MERIT RESEARCH JOURNALS
www.meritresearchjournals.org
Merit Research Journal of Medicine and Medical Sciences (ISSN: 2354-3238) Vol. 3(1) pp. xxx-xxx, January, 2015
Available online http://www.meritresearchjournals.org/mms/index.htm

Original Research Article

Anti-ulcerogenic and antioxidant properties of the aqueous leaf extract of *Ficus capensis* in Wistar albino rats

Patricia Eluka[1], Fred Nwodo[1], Peter Akah[2*] and Collins Onyeto[2]

[1]Department of Biochemistry, University of Nigeria, Nsukka, Nigeria

[2]Department of Pharmacology and Toxicology, University of Nigeria, Nsukka, Nigeria

***Corresponding Author's E-mail: peter.akah@unn.edu.ng; peterakah@hotmail.com**
Tel: +2348037750231

Abstract

The anti-ulcer effects of the aqueous extract of the leaves of *Ficus capensis* were evaluated in rats using diclofenac sodium induced-ulcer model. The possible mechanisms of the anti-ulcerogenic effect were explored by determining the antioxidant activity, as well as its effects on some biochemical parameters such as superoxide dismutase (SOD), catalase (CAT), malonaldihyde (MDA) and glutathione (GSH). The aqueous extract was evaluated for acute toxicity test, qualitative and quantitative phytochemical analysis. The results showed that the extract exhibited significant (P<0.05) and dose- dependent anti-ulcer activity. The percentage ulcer inhibition due to extract at 100, 150 and 200 mg/kg were 25, 41.7 and 43.3% respectively, while that of ranitidine (150mg/kg) was 66.7%. The extract significantly (P<0.05) decreased MDA activity, and increased the activities of CAT, GSH and SOD significantly (P<0.05) when compared to untreated control. The qualitative and quantitative phytochemical analysis revealed the presence of reducing sugar, saponins, tannins, flavonoids, soluble carbohydrates, alkaloids, steroids, hydrogen cyanide, glycosides, terpenoids and fats and oil. The acute toxicity test on the extract showed no death or obvious signs of toxicity up to 5000 mg/kg body weight. These findings revealed the potentials of the aqueous extract of *Ficuscapensis* as an anti-ulcerogenic, and as well as antioxidant agent

Keywords: Antioxidant, Antiulcer, *Ficus capensis*, Ranitidine, Rats

INTRODUCTION

Peptic ulcer disease (PUD) is mainly a disruption of the mucosal integrity of the stomach, duodenum or esophagus leading to a local defect or excavation due to active inflammation (Adreoli et al., 2008). There are two main approaches for treatment of peptic ulcer. The first is to reduce gastric acid production and the second is to enhance gastric mucosa protection (Valle, 2005). The current treatment of peptic ulcer is mainly achieved with H_2 receptor antagonists, antacids, proton pump inhibitors, prostaglandin analogues and antimuscarinics. Unfortunately, the prolonged use of these treatments are often associated with adverse reactions such as, hypersensitivity, arrhythmia, impotence, gynecomastia and hematopoietic disorders (Malfertheiner et al., 2009).Therefore, there is a need for novel effective drugs for peptic ulcer therapy with better tolerability.

Several medicinal plants have been reported to be safe and effective in peptic ulcer disease (Akah et al., 1998a, 1998b). The *Ficus species* are popular among Nigerian traditional doctors in the treatment of peptic ulcers and other gastrointestinal diseases (Akah et al., 1997 and Kunle et al., 1999). *Ficus capensis*, Thumb, (*Moraceae*) also known as the Cape figplant belongs to the mulberry family and is a native of tropical Africa and the Cape Islands. The plant is a deciduous tree with spreading roots and branches and broad green leaves. The plant is very common for the treatment of gastrointestinal ulcers among native doctors in many

parts of Nigeria. In addition to gastrointestinal problems, *Ficuscapensis* has been reported to possess other pharmacological properties such as antimicrobial (Oyeleke et al., 2008, Adebayo-Tayo and Adeniyi, 2012), relaxation of gastrointestinal tract (Ayinde andOwolabi 2009, Ayinde et al., 2013), antioxidant (Sirisha et al., 2010), immune booster (Daukwo et al., 2012) and tocolytic activity (Owolabi et al., 2009).The chemical composition of the plant has been documented (Francois et al., 2010, Adebayo-Tayo and Adeniyi, 2012). In this study an attempt was made to evaluate the anti-ulcerogenic effect of *Ficuscapensis* and the mechanisms underlying its effect.

