%)</td>
<td>1.73 ± 0.33</td>
<td>3.18 ± 0.38</td>
<td>3.98 ± 0.25</td>
</tr>
<tr>
<td>Saponins (mg/100 g)</td>
<td>2.03 ± 0.25</td>
<td>3.26 ± 0.45</td>
<td>4.02 ± 0.30</td>
</tr>
<tr>
<td>Steroids (mg/100 g)</td>
<td>2.49 ± 0.12</td>
<td>3.95 ± 0.21</td>
<td>3.02 ± 0.10</td>
</tr>
</tbody>
</table>

Values are expressed as means of three determinations ± SEM

3.3. The Acute Toxicity and Lethality (LD₅₀) of the Aqueous Extract, Chloroform and Ethanol Layers of the Chloroform-Ethanol Leaf Extract of D. edulis
There was no lethality or any sign of toxicity in the four groups of mice that received 10, 100, 1000 mg/kg body weight of the aqueous extract, chloroform and ethanol layers and 5 ml/kg body weight of the vehicle respectively at the end of the first phase of the study. At the end of the second phase of the study, no death was recorded in the groups of mice that received 1600, 2900 and 5000 mg/kg body weight.
weight of the aqueous extract, chloroform and ethanol layers within 24 hours of administration.

3.4. Effect of the Methanol Fraction of the Ethanol Layer of the Chloroform-Ethanol Leaf Extract of D. edulis on Ulcer Index

As shown in Fig. 2, the ulcer index (0.00 ± 0.00 mm) of the rats in the normal control group (group 1) was significantly (p < 0.05) lower when compared to the value (5.18 ± 0.17 mm) obtained for the rats in the ulcer-untreated group (group 2). Treatment with the 100, 200 and 400 mg/kg body weight of the methanol fraction significantly (p < 0.05) and dose-dependently decreased the ulcer indices of the rats in groups 4 (3.01 ± 0.20 mm), 5 (1.93 ± 0.06 mm) and 6 (1.02 ± 0.04 mm) respectively when compared to that of the rats in group 2 (5.18 ± 0.17 mm). The effect of the administration of the methanol fraction at the dose of 400 mg/kg body weight was comparable with that produced by treatment with the standard anti-ulcer agent [ranitidine (150 mg/kg body weight)] as there was no significant (p > 0.05) difference between the ulcer index of the rats in the group treated with 150 mg/kg body weight of ranitidine and that of the rats in the group treated with 400 mg/kg body weight of ranitidine (0.99 ± 0.11 mm).

3.5. Effect of the Methanol Fraction of the Ethanol Layer of the Chloroform-Ethanol Leaf Extract of D. edulis on Gastric Juice Volume

The gastric juice volume (4.36 ± 0.14 ml) of the rats in the ulcer-untreated group (group 2) was significantly (p < 0.05) higher when compared to the value (1.32 ± 0.04 ml) obtained for the rats in the normal control group (group 1) which received 5 ml/kg body weight of normal saline only. The gastric juice volumes of the rats in groups 3 (1.51 ± 0.03 ml), 4 (2.84 ± 0.04 ml), 5 (2.18 ± 0.04 ml) and 6 (1.67 ± 0.04 ml) treated with 150 mg/kg body weight of ranitidine, 100, 200 and 400 mg/kg body weight of the methanol fraction respectively were significantly (p < 0.05) reduced relative to that of the rats in group 2 (4.36 ± 0.14 ml). The effects of the treatments with the graded doses of the fraction were dose-related with the effect of the administration of the 400 mg/kg body weight of the fraction being similar to that produced by treatment with the standard anti-ulcer drug [ranitidine (150 mg/kg body weight)]. There was no significant (p > 0.05) difference between the gastric juice volume of the rats in group 3 (1.51 ± 0.03 ml) and the value obtained for the rats in the normal control group (1.32 ± 0.04 ml) [Fig. 3].

