INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES

(p-ISSN: 2348-5213: e-ISSN: 2348-5221)

www.ijcrcps.com

DOI: 10.22192/ijcrcps Coden: IJCROO(USA) Volume 8, Issue 5 - 2021

Research Article

DOI: http://dx.doi.org/10.22192/ijcrcps.2021.08.05.002

Gastroprotective Effect of the Aqueous Extract of *Borreria stachydea* Leaves

APPAH Joseph[1], AGATEMOR Uzuazokaro Mark- Maria[2], ELAH Sarah Onyeche[3], MOMOH Theophilus Boniface[4*]

[1]Department of Biological Sciences, Faculty of Sciences, Nigeria Defence Academy, Kaduna State, Nigeria

[2]Department of Pharmacology, College of Health Science, Novena University, Ogume, Delta State, Nigeria

[3]Department of Biochemistry, Faculty of Biological Sciences, University of Nigeria, Nsukka, Enugu State, Nigeria

[4]Department of Plant Science and Biotechnology, Faculty of Natural Sciences, Kogi State University, Anyigba, Kogi State, Nigeria

*Corresponding author: MOMOH Theophilus Boniface

E-mail: *momohtheophilus@rocketmail.com*

Abstract

In this study, we investigated the gastroprotective activity of the aqueous extract of *Borreria stachydea* Leaves (AEBS). Acute toxicity study was carried out on the extract using Lorke's method while the anti-ulcer activity of the extract was investigated using indomethacin, ethanol and histamine ulcer models. Results of acute toxicity showed that AEBS produced no signs of toxicity or mortality up to a dose of 5000 mg/kg. Results also showed that AEBS (at 200 and 400 mg/kg) evoked a dose-dependent gastroprotective activity as demonstrated by significant ($P< 0.05$) inhibition of the formation of ulcers induced by indomethacin, ethanol and histamine. It was concluded that the aqueous extract of *Borreria stachydea* leaves possess gastroprotective effect. Thus, it could be used as an alternative to orthodox anti- ulcer drugs or used as an add-on therapy.

Keywords: Gastroprotective, Aqueous, *Borreria stachydea*, Indomethacin, Ethanol, Histamine

Introduction

Peptic ulcer is a term used to describe a group of ulcerative disorders that occur in areas of the upper gastrointestinal tract. It represents a chronic health problem. Peptic ulcers develop due to excessive secretion of acid and pepsin, a diminished mucosal defence or a combination of these 2 abnormalities. Predisposing factors of gastric ulcer include *Helicobacter pylori* infection, Nonsteroidal anti-inflammatory drugs, cigarette smoking, stress, alcohol and chronic pancreatitis (Tariq *et al.*, 1986). Symptoms of peptic ulcer disease include epigastric pain of a burning or gnawing nature (postprandial pain and pain relieved by food or antacids), nausea, vomiting, belching and bloating.

Although a large number of anti-ulcer drugs are available, none produces complete remission of ulcers, with reduced side effects and without compromising the patient's wellbeing, which usually results in chronic use of these drugs. There is, therefore, the need to develop safe, effective and affordable alternatives in the symptomatic management of ulcers.

Borreria stachydea (DC) commonly known in English language as ant's wheat is an erect, hairy and weedy herb, about 30-60 cm high with mauve flowers. It belongs to Rubiaceae family (Dalziel, 1937). Through personal communication, we found out that this plant is used in traditional medicine to treat venereal diseases, inflammations, and gonorrhea. Borreria species possess wide variety of medicinal properties; however a few species have been screened for confirmation of their biological activities. Hence, this study investigated the gastroprotective potentials of the plant using different experimental ulcer models.

Materials and Methods

Materials

Chemicals and drugs

All chemicals used in this study were of analytical grade and were purchased from Sigma Chemical Co. Ltd (USA). The drugs used were purchased from a local pharmacy shop.

Animals

Male adult wistar rats weighing 120–180g were used for this study. They were kept in stainless steel cages under standard laboratory conditions. They were maintained on clean water and standard rodent feed.

