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Anti-ulcer and Wound-healing Activities of the Aqueous Leaf Extract of Cissampelos owariensis P.Beauv. ex DC.

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Abstract:

Cissampelos owariensis has been reported to be used in the treatment of diseases and conditions such as digestive problems, infertility and infections. The present study evaluated its effects on gastric ulcers and wound healing. Gastric ulcer was induced in albino rats with ethanol, indomethacin and cold stress following treatment with 50, 100 and 200 mg/kg of the aqueous extract of the leaf of C. owariensis (COLE). The free and total acidity of the gastric contents were assessed. Heat-inflicted wound was applied on the skin of albino rats and treated with the extracts for 3 weeks, measuring the reduction in wound size every 5 days. The extract acted dose-dependently and compared favourably with the reference drugs used for the three models. The extract exhibited lower gastric juice volume compared to the control (2.50 ml at 100 mg/kg as against 9.00 ml in the ethanol model). By the 20th day, 200 mg/kg of the extract achieved a mean percentage wound healing of 96%. COLE proved very plausible as an alternative remedy for ulcers and wounds.

Keywords: Cissampelos owariensis extract, Toxicity, Gastric ulcer, Wound

INTRODUCTION

Peptic ulcer is a disease characterized by sores, inflammation or ulceration of the lining of the mucosal wall of the stomach or duodenum. Peptic ulcer, stomach ulcer or gastric ulcer, also known as peptic ulcer disease (PUD), is a distinct breach in the mucosa of the stomach as a result of the caustic effects of acid and pepsin in the lumen. Helicobacter pylori, a bacterium, is one of the most common causes of peptic ulcer. Ulcers can also be caused or worsened by drugs such as aspirin, ibuprofen, and other non-steroidal anti-inflammatory drugs (NSAIDs) [1]. Untreated, peptic ulcers have a widely variable natural history. Some heal spontaneously, but recur within months or sometimes within a year or two. Other reports have confirmed a 50 to 80 percent recurrence rate during the 6 to 12 months following initial ulcer healing, although relapses are not always symptomatic [2]. NSAIDs can cause damage to the gastro-duodenal mucosa via several mechanisms, including the topical irritant effect of these drugs on the epithelium, impairment of the barrier properties of the mucosa, suppression of gastric prostaglandin synthesis, reduction of gastric mucosal blood flow and interference with the repair of superficial injury [3]. The most common signs or symptoms of peptic ulcers are classically epigastric pain which strongly correlated to mealtimes, bloating and abdominal fullness, water brash (rush of saliva after an episode of regurgitation to dilute the acid in esophagus - although this is more associated with gastro-esophageal reflux disease), nausea, and copious vomiting, loss of appetite and weight loss, Hematemesis (vomiting of blood); this can occur due to bleeding directly from a gastric ulcer, or from damage to the esophagus from severe/continuing vomiting and melena (tarry, foul-smelling feces due to oxidized iron from hemoglobin). Rarely, an ulcer can lead to a gastric or duodenal perforation, which leads to acute peritonitis and stabbing pain requiring immediate surgery [4].

Younger patients with ulcer-like symptoms are often treated with antacids or H_2-receptor antagonists before esophagogastroduodenoscopy (EGD) is undertaken. Patients who are taking non-steroidal anti-inflammatory drugs (NSAIDs) may also be prescribed a prostaglandin analogue (Misoprostol) in order to help prevent peptic ulcers, which are a side-effect of the NSAIDs. When H. pylori infection is present, the most effective treatments are combinations of two antibiotics (e.g. Clarithromycin, Amoxicillin, Tetracycline, Metronidazole) and one proton pump inhibitor (PPI), sometimes together with a bismuth compound [5]. In complicated treatment-resistant cases, 3 antibiotics (e.g. amoxicillin + clarithromycin + metronidazole) may be used together with a PPI (proton pump inhibitor) and sometimes with bismuth compound. An effective first-line therapy for uncomplicated cases would be Amoxicillin + Metronidazole + Pantoprazole (a PPI) [6]. In the absence of H. pylori, long-term higher dose PPIs are often used. Ranitidine and famotidine, which are both H_2-antagonists, provide relief of peptic ulcers, heartburn, indigestion and excess stomach acid, and prevention of these symptoms associated with excessive consumption of food and drink.