3.6. Effect of the Methanol Fraction of the Ethanol Layer of the Chloroform-Ethanol Leaf Extract of D. edulis on Gastric Juice pH

The gastric juice pH (4.03 ± 0.04) of the rats in the ulcer-untreated group (group 2) was significantly (p < 0.05) lower when compared to the value (6.98 ± 0.04) obtained for the rats in the normal control group (group 1) that received 5 ml/kg body weight of normal saline only as shown in Fig. 4. The gastric juice pH of the rats in groups 3 (6.95 ± 0.04), 4 (5.47 ± 0.04), 5 (6.84 ± 0.04) and 6 (6.91 ± 0.04) treated with 150 mg/kg body weight of ranitidine, 100, 200 and 400 mg/kg body weight of the methanol fraction respectively were significantly (p < 0.05) higher when compared to that of the rats in group 2 (4.03 ± 0.04). The effects of the treatments with the graded doses of the fraction were dose-dependent with the effects of the administrations of the 200 and 400 mg/kg body weight of the fraction being similar to that produced by treatment with the standard anti-ulcer drug, ranitidine at the dose of 150 mg/kg body weight. There were no
significant (p > 0.05) differences between the gastric juice pH of the rats in groups 3 (6.95 ± 0.04), 5 (6.84 ± 0.04) and 6 (6.91 ± 0.04) and that of the rats in the normal control group (6.98 ± 0.04).

**Fig. 4:** Effect of the methanol fraction of the ethanol layer of the chloroform-ethanol leaf extract of *D. edulis* on gastric juice pH

[Values for groups with different alphabets are significantly (p < 0.05) different]

3.7. Effect of the Methanol Fraction of the Ethanol Layer of the Chloroform-Ethanol Leaf Extract of *D. edulis* on the Architecture of the Stomach

Plate 1 shows normal histology of the mucosa (M), submucosa (SM) and the muscularis mucosa (MM) of the stomach of the rat in the normal control group (group 1) which received 5 ml/kg body weight of normal saline only. There were oedema and inflammatory cell infiltration of the submucosa (SM) as well as severe disruption of the surface epithelium (arrow) of the stomach of the rat in the ulcerated group (group 2) as shown by Plate 2. Plate 3 shows apparently normal histology of the submucosa (arrow) of the stomach of the rat in group 3 treated with 150 mg/kg body weight of ranitidine. There was mild oedema of the submucosa (arrow) of the stomach of the rat in group 4 administered 100 mg/kg body weight of the methanol fraction as shown by Plate 4. Plates 5 and 6 show apparently normal histology of the submucosa (arrows) of the stomachs of the rats in groups 5 and 6 treated with 200 and 400 mg/kg body weight of the methanol fraction respectively.

4. DISCUSSION

The results of the qualitative and quantitative phytochemical analyses of the aqueous extract, chloroform and ethanol layers of the chloroform-ethanol leaf extract of *D. edulis* showed the presence and amounts of such bioactive constituents as alkaloids (1.77 ± 0.26, 3.19 ± 0.14 and 3.52 ± 0.49 mg/100 g), flavonoids (2.21 ± 0.41, 5.25 ± 0.34 and 4.46 ± 0.53 mg/100 g), tannins (1.73 ± 0.33, 3.18 ± 0.38 and 3.98 ± 0.25%), saponins (2.03 ± 0.25, 3.26 ± 0.45 and 4.02 ± 0.30 mg/100 g) and steroids (2.49 ± 0.12, 3.95 ± 0.21 and 3.02 ± 0.10 mg/100 g) respectively. This indicates that the bioactive constituents present
in the aqueous extract, chloroform and ethanol layers of the chloroform-ethanol leaf extract of *D. edulis* resided more in the ethanol layer than in the chloroform layer and the aqueous extract. Similar finding had been reported by\[25\]. Resins, reducing sugars, glycosides and acidic compounds were not detected in any of them. The presence of alkaloids, flavonoids, tannins and saponins in the ethanol extract of the leaves of the plant had been documented\[26\].

The anti-ulcer properties of the methanol fraction as shown in the present study could be, in part, due to the presence of the afore-listed phytochemicals in the ethanol layer of the chloroform-ethanol leaf extract of *D. edulis*. In other words, it is likely that flavonoids and tannins, acting dually or in combination with other phytochemicals caused the observed anti-ulcer effects of the methanol fraction. Previous studies showed that flavonoids and tannins are among the cytoprotective active compounds for which anti-ulcer properties have been extensively confirmed\[6,27,28\]. While flavonoids are suggested to be able to stimulate the secretions of mucus, bicarbonate and prostaglandins and counteract the deteriorating effects of reactive oxidants in the gastro-intestinal lumen, tannins are known to “tan” the outermost layer of the mucosa and render it less permeable and more resistant to chemical and mechanical injuries\[29\].