Methods

Plant Collection and Identification

The leaves of *Borreria stachydea* were collected from a natural habitat in Aloma, Ofu Local Government Area of Kogi State, Nigeria. The plant was identified at the Department of Plant Science and Biotechnology, Kogi State University, Anyigba by Mr. Momoh.

Preparation of Extract

The leaves of the plant were shade- dried for five (5) days and pulverized using a laboratory mortar and pestle. 2000 g of the pulverized leaves was cold-macerated in distilled water for 48 h. The resulting mixture was filtered using Whatmann filter paper (Size No1) and the extract was concentrated using a water bath (60^{oc}). The extract will henceforth be reffered to as 'AEBS'.

Acute Toxicity Study

The oral median lethal dose (LD_{50}) of the extract was determined in rats according to the method of Lorke (1983).

Evaluation of antiulcer activity: Indomethacin-induced ulceration

Male adult albino rats were used for the experiment. They were randomly divided into 4 groups of 5 rats each. Food was withdrawn 24 h and water 2 h before the commencement of the experiment (Alphin and Ward, 1967). Group 1 (control) received only indomethacin (60 mg/kg p.o. dissolved in 5% Na_2CO_3); Groups 2 and 3 were pretreated with 200 and 400 mg/ kg p.o of AEBS respectively. Group 4 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80). One hour later, groups 2 and 3 were administered indomethacin. Four hours after indomethacin administration, animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al.*, 1996). Ulcer index (UI) and preventive ratio (PR) of each of the groups pretreated with extract was calculated using standard methods (Zaidi and Mukerji, 1985; Nwafor *et al.*, 2000).)

Ethanol-induced gastric ulceration

The procedure was similar to that used in indomethacin induced ulceration. The rats randomly assigned into 4 groups of 5 rats each based on their body weight. Food was withdrawn 24 h and water 2 h before the commencement of experiment (Alphin and Ward, 1967). Group 1 (control) received only ethanol (2.5 ml/kg p.o), Groups 2 and 3 were pretreated with 200 and 400 mg/ kg p.o of AEBS respectively, Group 4 received propranolol (40 mg/kg p.o. dissolved in distilled water). One hour later, groups 2- 4 were administered ethanol. Four hours after ethanol administration, animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al.*, 2000).

Histamine-induced gastric ulceration

Rats were randomized into 4 groups of 5 rats each. Food was withdrawn 24 h and water 2h before the commencement of experiment (Alphin and Ward, 1967). Group 1 (control) received only histamine acid phosphate (100mg/kg i.p. dissolved in distilled water) (Maity *et al.*, 1995); Groups 2 and 3 were pretreated with 200 and 400 mg/ kg p.o of AEBS respectively; Group 4 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80), 1 hour prior to histamine administration. One hour later, groups 2-4 were administered with histamine acid phosphate (100mg/kg, i.p). 18 hours after histamine administration, animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al.*, 1996). Ulcer indexes (UI) and preventive ratio (PR) of each of the groups pretreated with the extract were calculated using standard methods (Zaidi and Mukerji, 1985; Nwafor *et al.*, 2000).

Statistical Analysis

Statistical analysis was carried out using SPSS version 20.0. All the data were expressed as mean ± SEM and the statistical differences between the means were determined by one way analysis of variance (ANOVA) which was followed by Turkey-Kramer multiple comparison and difference between means at $P > 0.05$ were considered significant.

Results

Acute Toxicity Study

The results of acute toxicity studies showed no sign of toxicity or mortality up to a dose of 5000 mg/kg of the AEBS (Table 1). The oral LD_{50} of the extract was then taken to be > 5000 mg/kg.