Traditional medicine remains an important alternative for novel bioactive compounds derived from plants, especially those with ethnobotanical history in gastrointestinal and wound-related ailments. Plant remedies have been also reported for treating ulcers; examples of such plants include Ocimum tenuiflorum, Musa paradisiaca, Diospyros malabarica [7] among others. There are about 20 species of Cissampelos owariensis and originating from Sierra Leone east to Uganda, and south to Angola, Zambia and Mozambique as well as Nigeria. The plant is very variable in leaf form, hairiness and inflorescence size. It is a dioecious liana, with rhizome; stem and branchlets with spreading hairs. Throughout the distribution area of Cissampelos owariensis, people take an infusion of the bitter rhizome, leaves or stems to cure gastro-intestinal complaints such as diarrhoea, dysentery, colic, intestinal worms and digestive complaints. Preparations from the plant are also used to treat urogenital problems such as menstrual problems, venereal diseases, infertility, to induce contraction of the uterus to start labour or abortion and to expel the placenta [8]. In recent years, pharmacological studies have validated some of the folkloric uses of the plant. Omotosho et al [9] reported anti-ulcer activity of methanol leaf extract with doses of 100–500 mg/kg over 21 days; histological analysis revealed marked gastroprotective effects compared to controls. No study has evaluated the aqueous leaf extract of C. owariensis for its anti-ulcer and wound healing activities. Given that aqueous extracts resemble traditional infu-

sions used ethnomedically.

METHODOLOGY

Preparation of Extracts

Fresh samples of Cissampelos owariensis were collected at various locations in Ile-Ife, Osun State Nigeria, and the plant was identified in the Herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, with voucher number FPI 2309. The leaves (306 g) were dried in an oven at 60°C powdered and then soaked in distilled water for 48 h. The aqueous extract, a jelly-like, sticky product weighing 250g was obtained.

Acute toxicity test (Assessment of minimum lethal dose)

The method used is as described by Lorke [10]. This test was carried out in two phases. In phase one, three groups of 3 rats each were used. The rats in the three groups were administered orally with doses of 10, 100, and 1000 mg/kg of the extract respectively and monitored for 24 h observing for mortality. In phase 2 study, three groups of 3 rats were used. These were administered with doses of 1600, 2900, and 5000 mg/kg body weight of the extract respectively and monitored for 24 h observing for mortality. The phase 2 study was carried out based on the result of observation of mortality in phase 1 study. Using Lorke's method, the LD_{50} of the extract was calculated using the formula [11]:

$LD_{50} = \sqrt{(D_0 \times D_{100})}$ Where D_0 = Highest dose that gave no mortality, and D_{100} = Lowest dose that produced mortality.

Ethanol-induced gastric ulcer and effect of C. owariensis extract

Twenty-five rats divided into groups of 5 were fasted for 48 h [12]. Three groups were orally given doses of 50 mg, 100 mg and 200 mg/kg of the extract respectively, the negative control group received 10 ml/kg body weight of distilled water and the positive control group, ranitidine 4.4 mg/kg. The treatments were given at 16, 8 and 1.5 h before administering of 1 ml/kg of 50% ethanol to all the animals. One hour after ethanol administration, all rats were anaesthesized with ether, and the abdomen of each was cut open; the stomach rapidly removed, opened along their greater curvature, and gently rinsed with water to collect the gastric contents. Lesions in glandular part of the stomach were measured under illuminated magnifying lens. Lesions were counted, long lesions in the glandular part of the stomach were measured along their greater length. Petechial lesions were counted using 1 mm grid [13]. The sum of the total length of long ulcer and petechial lesions in each group of rat was divided by its number to calculate ulcer index (UI) (mm). The curative ratio was determined by the following equation [12].