Acute toxicity test on the aqueous extract, chloroform and ethanol layers of the chloroform-ethanol leaf extract of *D. edulis* using mice showed that each of them administered to the mice at a dose as high as 5000 mg/kg body weight by oral route within twenty-four hours of observation, had no fatal effect on the mice which indicates that the aqueous extract, chloroform and ethanol layers have low toxicity at high doses when administered by oral route.

Evaluation of the effects of the aqueous extract, chloroform and ethanol layers on gastric ulcer experimentally induced with diclofenac in rats showed that, they dose-dependently decreased the ulcer indices of the treated rats with the effect of the ethanol layer being the most pronounced. Also, the n-hexane, chloroform, ethyl acetate and methanol fractions caused reductions in the ulcer indices of the treated rats with the effect of the methanol fraction being remarkable. Investigation into the effects of the graded doses of the methanol fraction revealed that they remarkably and dose-dependently decreased the ulcer indices of the treated rats with the effect of the 400 mg/kg body weight of the fraction being the greatest. This indicates that the leaves of *D. edulis* contain anti-ulcer agents. The observation that the ethanol layer decreased the ulcer indices of the treated rats more than the chloroform layer and the aqueous extract might be attributed to the fact that the bioactive constituents responsible for the anti-ulcer effect resided more in the ethanol layer than in the chloroform layer and the aqueous extract as shown by the result of the quantitative phytochemical analyses. Also, the finding that diclofenac induced ulcer in all the rats is in accord with the reports of\[6,30,31,32\]. The mechanism by which diclofenac and other NSAIDs cause injury to the gastric mucosa is mainly due to the inhibition of cyclooxygenase and suppression of prostaglandin-mediated effects on mucosal protection. Besides, it has been proposed that neutrophil and oxygen radical-dependent microvascular injuries may be important processes that lead to mucosal damage in response to NSAID administration\[33\]. These agents cause the activation of neutrophils and their adherence to the vascular endothelium, hence, blocking capillaries and reducing local gastric blood flow. NSAIDs inhibit COX and thereby reduce the intrinsic ability of the mucosa to resist injury induced by endogenous and exogenous aggressors\[31\]. Administration of exogenous prostaglandins has also been shown to decrease or prevent gastric damage induced by NSAIDs\[34\]. Therefore, the decreases in ulcer indices of the treated rats observed with the methanol fraction of the ethanol layer of the chloroform-ethanol leaf extract of *D. edulis* in this study are in part, indications of the anti-ulcer properties of the leaves of *D. edulis*. This anti-ulcer effect of the methanol fraction might be due to some of the phytochemicals acting singly or in combination with one another.

Diclofenac induced higher secretion of gastric acid as typified by the increase and decrease in the gastric juice volume and gastric juice pH respectively in the ulcerated rats. Secretion of acid from the gastric mucosa and its pH are critically involved in the development of gastric ulcer\[35\]. The methanol fraction provoked a marked decrease in the gastric juice volume whereas it increased the gastric juice pH of the treated rats in a manner similar to the action of the standard anti-ulcer drug (ranitidine) and thus restored a balance that is highly desirable of an anti-ulcer agent in the ulcerated rats. These observed effects of the methanol fraction of the leaves of *D. edulis* which are indications of the inhibition of gastric acid secretion by the fraction, imply an anti-secretory effect of the fraction. The anti-secretory effect of the methanol fraction of the leaves of *D. edulis* in part, could be indicative of an anti-ulcer property of the leaves of *D. edulis*. These effects are in agreement with the findings of\[30\] which reported that the methanol extract of the leaves of *Punica granatum* remarkably decreased and increased the gastric juice volume and gastric juice pH respectively of ulcerated rats.

Histopathological evaluation of the stomach tissue of the rat in the ulcer-untreated group portrayed oedema and infiltration of the submucosa by inflammatory cells as well as severe disruption of the surface epithelium. Graded doses of the methanol fraction of the leaves of *D. edulis* were able to foreclose the aberrations caused by diclofenac as the tissues of the treated rats reflected seemingly normal.
histology. The effects might be due to the presence of anti-oxidant phytochemicals in the ethanol layer. Similar effects had been reported for *Dalbergia sissoo*.[2]

In conclusion, the observations of this study imply that the methanol fraction of the ethanol layer of the chloroform-ethanol leaf extract of *D. edulis* protects against gastric ulcer by decreasing the ulcer index and gastric juice volume and raising the gastric juice pH. These thus, support the use of the leaves of *D. edulis* in traditional medicine for the treatment of gastric ulcer.

**REFERENCES**


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