Table 1: Observed Effects of Aqueous Extract of *Borreria stachydea* Leaves (AEBS) on Rats

Phase	Treatment (mg/kg)	D/T
I	AEBS (10)	0/3
	AEBS (100)	0/3
	AEBS (1000)	0/3
II	AEBS (1600)	0/1
	AEBS (2900)	0/1
	AEBS (5000)	0/1

Key: D= Number of deaths, T= Number of treated animals

Indomethacin-induced Gastric Ulceration

Table 2 shows that indomethacin induced gastric ulcer in all experimental groups. AEBS at 200 and 400 mg/kg produced significant reduction ($p < 0.05$) in the gastric erosions formed compared to control as evident in the reduction of ulcer indices. AEBS (400 mg/kg) produced 92. 10% inhibition of ulcer, which was comparable to that of cimetidine, the anti-ulcer drug used, which had 94.69% inhibition.

Table 2 Effect of Aqueous Extract of *Borreria stachydea* Leaves (AEBS) on Indomethacin-induced Gastric Ulcer

Treatment (mg/kg)	Ulcer Index	% Ulcer Inhibition
Control (Indomethacin 60 mg/kg)	15.82±1.11	-
AEBS (200 mg/kg)	5.12±1.01*	67.64
AEBS (400 mg/kg)	1.25±0.88*	92.10
Cimetidine(100 mg/kg)	0.84±0.23*	94.69

Data were expressed as mean ± SEM. significant at *P < 0.05 when compared to control n = 5.

Ethanol- induced Gastric Ulceration

As shown in Table 3, AEBS at 200 and 400 mg/kg produced significant reduction ($p < 0.05$) in ethanol- induced gastric ulcer compared to control. This was evident in the reduction of ulcer indices. AEBS (400 mg/kg) produced 79.92 % inhibition of ulcer which was less than that of propranolol (90.89%).

Table 3 Effect of Aqueous Extract of *Borreria stachydea* Leaves (AEBS) on Ethanol- induced Gastric Ulcer

Treatment (mg/kg)	Ulcer Index	% Ulcer Inhibition
Control (Ethanol)	10.21±2.23	-
AEBS (200 mg/kg)	5.32±1.08*	47.89
AEBS (400 mg/kg)	2.05±0.89*	79.92
Propranolol (40 mg/kg)	0.93±0.19*	90.89

Data were expressed as mean ± SEM. significant at *P < 0.05 when compared to control n = 5.

Histamine– induced Ulceration

Table 4 shows that Histamine induced gastric ulcer in all experimental groups. AEBS dose-dependently produced significant reduction ($p < 0.05$) in the gastric erosions formed compared to control as evident in the reduction in the ulcer indices. At 400 mg/kg AEBS produced 82.72% inhibition of ulcer, which was less than that of cimetidine, the standard anti-ulcer drug used, which produced 92.93% inhibition.

Table 4 Effect of Aqueous Extract of *Borreria stachydea* Leaves (AEBS) on Histamine-induced Gastric Ulcer

Treatment (mg/kg)	Ulcer Index	% Ulcer Inhibition
Control (Histamine 100 mg/kg)	12.44±2.24	-
AEBS (200 mg/kg)	4.21±1.23*	66.16
AEBS (400 mg/kg)	2.15±0.92*	82.72
Cimetidine(100 mg/kg)	0.88±0.06*	92.93

Data were expressed as mean ± SEM. significant at *P < 0.05 when compared to control n = 5.

Discussion

The acute toxicity studies carried out on the extract revealed no mortality or physical changes in skin and fur, eyes and mucus membrane, respiratory rate, circulatory signs, autonomic and central nervous system effects up to a dose of 5000 mg/kg. The oral LD_{50} of the extract was then taken to be > 5000 mg/kg for. Judging from this study, the extract of *Borreria stachydea* could be considered to be relatively safe.