Curative ratio = [(Control ulcer index) – (Test ulcer index)] / (Control ulcer index)

Indomethacin induced gastric ulceration

The modified method of Goel [14] was used for production of experimental gastric ulceration. After fasting the rats for 48 h they were given 1 ml/kg of Tween 80 orally. One hour later, they were treated with the respective doses of the test agents as described above and orally also one hour after with 50 mg /kg of indomethacin suspended in 2% Tween 80. Observations and recordings were then taken as described in the experiment above.

Cold-stress induced ulcer

After fasting the rats for 36 h with free access to water, the treatments commenced, the rats being grouped and treated as stated above. The animals were then put in cold-restraint in a refrigerator for 12 h [15] . Observations and recordings were then taken as above.

Determination of free acidity and Total acidity of the gastric contents

In all the three models, titratable acidity which is a total amount of acid in the solution as determined by titration using a standard titrant 0.01 M sodium hydroxide (NaOH) against the gastric juice was determined. The gastric content of the stomach was centrifuged at 500 rpm, 1 ml of the supernatant was diluted with 10 ml of distilled water and titrated against standardized 0.01 M NaOH using phenolphthalein as indicator. To this mixture, methyl orange indicator was added and the solution further titrated against NaOH, until solution changed to pink from yellow. This

volume is half of total acid, multiplying this by 2 gives total acidity of the gastric juice. When this is subtracted from the initial volume the volume of free acid is calculated.

$HCl + NaOH \rightarrow NaCl + H_2O$

$H_2X + NaOH \rightarrow NaHX + H_2O$ Phenolphthalein end-point

$NaHX + NaOH \rightarrow NaX + H_2O$ Methyl orange end-point

Methyl orange volume x 2 = total titratable acid

Total Titratable acid – methyl orange end-point volume = Free acid volume

Calculation of the Ulcer Index and % Protection

$UI = (UN + US + UP) \times 10^{-1}$

UI = Ulcer index

UN = Average of number of ulcer per animal

US = Average of severity score

UP = Percentage of Protection

$$UP = \frac{\text{(Mean ulcer index of control – Mean ulcer index of test)}}{\text{(Mean ulcer index of control)}} \times 100$$

Wound healing test with C. owariensis extract

The animals were shaved on the side to be inflicted using electric clipper, the right-hand side of the abdomen. The rats were inflicted using a hot-stainless steel carved into 8 mm^2. The area of the wound was outlined on the side of the animal with methylene-blue using a rectangular stencil, a full thickness stamping area 8 mm^2. Animals were closely observed for infection and those which showed signs of infection were discarded and the wound left opened. Animals were divided into five groups of 5 animal each, group 1 normal treated with Vaseline, group 2, 3 and 4 were treated with leaf extract of 50, 100 and 200 mg/kg, while group 5, was treated with carboxyl methylcellulose gel 100 mg/kg (intrasite gel). The treatment of the groups was done topically in all cases. The extract was applied daily for three weeks, and wound area measured on 0, 5, 10, 15, and 20 days respectively using transparent sheet and permanently marked to trace the reduced area. The day of falling off of the transparent sheet was considered the period of epithelization [16] .

Data analysis:

The data was analysed using One Way Analysis of Variance (ANOVA) followed by Duncan post hoc test, the significance was set at $p<0.05$. Values are expressed as mean ± standard error of mean (SEM).

RESULTS

Acute toxicity test

There was no mortality recorded after the 2 phases of the assay. According to Lorke [10], LD_{50} values above 5000 mg/kg is of no practical interest. The extract can then be considered non-toxic.

