

Research Article

# Gastric Ulcer-Healing Properties of Diets Containing Seeds of *Buchholzia coriacea* Englar in Rats

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## Abstract

The effect of diets containing seeds of *Buchholzia coriacea* (wonderful kola) on the healing of experimental gastric ulceration was investigated in Wistar albino rats. *Buchholzia coriacea* seeds were collected, authenticated, dried, milled and then mixed with normal rat feed in dose-dependent proportions of 12.5%, 25% and 50% in relation to the rat feed. The animals were fed with the diets for six weeks. Acid secretory rate was estimated using the continuous stomach perfusion method. In another study, experimental gastric ulceration was induced by serosal application of 20% acetic acid to the wall of the rat stomach. Healing was assessed by scoring ulcers 10 days post-induction. Lipid peroxidation was estimated in the homogenized stomach samples. Histopathologic analysis of the stomach sections were also carried out. Results showed that the various doses of the *B. coriacea* preparation significantly reduced experimentally induced acetic acid gastric ulceration in pre-treated rats in a dose dependent fashion as shown in mean ulcer indices ( $p < 0.05$ ) observed ten days after ulceration, the healing being more effective with the 50% dose. Lipid peroxidation was significantly increased the stomach of all the rats with acetic acid induced ulcer when compared with the ulcerated (normal) rats ( $p < 0.05$ ). However, lipid peroxidation decreased dose dependently with increasing percentage of *Bulchorzia* incorporation into the diet. Evidence of restoration towards normal were observed in the analysis of the prepared histologic slides. The results of this study suggest that *Buchholzia coriacea* seeds promote the healing of experimental gastric ulcers in rat.

Keywords: *Bulchorzia coriacea*, wonderful kola, ulcer, stomach, inflammation

## INTRODUCTION

The gastrointestinal tract is constantly exposed to several aggressive and protective substances which may be either exogenous or endogenous in origin. Among the exogenous substances are the foods we take in, drugs and many substances from the environment (Wallace, 2008; Olaleye *et al*, 2010). This is aided by the natural aggressors such as hydrochloric acid, gastrin and pepsin (secreted by the gastric glands into the mucosal lumen) as well as *Helicobacter pylori*. Under physiological conditions however, the stomach is protected from these substances by factors such as the bicarbonate barrier, the adherent mucous lining as well as a constantly renewing glandular columnar epithelium (Karam and Leblond, 1993; Karam *et al*, 2003). Gastric mucosal damage occurs as a result of imbalance between the aggressive factors and defensive factors.

Peptic Ulcer Disease (PUD, a form of gastric or duodenal mucosal damage) was thought to be caused mainly by *Helicobacter pylori* infection. However, it is now known to be more associated with the use of acetylsalicylic acid and nonsteroidal anti-inflammatory drugs (Laine, 1996; Yuan *et al*, 2006; Remakrishan and Salinas, 2007). PUD affects millions of individuals worldwide and is considered one of the most important common diseases in the world. Sung *et al*, (2009) put the annual incidence rates of PUD as 0.10–0.19% for physician diagnosed PUD and 0.03–0.17% when based on hospitalization data and concluded that disease remains a

common condition despite reported decreases in incidence and prevalence.

Based on its etiology, antiulcer agents are directed at either increasing the activity of the mucosal defensive or decreasing those of the aggressive factors, or both. Although there are drugs currently used in the management of PUD, a number of reported side effects and the high rate of relapse make the search for better products imperative, hence the need for more research into medicinal plants with potential gastroprotective activities.

*Buchholzia coriacea* commonly called musk tree or wonder cola and belonging to the family capparaceae, is found widely distributed in many African countries such as Nigeria, Ivory Coast, Gabon, Sierra Leone, Ghana, Liberia and Cameroon. In Nigeria, it is locally called Uke by the Ibo of South East (Meregini, 2005), Obi-ata by the Yoruba of the South West and Ovu by the Bini tribe (Keay and Onoche 1964). The plant's fruit, which and resembles avocado pear, is yellowish when ripe with a yellow flesh containing a few large, blackish seeds about 1 inch long. The fruit is edible and taste peppery (Koudogbo *et al.*, 1972). A number of folkloric uses of the plant are available in literature. For example, in Ghana, fresh bark of the plants is used for ear ache (Irvine, 1961) while in Cameroon, the hot water extract of the stern bark is used as an aphrodisiac (Mbi, 1985). In Nigeria, the seed, when mixed with palm oil is employed in treatment of malaria (Adjanohoun *et al*, 1996) while in Ivory coast, the decoction of the bark is used to relieve headache, sinusitis and eye infection (Burkill, 1985).