Indomethacin is known to cause ulcer especially in an empty stomach (Bhargava *et al*., 1973) and mostly on the glandular (mucosal) part of the stomach (Evbuonwa and Bolarinwa, 1990; Nwafor *et al*., 1996) by inhibiting prostaglandin synthetase through the cycloxygenase pathway (Rainsford, 1987). Prostaglandins function to protect the stomach from injury by stimulating the secretion of bicarbonate and mucus, maintaining mucosal blood flow and regulating mucosal turn over and repair (Hayllar and Bjarnason, 1995; Hiruma-Lima *et al*., 2006). This suppression of prostaglandins synthesis by indomethacin results in increased susceptibility of the stomach to mucosal injury and gastro-duodenal ulceration. In this study, the aqueous leaf extract of *Borreria stachydea* at doses of 200 and 400 mg/kg significantly inhibited the ulcer- induced in rats by indomethacin. This observation suggests a possible mobilization of prostaglandin in the anti-ulcer effect of the extract.

Ethanol via the release of superoxide anion and hydroperoxy during metabolism has been found to be involved in the mechanism of acute and chronic ulceration in the gastric mucosa (Pihan *et al*., 1987). In our study, the ulcer-inducing effect of ethanol was observed as seen in the control group. Treatment with 200 and 400 mg/ kg of the extract significantly produced ulcer inhibition. This observation may be due to cytoprotective effect of the extract via antioxidant effects. Ethanol is also reported to cause gastric mucosal damage by stimulating the formation of leukotriene C4 (LTC4) (Whittle *et al*.,1985).The gastroprotective effect of the extract may in part be due to the suppression of lipoxygenase activity (Nwafor *et al*.,1996).

Histamine-induced ulceration is known to be mediated by enhanced gastric acid secretion as well as by vasospastic action of histamine (Cho and Pfeiffer, 1981). The inhibition of ulcer due to histamine by the extract at 200 and 400 mg/kg may be due to its suppression of histamine-induced vasospastic effect and gastric secretion.

Antioxidants such as quercetin have been reported to prevent gastric mucosal lesions in various experimental models (Di Carlo *et al*., 1999; Zayachkivska, 2005) by increasing the amount of neutral glycoproteins (Di Carlo *et al*., 1999). Antioxidants such as flavonoids have been reported to 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. Free radical scavenging ability of flavonoids has been reported to protect the gastrointestinal tract from ulcerative and erosion lesion (Borrelli and Izzo, 2000). Saponins, especially triterpenes type have been implicated in antiulcer activity mediated by formation of protective mucus on the gastric mucosa and also protect the mucosa from acid effects by selectively inhibiting PGF2α (Agwu and Okunji, 1986; Lewis and Hanson, 1991). These phytochemicals therefore must have been responsible for the anti-ulcer potentials of the extract. Conclusively, the anti- ulcer effect of the aqueous extract of *Borreria stachydea* leaves has been proven in different experimental models of ulcer. Hence, it could be used as an alternative to the orthodox anti- ulcer drugs or as an add-on therapy.

References

Agwu, C. N., Okunji, C. O. 1986. Gastrointestinal studies of *Pyrenacantha staudtii* leaf extracts. *Journal of Ethnopharmacology* 15: 45 – 55.

Alphin, R. S. and Ward, J. W. 1967. Action of hexopyrronium bromide on gastric secretion in dogs and on gastric secretion and ulceration in rats. *Archives Internationales de Pharmacodynamie et de Therapie;* 6(15) 10-16

Bhargava, K. P., Gupta, M. B., Tangri, K. K. 1973. Mechanism of ulcerogenic activity of indomethacin and oxyphenbutazone. *European Journal of Pharmacology* 22: 191 – 195.

Bhargava, K. P., Gupta, M. B., Tangri, K. K. 1973. Mechanism of ulcerogenic activity of indomethacin and oxyphenbutazone. *European Journal of Pharmacology* 22: 191 – 195.

Borrelli, F. and Izzo, A. A. 2000. The plant kingdom as source of anti-ulcer remedies. *Phytotherapy Research* 14: 581 – 591.

Cho, C. H. and Pfeiffer, C. J. 1981. Gastrointestinal ulceration in the guinea pigs in response to dimaprit, histamine and H1 and H2 blocking agents. *Digestive Disease Science* 26:306 – 311.