Ethanol-induced gastric ulceration in rats

The values recorded for % protection are 0, 90.00±0.5, 87.00±0.5, 91.00±0.5, 92.00±0.5, 0.00; gastric pH 2.4±2.0, 4.0±1.0, 4.2±1.0, 3.8±1.0, 4.4± 1.0, 2.4±1.0; and gastric juice volumes 9.00±2.0, 3.50±1.0, 3.60±1.0, 2.50±1.0, 4.10±1.0, 2.40±1.0 respectively for the negative control, ranitidine (300mg/kg), the extract doses of 50, 100 and 200mg/kg and blank. The extract thus acted dose-dependently and compared favourably with the reference drug. The results are presented in Table 1.

Table 1: Effects of C. owariensis leaf extract on ethanol-induced gastric ulcers in rats

Grp	Treatment (mg/kg)	Ulcer Index	% Protection	Gastric juice pH	Gastric juice (ml)
I	Negative control	14.40±1.5	0.00±1.5	2.40±2.0	9.00±2.0
II	Ranitidine (300)	1.50±0.5*	90.00±0.5	4.00±1.0††	3.50±1.0*
III	Extract (50)	1.90±0.5*	87.00±0.5	4.20±1.0††	3.60±1.0*
IV	Extract (1000)	1.30±0.5*	91.00±0.5	3.80±1.0††	2.50±1.0*
V	Extract (2000)	1.20±0.1*	92.00±0.5	4.40±1.0	4.10±1.0*
VI	Blank	0	0	2.4±1.0	2.40±1.0*

Key: * = Significantly ($p<0.05$) reduced compared to negative control but not different from each other. †† = significantly ($p<0.05$) increased compared to negative control but not different from each other.

Indomethacin-induced gastric ulceration in rats

The values obtained for % protection are 0, 81.20±0.5, 79.00±0.5, 85.00±0.5, 86.00±0.5, 0.00; gastric pH 2.4±2.0, 4.0±1.0, 3.9±1.0, 4.0±1.0, 2.5±1.0, and gastric juice volumes 9.0±2.0, 3.5±1.0, 3.6±1.0, 2.5±1.0, 4.10±1.0, 4.5±1.0, respectively for the negative control, ranitidine (300 mg/kg), the extract doses of 50, 100, and 200 mg/kg and blank. The extract thus acted dose-dependent and compared favourably with the reference drug. The results are presented in Table 2.

Table 2: Effects of C. owariensis leaf extract on Indomethacin-induced gastric ulcers in rats

Group	Treatment (mg/kg) (ml)	Ulcer Index	% Protection	Gastric juice pH	Gastric juice
I	Negative control	8.40±1.5	0	2.40±2.0	9.00±2.0
II	Ranitidine (300)	1.50±0.5*	89.60	4.00±1.0††	3.50±1.0*
III	Extract (50)	1.80±0.5*	85.00	4.20±1.0††	3.60±1.0*
IV	Extract (1000)	1.30±0.5*	78.00	4.20±1.0††	3.60±1.0*
V	Extract (2000)	I.20±0.1*	83.00	4.40±1.0††	4.10±1.0*
VI	Blank	0	0	2.50±1.0	4.50±1.0*

Key: * = Significantly ($p<0.05$) reduced compared to negative control but not different from each other. †† = significantly ($p<0.05$) increased compared to negative control but not different from each other.

Effects of C. owariensis extract on the stress-induced gastric ulceration in rats

The values obtained for % protection are 0, 77±1.30, 64±0.10, 67±0.10, 69±0.10, 0; gastric pH 2.10±1.0, 4.5±1.0, 4.6±1.0, 4.5±1.0, 2.1±1.0; and gastric juice volumes 8.7±1.0, 3.2±1.0, 3.4±1.0, 3.2±1.0, 3.4±1.0, respectively for negative, ranitidine (300 mg/kg), the extract doses of 50, 100, 200 mg/kg and blank. The extract thus acted dose-dependent and compared favourably with the reference drug. The results are presented in Table 3.