Scientific insight into the medicinal properties of *Buchholzia coriacea* shows that the stem bark and seeds of the plant possess potent antimicrobial activities (Ajayeoba *et al*, 2003; Ezekiel and Onyeoziri, 2009; Oluseyi and Onyeoziri, 2009). Nweze *et al* (2008) also reported the potency of the stem and bark extract as an anthelmintic. Nwaehujor *et al* (2012) reported its antidiabetic activity). The anti-inflammatory and analgesic properties of the plant have also been reported (Ezeigbo and Madubuike, 2011; Olaleye *et al*, 2012). In a recent study, *Bulchorzia coriacea* was reported to protect against indomethacin-induced ulceration (Enechi and Nwodo, 2014). In the present study, the effect of the plant on acetic acid-induced ulcer is investigated.

## MATERIALS AND METHODS

### Plant material

The seeds of *Buchholzia coriacea* were obtained from Bodija market, Ibadan, Nigeria and identified by Prof. Egunyomi of the Department of Botany, University of Ibadan. A voucher specimen is available in the herbarium of the same institution.

### Preparation of *B. coriacea*/rat diet mixture

The seeds were initially soaked in water for five days. Over this period, the covering of the seeds were peeled off after the kernel had softened. The seeds were later chopped into smaller pieces and completely dried in the sun for another four days and then milled completely into fine powder. The standard commercial rat diet was similarly milled. The two were then mixed in such a way as to contain 12.5%, 25% and 50% wonder cola for groups B, C and D, respectively. The prepared mixtures were thereafter pelletized by a local pelletizer.

### Animals

Male albino rats of the Wistar strain (60–90 g) were used. The control group (A) were fed on standard rat diet (Ladokun feeds, Ibadan; Nigeria) while the other groups (B, C and D) were fed on standard diets containing 25%, 50% and 75% by weight of *B. coriacea* respectively for five weeks. Tap water was given *ad libitum*. A separate group of six rats were given the normal laboratory rat chow but were not taken through the ulceration process. These served as normal control.

### Gastric acid secretion study

The gastric acid secretion was measured using the continuous perfusion method of Ghosh and Schild (1958), modified by Amure and Ginsburg (1964). Rats anaesthetized with a mixture of 4:3 ketamine HCl- xylazine were surgically prepared for *in situ* stomach perfusion. A tracheal cannula was inserted via an incision on the neck to ensure normal breathing throughout the course of the experiment. An abdominal incision through the *linea alba* was made to expose the stomach and a semi-transection made at the junction of the pylorus with the duodenum. A pyloric cannula was inserted and tied to collect gastric contents. An orogastric cannula was inserted for perfusion of pre-warmed (at temperature 37°C) 0.9% normal saline (pH 7.00) at a rate of 1ml/minute using a perfusion pump. Gastric acid was collected via the pyloric cannula at 10 minutes intervals. In order to determine acidity, 10ml of the stomach perfusate was titrated against 0.01M sodium hydroxide (NaOH) solution with phenolphthalein as indicator. Titrable acidity was expressed in mmol/10mins after calculation in each sample. After steady basal effluent

collection was attained, histamine was administered via a femoral cannula vein for the stimulated acid secretory response.

### Induction of ulcer using Acetic acid

Gastric ulcers were induced using acetic acid following the type 2 serosal application method described by Tsukimi and Okabe (1994). After 24 hours of fasting, the rat's stomach was exposed under light ether anaesthesia. A laparotomy was then performed through a midline epigastric incision and the stomach was exposed. Using a cotton ball placed at the tip of a local cylindrical ball point pen casing (biro) Glacial acetic acid (0.05 mL) was applied topically onto the serosal surface of the stomach for one minute, after which the area was rinsed with normal saline to prevent possible damage to the surrounding tissues close to the point of application. The stomach was carefully placed back and the abdomen was sutured, and rats allowed to recover. All the animals were fed normally throughout the experiment. All rats were sacrificed on the 10th day post ulcer induction. The stomachs were removed and cut open along the greater curvature, rinsed with normal saline and placed on a white tile. Gastric lesions were evaluated by examination of the inner gastric surface with a dissecting magnifying glass. All the animals were subjected to a gross autopsy according to WHO (1993) and OECD (1998) standards. The lesions examined independently by two observers. The total area of ulcer as well as the total mucosal surfaces were measured. The ulcer index was determined for each rat according to Ganguly (1969) as follows:

$$\text{Ulcer Index} = 10/X$$

where X = Total mucosal area/Total ulcerated area.