MATERIALS AND METHODS

Animals

Adult Swiss albino mice (19-25g) rats (90-240g) of both sexes obtained from the Laboratory Animal Facility Center of the Faculty of Biological Sciences University of Nigeria Nsukka were used in the study. The animals were maintained freely on standard pellets and water. All animal experiments were in compliance with the National Institute of Health Guide for Care and Use of Laboratory Animals (Pub No. 85 – 23, revised 1985).

Plant Material and Preparation of Aqueous Extraction

Fresh leaves of *Ficus capensis* were collected from Ituku Ozalla in Nkanu L.G.A. Enugu State in the month of October 2012. It was authenticated by Mr. Alfred Ozioko of Bioresource Development and Conservation Programme (BDCP) Research Centre, Nsukka Enugu State. The leaves were room-dried to constant weight and then ground with Thomas – Willey Laboratory Mill, the ground leaves were boiled for 1 h in distilled water. The decoction was left overnight to cool. The aqueous extraction was filtered, using calico and vacuum pump. The filtrate was then lyophilized and afforded 0.448g aqueous extract (2.24%).

Phytochemical Analysis

The procedure as outlined by Harborne(1998) was used for the study. The presence of reducing sugar, saponins, tannins, flavonoids, soluble carbohydrates, alkaloids, steroids, hydrogen cyanide, glycosides, terpenoids, fats and oil were determined.

Acute Toxicity Test

The acute toxicity and lethality of aqueous extract (LD_{50}) was studied in mice using the method of Lorke (1983). Briefly, nine mice of both sexes randomly divided into three groups (n = 3) received oral administration of one of 10, 100, and 1000 mg/kg of the aqueous extract and were observed for 24h for death. Since no death was recorded, further doses of 1,600, 2,900 and 5000mg/kg of aqueous extract were administered to a fresh batch of animals (n = 1) and the number of deaths in 24h was recorded. The LD_{50} was calculated as the geometric mean of the highest non-lethal dose and the lowest lethal dose (Lorke, 1983).

Induction of Ulcer

The modified method of Brzozowskiet al. (1998) was employed in this study. The animals were starved for 24 hours with free access to drinking water. Thirty (30) male albino rats (102-240 g) divided into seven (6) groups of five (n=6) rats each were used for the study. The animals were maintained under optimal atmospheric and hygienic conditions, with feed and water *ad libitum* for fourteen (14) days. The rats were pre-treated with doses of aqueous extract for ten days before the induction of ulcer with diclofenac sodium (100 mg) orally on the 11th day. The groups and doses administered were as follows.

Group 1: Normal saline (negative control) + Diclofenac
Group 2: Ranitidine (150 mg/kg, positive control) + Diclofenac
Group 3: Extract (100 mg/kg) + Diclofenac
Group 4: Extract (150 mg/kg) +Diclofenac
Group 5: Extract (200 mg/kg) +Diclofenac

After the experiment, blood was collected through rectobulba plexus in the eye and carefully mixed with the anticoagulant, EDTA (10% w/v) in distilled water to prevent clotting and into non-heparinized sample bottles to obtain serum for the determination of some biochemical parameters SOD, CAT, MDA and GSH. MDA (Wallin et al., 1993, Aebi, 1983, Xin et al., 1991, King and Wotton, 1959). The animals were euthanized after 1 hour, their stomach removed and cut open through the greater curvature and washed gently in normal saline, collected in small bottles containing 10% formalin solution and was observed under low and high magnification. The ulcer index (UI) of the control group and preventive ratio (PR) of the treated groups were calculated using the following relations:

$$UI = (A \, x \, B)/100,$$

where A = degree of ulceration and B = percentage of group ulcerated, and

where UI_U = Ulcer index of ulcerated group and UI_P = Ulcer index of the protected group.