Dalziel, J.M. (1937). The Useful Plants of West Tropical Africa. London: The Crown Agents for the Colonies, pp. 52- 560.

Di Carlo, G., Mascolo, N., Izzo, A. A. and Capasso, F. 1999. Flavonoids: old and new aspects of a class of a natural therapeutic drug. *Life sciences* 64: 337 – 353.

Evbuonwa, M. T and Bolarinwa, A. F. 1990. Effect of diet on indomethacin-induced peptic ulceration in pregnant rats. *Nigerian Journal of Physiological Sciences* 6:189 – 191.

Hayllar, J. and Bjarnason, I. 1995. NSAIDS, COX-2 inhibitor and the gut .*Lancet* 346 - 522.

Hiruma-Lima, C. A., Calvo, T. R., Rodriguez, C. M., Andrade, F. D. P., Vilegas, W. and Brito, ARM. 2006. Antiulcerogenic activity of *Alchornea castaneaefolia* effects on somatostatin, gastrin and prostaglandin. *Journal of Ethnopharmacology* 104: 215 – 224.

Lewis, D. A., Hanson, D. 1991. Anti-ulcer drugs of plants origin. *Progress in Medicinal Chemistry* 28:208 – 210.

Lorke, D. 1983. "A new Approach to Practical Acute Toxicity Testing." *Archives of Toxicology* 54: 275-287.

Maiti, R., Jana, D., Das, U. k, Hosh, D. 2004. Antidiabetic effect of aqueous extract of seed of *Tamarindus indica* L. in streptozotozin-induced diabetic rats. Journal of *Ethnopharmacology*; 92:85-91.

Nwafor, P. A., Effraim, K. D. and Jacks, T. W. 1996. Gastroprotective effects of aqueous extracts of Khaya *senegalensis* bark on indomethacin – induced ulceration in rats. *West African Journal of Pharmacology and Drug Research* 12:46 – 50.

Nwafor, P. A., Okwuasaba, F. K. and Binda, l. G. 2000. Antidiarrhoeal and antiulcerogenic effects of methanolic extracts of *Asparagus pubescens* root in rats. *Journal of Ethnopharmacology* 72:421 – 427.

Pihan G., Regillo, C., Szabo S. 1987. Free radicals and lipid peroxidation in ethanol or aspirin – induced gastric mucosa injury. *Digestive Diseases and Sciences*; 5(3): 23-24

Rainsford, K. D. 1987. The effects of 5-lipoxygenase inhibitors and leukotriene antagonists on the development of gastric lesions induced by nonsteroidal anti-inflammatory drugs in mice. *Agents and Action* 21:316 – 319.

Tariq M, Parmar N. S, Al Yahya M. A, Ageel A. M, Al Said M. S. (1986) Evaluation of Aloe vera leaf exudate and gel from gastric and duodenal anti-ulcer activity. *Fitoterapia* 57: 380-383.

Zaidi, S. H. and Mukerji, B. 1958. Experimental peptic ulceration. Part 1. The significance of mucus barrier. *Indian Journal of Medical Research* 46:27 – 37.

Zayachkivska, O. S., Konturek, S. J., Drozdowicz, D., Konturek, P. C., Brzozowski, T. and Ghegotsky, M. R. 2005. Gastroprotective effects of flavonoids in plants extracts. *Journal of Physiology and Pharmacology* 56: 216 - 231.

Access this Article in Online

Website: www.ijcrcps.com

Subject: Pharmacology

Quick Response Code

DOI: 10.22192/ijcrcps.2021.08.05.002

How to cite this article:

APPAH Joseph, AGATEMOR Uzuazokaro Mark- Maria, ELAH Sarah Onyeche, MOMOH Theophilus Boniface. (2021). Gastroprotective Effect of the Aqueous Extract of *Borreria stachydea* Leaves. Int. J. Curr. Res. Chem. Pharm. Sci. 8(5): 14-20.

DOI: http://dx.doi.org/10.22192/ijcrcps.2021.08.05.002