### Histology and histomorphometry

Stomach samples were fixed in 10% neutral buffered formalin, embedded in the paraffin wax, sectioned at 5 µm, stained with hematoxylin and eosin and then examined by the light microscopy for any inflammatory/other pathologic changes including infiltration of cells, necrosis or damage to nucleus or tissue structures. For histomorphometric analysis, a graticule with 1-100µm calibration was attached to the microscope and using the histological slides, ulcer depth and width were measured and recorded.

### Lipid peroxidation

Assessment of lipid peroxidation was carried out following the procedure described by Varshney and Kale (1990), based on the reaction of malondialdehyde (MDA) produced during lipid peroxidation with thiobarbituric acid (TBA) forming a pink coloured MDA-TBA adduct that absorbs strongly at 532nm. Animals were sacrificed after the experimental period, and the stomach of each rat was dissected. Stomach from each animal was cut open along the greater curvature, rinsed with normal saline, the mucosa of the ulcerated area was scraped and homogenised in phosphate buffer (tissue to buffer ratio - 1:3), and 0.2ml of test sample was added to 0.8ml of Tris-KCl. The solution was quenched with 0.25ml of TCA. 0.25ml of TBA was then added and the solution was then incubated for 45minutes at 80°C. A pink coloured reaction mixture was formed. The reaction mixture was then centrifuged at 1400 rpm for 15 minutes. The absorbance of the supernatant was read at 532 nm. MDA was calculated for each sample as described in a previous report by Adeniyi *et al* (2014).

**Statistical analysis**

All results were expressed as mean ± S.E.M. and the difference between groups were determined by ANOVA at p<0.05

**RESULTS**

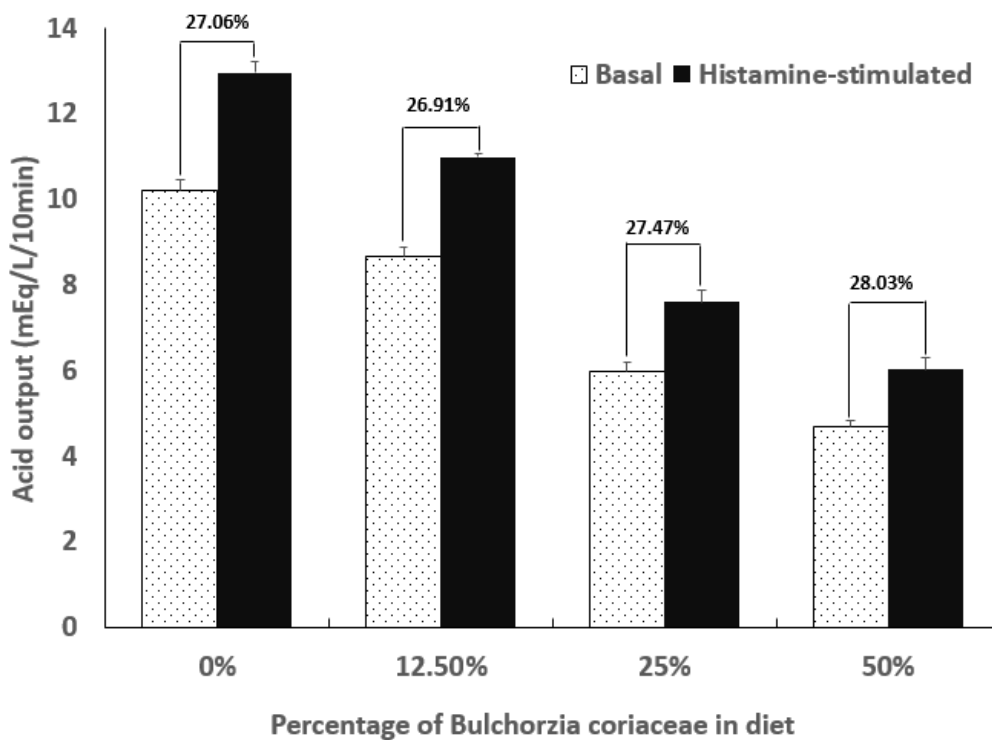
**Effect of Diets Containing the Seeds of *Buchholzia Coriacea* on gastric acid secretion**