Degree of ulceration (DU) was calculated using the relation

DU = (total ulcer score/number of ulcerated animals) (Ezike et al., 2009).

Table 1. Qualitative phytochemical screening of aqueous leaf extract of *F. capensis*

Phytochemical Constituents	Composition
Alkaloids	++
Carbohydrates	++
Flavonoids	+
Glycosides	++
Reducing sugar	+++
Saponins	++
Steroids	+
Tannins	++
Terpenoids	+
Fats and oil	+
Hydrogen cyanide	+

Key: Slightly present +, moderately present ++, highly present +++

Table 2. Quantitative phytochemical constituents of aqueous leaf extract of *F. capensis*

Phytochemical Constituents	Composition (mg/100g)
Alkaloids	3.92 ± 0.003
Carbohydrates	1.27 ± 0.032
Flavonoids	2.37 ± 0.005
Glycosides	543.47 ± 0.004
Reducing sugar	2.39 ± 0.003
Saponins	7.57± 0.002
Steroids	0.89 ± 0.002
Tannins	1.61 ± 0.003

Statistical Analysis

The results were expressed as mean ± SEM. The data were analyzed using Graph pad Prism (version 5.0) and One way analysis of variance (ANOVA) followed by Dunnet Post hoc test.. Differences between means were accepted to be significant at $P < 0.05$.

RESULTS

Qualitative and Quantitative Phytochemical Screening

Phytochemical analysis showed that aqueous extract of *F.capensis* tested positive for reducing sugar, alkaloids, saponins, tannins, soluble carbohydrates, glycosides, flavonoids, steroids, hydrogen cyanide, terpenoids and fat and oil (Tables 1 and 2).

Acute Toxicity (LD_{50}) test

Oral administration of aqueous extract of *F. capensis* up to 5 g/kg caused no death in mice. Therefore, the oral LD_{50} of the aqueous extract in mice was >5 k/kg. Also there were no signs of obvious behavioural and physical adverse effects.

Effect of the extract on Diclofenac sodium -induced ulcer

The aqueous extract exhibited significant (P<0.05) and dose-dependent anti-ulcer activity. The percentage ulcer inhibition due to extract at 100, 150 and 200mg/kg were 25, 41.7 and 43.3% respect-tively, while that of ranitidine (150mg/kg) was 66.7% (Table 3).

Effects of the extract on biochemical markers

The aqueous extract significantly (P<0.05) decreased MDA activity, and increased the activities of CAT, GSH and SOD significantly (P<0.05) when compared to untreated control (Table 4)

Table 3. Effect of the extract on Diclofenac sodium -induced ulcer

Treatment group	Dose(mg/kg)	Ulcer index (mm)	Preventive ratio (%)
Normal saline	10 ml/kg	1.2±0.04	0
Ranitidine	150	0.4±0.01	66.7
Extract	100	0.9±0,03	25
	150	0.7±0.04	41.7
	200	0.68 ±0.02	43.3

Table 4. Effects of the extract on biochemical markers

Treatment group	Dose (mg/kg)	SOD	CAT	MDA	GSH
Normal saline	10 ml/kg	54.80±2.70	52.60±5.75	59.80±1.497	55.00±3.11
Ranitidine	150	56.00±2.51*	54.60±3.29*	33.40±2.22*	60.000±4.88*
Extract	100	58.20±2.92*	55.20±2.55*	52.00±3.08*	56.400±2.54*
	150	60.60±2.29*	56.00±4.49*	35.20±4.24*	57.000±3.42*
	200	63.00±5.29*	59.20±5.20*	32.80±2.22*	60.200±5.57*

P>0.05 vs Normal saline control

DISCUSSION

In this study, the potential effects of the aqueous leaves extract of *Ficus capensis* on some serum biochemical parameters that are indicators of gastric lesions were investigated. The results of the phytochemical studies corroborated the findings of Adebayo-Tayo and Adeniyi (2012). The results indicated that the extract possessed some biologically active compounds which could serve as potential sources of drugs. The oral acute toxicity studyin mice revealed that it has a high safety profile, as the extracts was well tolerated by the animals up to 5000 mg/kg body weight.