Table 3: Effects of C owariensis leaf extract on stress-induced gastric ulcers in rats

Group	Treatment (mg/kg)	Ulcer Index	% Protection	Gastric juice pH	Gastric juice (ml)
I	Negative control	6.40± 1.3	0	2.10±1.0	8.70±2.0
II	Ranitidine (300)	1.50±0.5*	77	4.50±1.0††	3.20±1.0*
III	Extract (50)	2.30±0.5*	64	3.50±1.0††	3.40±1.0*
IV	Extract (100)	2.10±0.5*	67	4.60±1.0††	3.30±1.0*
V	Extract (2000)	2.00±0.5*	69	4.50±1.0††	3.20±1.0*
VI	Blank	2.40±0.5	0	2.10±1.0	4.3±1.0*

Key: * = significantly ($p<0.05$) reduced compared to negative control but not different from each other. †† = significantly ($p<0.05$) increased compared to negative control but not different from each other.

Effects of C. owariensis extract on wound healing in rats

At Day 1, there was no significant ($p>0.05$) difference in the wound sizes of all treated rats relative to the control group (Group I, No treatment). Day 5: 50, 100 and 200 mg/kg extract induced 18%, 12% and 25% would healing respectively compared to 12% in rats with no treatment (Group I). Day 10: 50, 100 and 200 mg/kg extract achieved 64%, 67% and 77% wound contraction compared to 58% for negative control (no treatment) and 56% with modified sodium carboxymethyl cellulose - Intrasite Gel^{R}). Day 15: 50, 100 and 200 mg/kg extract produced higher wound healing effects of 83%, 82% and 92% relative to 79% in Group I (no treatment and 76% in rats treated with modified sodium carboxymethyl cellulose - Intrasite Gel^{R}). Again at Day 20, the extract at 50, 100 and 200 mg/kg was able to achieve greater wound healing effects of 92%, 95% and 96% but rats with no treatment had 89% while modified sodium carboxymethyl cellulose - Intrasite Gel^{R}) produced 84% wound healing within the same period (Table 4).

Table 4: Wound Healing Effect of the leaf extract of C. owariensis on rat's skin

	Wound area measurement (x 10 mm^2) ± SEM; % Wound healing in parenthesis				
Days of treatment	**Group 1 (No treatment)**	**Group II Extract (50 mg/kg)**	**Group III Extract (100 mg/kg)**	**Group IV Extract (200 mg/kg)**	**Group V (0.345g modified sodium carboxymethyl cellulose - Intrasite Gel®)**
Day 1	80.00±0.30(0%)	80.00±0.20(0%)	80.00±0.30(0%)	80.00±0.20 (0%)	80.00±0.20(0%)
Day 5	70.70±0.20(12%)	65.50±0.20(18%)	70.30±0.20(12%)	60.20±0.10(25%)	72.50±0.20 (9%)
Day 10	33.50±0.20(58%)	28.70±0.25(64%)	25.20±0.10(67%)	18.50±0.10(77%)	35.60±0.10(56%)
Day 15	17.00±0.20(79%)	13.40±0.10(83%)	14.30±0.10(82%)	07.00±0.20(91%)	19.30±0.20(76%)
Day 20	09.00±0.20(89%)	6.10±0.10(92%)	04.10±0.10(95%)	03.10±0.10(96%)	12.10±0.20(84%)

All the values obtained were statistically significant with one another and only the value for 100 mg/kg is not significant with the negative control in day 5. But for all the other days, all the values were significant with one another and both controls.

DISCUSSION

Peptic ulcer diseases is a serious gastrointestinal disorder characterized by abrassion, irritaion and inflammation of the lining of the mucosal wall of the stomach or duodenum which result from the caustic effects of acid and pepsin in the lumen coupled with a breakdown in mucosal defense [17]. Drug treatment of peptic ulcers is targeted at either counteracting aggressive factors such as acid, pepsin, active oxidants, platelet aggravating factor (PAF), leukotrienes, endothelins, bile or exogenous factors including NSAIDs, or stimulating the mucosa defenses such as mucus bicarbonate normal blood flow, prostaglandins (PG), and nitric oxide [18].