Basal acid secretion from the stomach of the rats placed on standard rat diet was 10.2±0.24mEq/L. Incorporation of the seeds of *Bulchorzia coriacea* into the rat feeds produced significant (p<0.05) dose-dependent decreases in basal gastric acid secretory rate. Although histamine significantly stimulated acid output in each animal group, there were no significant differences in the percentage increases over the basal values (Fig. 1).

**Effect of Diets Containing the Seeds of *Buchholzia Coriacea* on gastric ulcer scores**

In all the animals used, acetic acid produced visible gastric ulcers. In particular, the acetic acid model results in ulcers of consistent size and severity at incidence of 100%. The ulcers resemble human ulcers in terms of both pathological features and healing mechanisms.

Table 1 shows the effect of diets containing seeds of wonder cola on ulceration in rat stomach 10 days post ulcer induction. Ulcer index in the rats fed with the standard control diet was 0.35 ± 0.01. In the rats with 12.5%, 25% and 50% *Bulchorzia* diet, ulcer indexes were 0.246±0.02, 0.105±0.01 and 0.0825±0.01 respectively. These values were significantly lower than the control values. No visible ulcers were seen in the un ulcerated normal rats.



**Fig. 1**

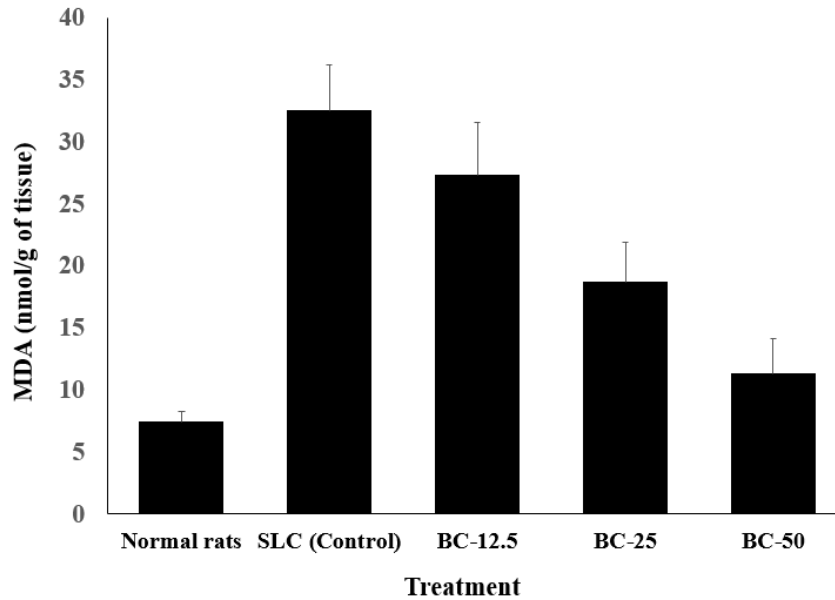
Basal and histamine stimulated from the stomach of rats fed diets containing 0, 12.5 and 50% *Bulchorzia coriacea*. Each bar represents the Mean ± SEM of six rats per group.