Ulcers are caused as a result of imbalance between aggressive and defensive factors. An increase in aggressive factors or a decrease in defensive factors will lead to loss of mucosal integrity. Ulcer index is an established indication of ulceration in experimental animals (Ezike et al., 2009).

The ulcer index decreased significantly (P<0.05) in the extract treated groups when compared with the normal saline control group. The ulcer inhibition by the extract was not only significant (P<0.05), but also dose-related. This effect may be attributed to the presence in high amount of some bioactive compounds, especially tannins and flavonoids which have been reported to exhibit potent anti-ulcerogenic and anti-gastric activity (Nwagba et al., 2013),

The mean MDA activity showed significant decrease (P<0.05) in the extract treated groups compared to the ranitidine group. The reduction in the mean MDA levels of the treated groups could be attributed to the ability of the extract to scavenge free radicals generated by the inducing agent thereby preventing lipid peroxidation Increased lipid peroxidation during ulcer as found in the present study may be due to oxidative stress. Oxidative stress results from the imbalance between production and removal of reactive oxygen species (ROS), and Increased oxidative stress, which contributes substantially to the to the pathogenesis of ulcer complications, is the consequence of either enhanced ROS production or attenuated ROS-scavenging capacity (Ahmed et al., 2011). The increase could also be due to the failure of the antioxidant defense mechanisms to prevent formation of excess free radicals in the system.

Antioxidant enzymes (CAT, GSH and SOD) activities increased significantly (P<0.05) compared in the extract treated group. Sirishaet al*.,* (2010) had earlier reported that *Ficus* species are rich source of antioxidants that help in prevention of oxidative stress related diseases. A possible reason for these protective mechanisms against mucosal damage could be due to the gel-like nature of the extract that may likely adhere to mucosal wall, thus acting as a physical barrier and preventing acids, pepsins and bile from damaging the mucosal surface. It is known that the cytoprotective action of some anti-ulcer drugs is mediated by the action of endogenous prostaglandins which promote mucus secretion and play an important role in maintaining mucosal integrity against the action of various damaging agents (Sirisha et al., 2010).

CONCLUSION

These results revealed that the aqueous leaf extract of *Ficus capensis* possesses a potent ulcer healing effect, which could be attributed to the free radical scavenging activity, and its ability to inhibit lipid peroxidative processes as well as elevation in the levels of the antioxidant enzymes.

Conflict of Interest

Nil. The study was funded by the authors' personal contributions

REFERENCES

Adebayo-Tayo R, Odeniyi A (2012). Phytochemicals screening and Microbial inhibitory. Activities of *Ficus capensis*. Afr. J. Biomed. Res;15: 35-40

Adreoli T, Chan PD, Cowell JC, Gilbert DM, Green G, Johnson M. et al., (Provide names of other authors) (2008). Management Of Patients with Gastric and Duodenal Disorders. In: Brunner and Suddarth; Textbook of Medical Nursing. 11th Edn. Elserview, Philaldephia,USA .P. 1203-1279.

Aebi HE (1983). Catalase. In: Methods of Enzymatic Analysis. 3rd Edition. Academic Press, New York . P. 673-644.

Ahmed M, Ahmed A, Hala S, Gehan M, Fehad A (2011). Protective effects of simvastatin, an HMG-CoA reductase inhibitor against oxidative damage in experimental diabetic rats. Intern J Pharm. Tech Res; 3(3): 1780-1795.

Akah PA, Gamaniel KS, Wambebe CON, Shittu A, Kapu SD, Kunle OO (1997). Studies on the gastrointestinal properties of *Ficus capensis*. Fitoterapia; 68: 17-20.

Akah PA, Orisakwe OE, Gamaniel KS, Shittu A (1998a) Evaluation of Nigerian traditional medicines: 11. Effects of some Nigerian folk remedies on peptic ulcer. J .Ethnopmarmacol; 62:123-128.