The complicated nature of the current drugs prescribed for peptic ulcer is contending both in terms of side-effects [19] and patients' compliance. When H. pylori infection is present, the most effective treatments are combinations of 2 antibiotics (e.g. Clarithromycin, Amoxicillin, Tetracycline, Metronidazole) and 1 proton pump inhibitor (PPI), sometimes together with a bismuth compound. aIn complicated, treatment-resistant cases, 3 antibiotics (e.g. amoxicillin + clarithromycin + metronidazole) may be used together with a PPI and sometimes with bismuth compound [20]. An effective first-line therapy for uncomplicated cases would be Amoxicillin + Metronidazole + Pantoprazole (a PPI). In the absence of H. pylori, long-term higher dose PPIs are often used. Treatment of H. pylori usually leads to clearing of infection, relief of symptoms and eventual healing of ulcers. Recurrence of infection can occur and retreatment may be required, if necessary, with other antibiotics. Perforated peptic

ulcer is a surgical emergency and requires surgical repair of the perforation. Most bleeding ulcers require endoscopy urgently to stop bleeding with cautery, injection, or clipping [21].

The use of herbs for the treatment of diseases has been practiced by different people of different cultures of the world for many centuries. These medicinal plants have proven useful either in the crude or in isolated compounds which include alkaloids, saponins, anthraquinones, glycosides, steroids, etc. [21].

Ethnomedical reports claim the use, among other uses, of the plant Cissampelos owariensis to treat ulcer and other gastrointestinal disorders. The main reasons for going into this research is to validate the claim of traditional practitioners in using the leaves for palliative treatment of peptic ulcer, which is regarded as wound or sore of the stomach. It's reported that, on taking the aqueous extract of the leaves of C. owariensis, the patient is relieved of the pain to the extent that he/she goes into sleep, for closely to 30 minutes after the ingestion.

This present work focus on the assessment of external wound healing and anti-inflammatory activities as the likely medicinal properties of the extract.

In ethanol-induced gastric ulcer, the percentage protection of the extract was highly comparable to the standard drug, Ranitidine. The results also showed that the stomach secretion reduces on administration of the extract, right from 50 mg/kg, which could be correlated to decrease in acidity of the stomach. These are the trend in the three models used, proving right the traditional use of the leaf extract in controlling peptic ulcers. Malairajan, et al. [22] similarly observed that the leaf extract of Polyalthia longifilia exhibited significant reduction in gastric volume, free acidity and ulcer index as well as ulcer inhibition and protection index in stress-induced ulcer.

When the pH of the stomach of the three models were compared, the pH content of the stomach became less acidic on administration of the standard drug and the leaf extract, showing the ability of the extract to control the acidity as well as the secretion of the stomach. Augmentation of the acidity in animal model was similarly demonstrated in previous studies [23, 24].

The mechanism of how the leaf extract achieved this was viewed when wound healing processes of the leaf extract was compared with that of "modified carboxymethyl cellulose (Intrasite gel^{R})" which is routinely used topically in clinical settings for wound healing due to its high capacity to absorb

wound exudates. The leaf extract had higher rate of wound healing at various doses (50, 100 and 200 mg/kg) compared to the Intrasite gel^{R} throughout the duration of the test. This could be due to the fact that the leaf extract either has higher capacity to absorb liquid, than the Intrasite gel^{R}, and could also complement some other healing factors not present in the Intrasite gel^{R}. The same mechanism of action could have been responsible for controlling the ulcer of the stomach.