**Table 1:**

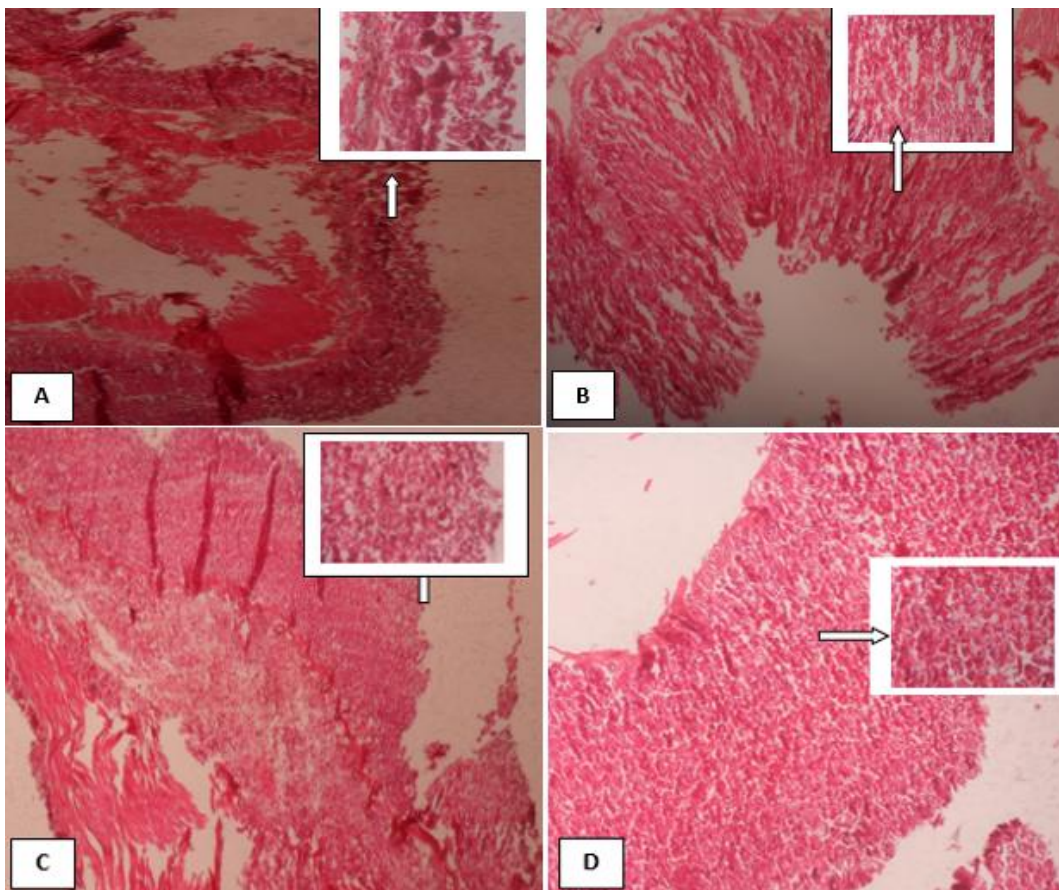
Effect of Diets Containing the Seeds of *Buchholzia Coriacea* on Mean Ulcer scores six and nine days post-acetic acid induced gastric ulceration

Diet	Ulcer parameters on Day 10		
	Ulcer index	Ulcer width	Ulcer depth
Normal rats (no ulcer)	Nil	Nil	Nil
100% SLC (control)	0.35 ± 0.01	71.4±2.3	16.5 ± 0.4
12.5% B.C.S + 87.5% SLC	0.246±0.02	61.5±3.2*	10.3 ± 0.2
25% B.C.S + 75% SLC	0.105±0.01	40.3 ±5.3 *	6.2 ± 0.4
50% B.C.S + 50% SLC	0.0825±0.01	33.2±4.7*	5.3 ± 0.2

\* Significant healing when compared to control at P≤0.05. Values are Mean ± SEM.



**Fig. 2.** Lipid peroxidation in gastric tissue 10 days after acetic acid induced ulceration in rats given standard rat diet (BC 0%) and diets containing 12.5% (BC-12.5%), 25% (BC-25%) and 50% ((BC-50%) *Bulchorzia coriacea*.



**Plate 1**  
 Longitudinal sections of the layers of the stomach wall at low magnification (X100) and higher magnification (X400) of specific areas in boxes, showing different stages of healing 10 days after acetic acid-induced ulceration. (A) Control group with standard diet. The cells of the surface epithelium and the lamina propria of the stomach mucosa are not packed together showing distortion especially in the surface epithelium (B) Animals fed 12.5% *Bulchorzia* diet. The fundic part of the stomach, showing the mucosa majorly with intracellular canaliculi clearly present, moderate erosion within the mucosal layer and also the submucosal layer. The gastric pits are also visible. (C) Animals fed 25.0% *Bulchorzia* diet The 4 layers (mucosa, muscularis mucosae, submucosa and the muscularis externa) of the stomach wall were shown and appear normal towards the left. At higher magnification parietal cells were not clearly visible, dark stained cells suggest inflammatory cells infiltration. Arrow base shows an erosion of the gastric mucosa from the surface epithelium down to the level just above the muscularis mucosae. (D). Animals fed 50% *Bulchorzia* diet. Slide shows the mucosa layer that appears normal. Parietal cells are clearly visible, which suggest stomach acid secretion, with inflammatory infiltrate appearance at higher magnification (reddish cells with faintly stained nuclei)