Akah PA, Orisakwe OE, Nwafor SV, Gamaniel KS (1998b). Prospect of plant natural products as anti-ulcer agents. J Pharm Res Dev: 3: 57-62.

Ayinde BA, Owolabi OJ (2009). Effects of the aqueous extract of *Ficuscapensis* Thumb (Moraceae) leaf on gastrointestinal motility. J Pharmacognosy Pharmacotherapy: 8(53): 32-35.

Ayinde BA, Owolabi OJ, Jesuoroba RI (2013). Active ileum relaxant fraction from the leaves of *Ficuscapensis*, Thumb (Moraaceae). Nig J Pharm: 10 (1): 1-10.

Brzozowski T, Konturek SJ, Kwiecien SS, Pajdo R, Brzozowski I, Hahn EG (1998). Involvement of endogenous cholecystokinin and somatostatin in gastro protection induced by intra duodenal fat. J ClinGastroenterol;27: 125-137.

Daukwo OA, Tende JA, Okey ED, Ias AS (2012). The effect of aqueous extract of Thumb, (Moraceae) on in vivo leukocyte mobilization in rats. Bri J Pharmacol Toxicol: 3(3); 110-114.

Ezike AC, Akah PA, Okoli CO, Nnamani CM, Ojike CO, Eze FS. et al (2009). Studies on the anti-ulcer and gastrointestinal effects of stem bark extract of *Bridelia femiginea* J. Comp Integ Med; 8 (1): 1553-3840.

Francois MN, Amadou D, Rachid SC (2010). Chemical composition and biological activities of *Ficus capensis*. J Nat: Prod 3: 149-160.

Harbone J (1998). Phytochemical Methods A Guide to Modern Technology of Plant Analysis 3rd Ed Chapman and Hall New York. P 88-185.

King EJ, Wotton DP (1959). Microanalysis. In Medical Biochemistry. New York, NY: Mc Graw Hill. P. 14.

Kunle OO, Akah PA, Shittu A, Naspuri RN, Wambebe C (1999). The gastrointestinal properties of of some estracts of *Ficus sur*. Fitoterapia:70: 542-547.

Lorke D (1983). A new approach to practical acute toxicity testing. Arch Toxicol; 55: 275-287.

Malfertheiner P, Chan K, McColl E (2009). Peptic ulcer disease. Lancet; 374(9699): 1449-1461.

Nwagba C, Ezugwu C, Eze C, Anowi F, Ezea S, Nwakile C (2013). Anti-ulcer activity of *Bombax buonopozense*P. Beauv. Aqueous leaf extract (Fam.: Bombacaceae). J Applied PharmaceutSci; 3(2): 139-142.

Owolabi JO, Nworgu ZA, Falodun A, Ayinde BA, Nwako CN (2009). Evaluation of the tocolytic activity of the ethanol extract of the stem back of *Ficus capensis* Thumb, (Moraceae). Natural Drugs: 66(13): 293-296.

Oyeleke SB, Dauda BEN, Boye OA (2008). Antibacterial activity of *Ficus capensis*. Afr. J Biotechnol: 7(10): 1414-1417.

Sirisha N, Screenivasulu M, Sangeeta K, Madhusudhana C (2010). Antioxidant Properties of Ficus Species A Review. Intern J Pharm. Tech. Rese;2(4):2174-2182.

Valle L (2005). Peptic ulcer diseases and related disorders. In: Braunwald E, Fauci S., Kasper L., Hauser L., Longo L., Jameson L. Editors. Harrison's principles of internal medicine. 16th ed. New York: McGraw-Hill Professional, p. 1746- 1762.

Wallin B, Rosengren B, Shertzer HG, Camejo G (1993). Lipoprotein oxidation and measurement of TBARS formation in single microliter plate; its use for evaluation of antioxidants. AnalytBiochem; 208: 10-15.

Xin Z, Waterman DF, Henken RM, Harmon RJ (1991). Effect of copper status on neutrophil function, superoxide dismutase and copper distribution in steers. J Diary Sci; 74: 3078-3082.