In oedema formation, the percentage inhibition of the oedema by the leaf extract was significantly different from indomethacin. The rats treated with Intrasite gel^{R} as control group and C. owariensis-treated rats as experimental groups during the repair process were compared. In contrast, the progress of wound healing in the control and negative control groups appeared to be impaired. In all groups, wounds were covered by a dehydrated wound crust or scab at day one after stamping, and the scab was almost gone at day 14, revealing a thin residual skin defect. At day 21 after the stamping, the wounds fully healed in all C. owariensis-treated rats based on the macroscopic closure of the stamped interface and restoration of an epithelial cover. In most C. owariensis-untreated rats, the scab remained until 21 days, or there was a still gapping and red wound field with a scaly surface lacking an epidermal covering. It took over 3 weeks for these aberrant wounds to heal and to be covered with an epidermis. The wound diameter in the experimental group, which was treated with C. owariensis (50, 100 and 200 mg/kg), experienced a faster reduction than both the negative control and the reference drug. In addition, according to the results of measurement of the longitudinal or the perpendicular length of wounds, the wound sizes of negative control and control groups were significantly larger than that of experimental group at all days after the stamping.

However, the mechanism of action of the extract could be attributed to that of prostaglandins of E series, which provides protective cover for the gastric mucosa, thus with this the aggressive factors such as hydrochloric acid, pepsin and the bicarbonate secretion would be neutralized by the extract [25]. Mucus exists in the stomach as an insoluble gel layer adherent to the mucosal surface and as a soluble mucus mixed with the luminal juices. It is the former that is regarded as important in mucosal protection. A two-component system for mucosal protection consisting of an alkaline mucus cover overlying a rapidly regenerating epithelial cell layer. This concept was further developed considering that mucus is easily permeable to hydrogen ions, it must act as an unstirred layer, where acid diffusing in from the lumen could be neutralized by an alkaline mucosal bicarbonate secretion. Previous studies

[26, 27] have confirmed that this is indeed true and that there is a pH gradient demonstrable from a low pH on the luminal surface of the mucus to a near neutral pH on its mucosal surface. Whilst the mucus layer is permeable to small ions and solutes it is impermeable to pepsins (MW 35,000). Therefore, as long as there is a continuous layer of mucus covering the surface of the mucosa, there is no way in which pepsin can damage the surface epithelial layers. Mucosal defense can be compromised, however, because pepsin can break down the mucus. There must therefore be a balance between the secretion of new mucus and its erosion on the luminal surface.

Another aspect is the structure of the glycoprotein constituent of gastric mucus. The gastric mucus glycoprotein is a polymer of approximately four equal sized subunits joined by disulphide bonds. Each subunit consists of a glycosylated part (consisting of a protein core surrounded by carbohydrate side chains\'bottle-brush') and a non-glycosylated part. It is the latter that is attacked by proteolytic enzymes, breaking the molecule down into its subunits. The importance of this lies in the change that occurs in the physical properties of the glycoprotein during the breakdown. In its native polymeric form, the glycoprotein forms a water insoluble elastic gel of high viscosity [28]. As a gel it has important physical properties, including high adhesiveness which makes it adhere closely to the underlying mucosal surface, resistance to shear, ability to self-anneal (reform when cut) and capacity to flow over a surface to form a continuous layer. These properties, characteristic of the native glycoprotein, are greatly affected by breakdown of the glycoprotein into subunits. When broken down entirely to subunits the glycoprotein is no longer able to form a gel, but remained soluble in water and behaved as a viscous fluid. In patients with peptic ulcer disease the mucus covering the antral mucosa contains less 'native' glycoprotein, the greatest change being found in patients with gastric ulceration. This would suggest that the mucus is less effective as a gel covering of the mucosa, more liable to breakdown and may be less able to resist the passage of large molecules through its interstices.

The present study showed that the extract C. owariensis promotes healing either by absorbing the exudates from the wound, or better still by acting as anti-oxidant, mopping out oxidative species generated by the wound. This could be attributed to some of the phyto-chemicals in the leaf extract.

CONCLUSION

The findings from the research showed that C. owariensis possessed good gastro-protective prop-

erties that support its traditional use as a remedy for peptic ulcer. The gastro-protective activities of the aqueous extract were comparable to the standard drug (Ranitidine). This conclusion is attributed to wound healing activities of the extract as well as anti-inflammatory activity of the plant extract. Also, the leaf extract was more effective in external wound healing than anti-inflammatory activities in oedema reduction.

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