## Histology

Plate 1 shows the results of the histological examination of the gastric tissues of the normal and ulcerated rats exposed to different levels of *Bulchorzia coriaceae* diet. The plates shows evidence of erosion of the mucosal surface in all slides, confirming the acetic acid challenge to the stomach. However, the closest of the slides to a normal gastric mucosal was observed in the rats with diets containing 50% *Bulchorzia coriaceae* diet (Plate 1D) with the mucosal surface appearing normal, clearly visible parietal cells although evidence of infiltration with inflammatory cells is still evident in the higher magnification.

## DISCUSSION

In the present study, the pro-healing effect the seeds of *Buchholzia coriacea* (BC) on acetic acid induced ulceration was investigated in rats. *Buchholzia coriacea* was incorporated into the standard laboratory diets of rats in proportions of 12.5, 25 and 50%. The results indicate that incorporation of B.C up to 50% increased the rate of gastric ulcer healing in the animals used as evidenced by the reduced sizes of ulcerated areas areas of the stomach 10 days after acetic acid induced ulceration in the rats fed B.C diets when compared with the control rats fed with standars laboratory rat chow.

The acetic acid model of experimental gastric ulceration, developed by Takagi et al (1969) has been a useful tool in assessing the efficacy of anti-ulcer and ulcer-healing effects of potential drugs. This is because this model mimics clinical ulcers in terms of location, chronicity and severity (Okabe et al, 1971; Okabe and Pfeiffer, 1972; Okabe and Amagase, 2005). Furthermore, the model is regarded as the most reliable to study gastric ulcer healing processes as it easily and reliably produces round, deep ulcers in the stomach and duodenum of several species such as mice, rats, Mongolian gerbils, guinea pigs, cats, dogs, miniature pigs, and monkeys.

Reduction in gastric acid secretion has been demonstrated as a valuable tool in ulcer healing process. In the first study, basal gastric acid secretion was significantly reduced by wonder kola incorporation into the rat diet, the reduction increasing with the extent of incorporation. It is well known that one of the potent causative factors of gastric ulcer is excessive gastric acid (Fornai *et al*, 2011). In order to prevent gastric ulcer, its production must be endogenously regulated. The results of this study agrees with those reported earlier by Nwodo and Elechi (2014) in which ethanol extract of *Buchholzia coriacea* was reported to decrease histamine induced gastric acid secretion and also blocked histamine induced contractile responses in isolated guinea-pig ileum

The seeds of *Buchholzia coriacea* have been shown to contain phytochemicals which promote gastroprotection and ulcer healing activities, especially flavonoids (Onyekaba et al, 2011; Enechi and Nwodo, 2014). Many flavonoid-containing plants with seeds in the kola group have been shown to possess ant-ulcer activities. Examples include *Garcinia kola* (Ibironke et al, 1997; Olaleye 2005; Olaleye and Farombi, 2006; *Garcinia cambogina* (Mahenrea *et al*, 2012) and *Centella asiatica* (Cheng et al, 2000; Guo et al, 2004). Flavonoids display several pharmacological properties in the gastroprotective area, acting as anti-secretory, cytoprotective and antioxidant agents. Besides their action as gastroprotectives, flavonoids also act in healing of gastric

ulcers and additionally these polyphenolic compounds can be new alternatives for suppression or modulation of peptic ulcers associated with *H. pylori*. The flavonoid content of *Bulchorzia coriaceae* may account for its action as potent ulcer healing candidate.

The role of active oxygen species and lipid peroxidation in the pathogenesis of duodenal ulcers is well reported. It has been shown by several authors that the concentration of lipid peroxides in the gastric mucosa increase in the presence of ulcer. For healing to be accomplished therefore, therapeutic agents should also be able to reduce lipid peroxidation towards the normal values. In this study, B.C diets produced significant and a dose-dependent inhibition of lipid peroxidation. Lipid peroxidation is mediated by reactive oxygen species, which are generated in the cell during reduction of molecular oxygen (Yoshikawa et al, 1993).

In conclusion, the results of this study suggests that seeds of *Bulchorzia coriaceae* possess potent ulcer-healing properties. Further studies on the exact mechanism and active principles responsible for this action are necessary in order to throw light on the therapeutic potential of this plant.

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