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Anti-ulcer Activity of the Aqueous Root Extract of *Leptadenia hastata*

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Abstract

Leptadenia hastata (family: Asclepiadaceae) is a medicinal plant used in folk medicine against peptic ulcers**.** The anti- ulcer activity of the aqueous root extract of *Leptadenia hastata* (AELH) was evaluated using indomethacin and ethanol ulcer models. Results of the study showed that the extract displayed dose- dependent gastroprotective activity as demonstrated by significant (P< 0.05) inhibition of the formation of ulcers induced via the ulcer models. It was concluded that the extract could be useful in the management of peptic ulcers.

Keywords: *Leptadenia hastate*, peptic ulcers, gastroprotective activity, anti- ulcer activity.

1.0 Introduction

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, non-steroidal anti-inflammatory drugs, cigarette smoking, stress, alcohol and chronic pancreatitis (Tariq *et al.*, 1986).

Although there is a large arsenal of drugs with antiulcerogenic activity on the market, none produces 100% remission of ulcers, with reduced side effects and without compromising the patient's wellbeing, which usually results in chronic use of these drugs. Studies have reported the widespread use of herbs and polyherbal formulations with antiulcerogenic properties. This global upsurge in the use of herbs and herbal products is largely due to the wide acceptability; accessibility and affordability of these herbs/ herbal products (Idakwoji and Uzuazokaro, 2018b). This study was aimed at evaluating the anti- ulcer activity of aqueous root bark extract of *Leptadenia hastata*.

Leptadenia hastata belongs to the family asclepiadaceae widely used in Tropical Africa as vegetable (Burkil, 1985). The plant is medicinally important in the treatment of many ailments (Burkil, 1985; Oliver-Boyer, 1986; Aliero *et al*., 2001). Ethnobotanical information obtained from traditional medical practitioners in northern Nigeria revealed that *L. hastata* is used for the treatment of diabetes mellitus. The antibacterial and antimicrobial effects of *L. hastata* have been reported (Aliero and Wara, 2009) and the result of its toxicity studies showed that the plant is relatively safe (Tambuora *et al*., 2005). There is however paucity of information confirming the anti-ulcer potential of *L. hastata* roots.

2.0 Materials and Methods

2.1 Materials

2.1.1 Chemicals and drugs

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

2.1.2 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.

2.2 Methods

2.2.1 Plant Collection and Identification

The roots of *Leptadenia hastata* were collected from a natural habitat in Okpella Area of Edo State, Nigeria. The plant was identified at the herbarium unit of the Department of Biological Sciences, Federal University Lokoja.

2.2.2 Preparation of Extract

The roots were washed and shade- dried for ten (10) days and pulverized using an electric blender. One thousand and five hundred (1000) gram of the pulverized root was soaked in distilled water for 72- hours. The resulting mixture was filtered using Whatmann filter paper (Size No1) and the extract was concentrated using a free- dryer. The extract will henceforth be reffered to as AELH.

2.2.3 Acute Toxicity Study

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

2.2.4 Evaluation of antiulcer activity

2.2.4.1 Indomethacin-induced ulceration

Male adult albino rats were used for the experiment. They were randomly divided into 5 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 (Sigma, 60 mg/kg p.o. dissolved in 5% Na_2CO_3); Groups 2 – 4 were pretreated with 100, 200 and 400mg/ kg p.o of AELH respectively. Group 5 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80). One hour later, groups 2-5 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).)

2.2.4.2 Ethanol-induced gastric ulceration

The procedure was similar to that used in indomethacin induced ulceration. The rats randomly assigned into 5 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 - 4 were pretreated with 100, 200 and 400mg/ kg p.o of AELH respectively, Group 5

received propranolol (40 mg/kg p.o. dissolved in distilled water). One hour later, groups 2- 5 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).

2.2.5 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.

3.0 Results

3.1 Acute Toxicity

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

Table 1: Observed Effects of the Aqueous Root Extract of *Leptadenia hastata* (AELH) on Rats

Phase	Group	Treatment (mg/kg)	D/T	Observed Sign of Toxicity
I	1	AELH (10)	0/3	-
	2	AELH (100)	0/3	-
	3	AELH (1000)	0/3	-
II	1	AELH (1600)	0/1	-
	2	AELH (2900)	0/1	-
	3	AELH (5000)	0/1	-

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

3.2 Indomethacin-induced Gastric Ulceration

Table 2 shows that indomethacin induced gastric ulcer in all experimental groups. The extract dose-dependently produced a significant reduction ($p < 0.05$) in the gastric erosions formed compared to control as evident in the reduction of ulcer indices. The 100 and 200 mg/kg extract produced a 45.47 and 78.76% ulcer inhibition respectively while the 400mg/ kg produced 78.76 produced 87.56% ulcer inhibition which was more that of cimetidine (84.91%).

Table 2: Effect of the Aqueous Root Extract of *Leptadenia hastata* (AELH) on Indomethacin-induced Gastric Ulcer

Treatment (mg/kg)	Ulcer Index	% Ulcer Inhibition
Control (Indomethacin 60 mg/kg)	15.11±2.31	-
AELH (100 mg/kg)	8.24±1.01*	45.47
AELH (200 mg/kg)	3.21±0.88*	78.76
AELH (400 mg/kg)	1.88±0.73*	87.56
Cimetidine(100 mg/kg)	2.28±0.22*	84.91

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

3.3 Ethanol- induced Gastric Ulceration

As shown in Table 3, the extract also produced a dose- dependent significant reduction ($p < 0.05$) in the gastric erosions formed compared to control. This was evident in the reduction of ulcer indices. The potency of the formulations in reducing the ethanol- induced ulcer were 49.70 % for the 100mg/kg extract, 71.25% for the 200mg/ kg dose and 85.26% for the 400mg/ kg extract which was comparable to that of propranolol which had 87.94% inhibition.

Table 3: Effect of the Aqueous Root Extract of *Leptadenia hastata* (AELH) on Ethanol- induced Gastric Ulcer

Treatment (mg/kg)	Ulcer Index	% Ulcer Inhibition
Control (Ethanol)	8.21±0.99	-
AELH (100 mg/kg)	4.13±0.71*	49.70
AELH (200 mg/kg)	2.36±0.45*	71.25
AELH (400 mg/kg)	1.21±0.98*	85.26
Propranolol (40 mg/kg)	0.99±0.15*	87.94

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

4.0 Discussion

The aqueous root extract of *L. hastata* showed dose-dependent anti-ulcer activity against experimentally - induced gastric ulcer models used in this study.

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. The extract dose- dependently and significantly reduced the mucosal damage in the indomethacin– induced ulcer model, suggesting the possible extract mobilization and involvement of prostaglandin in the anti- ulcer effect of the extract.

Ethanol-induced ulcers which is predominantly in the glandular part of stomach has been reported to stimulate the formation of leukotriene C4 (LTC4) resulting in the damage of rat gastric mucosa (Cho *et al.,* 1987). Chronic alcohol misuse is associated with significantly reduced capacity for prostaglandin synthesis in gastric mucosa (Bode *et al.,* 1996). In the rat gastric mucosa, inflammation, erosion and necrosis elicited by exogenous LTC4 resemble those produced by ethanol (Szabo *et al.*, 1985). Other studies have indicated that an alcohol dependent increase in the production of leukotriene- compounds produced by the immune system that cause allergic and inflammatory reactions might also contribute to the development of alcohol-induced mucosa injury (Bode and Bode, 1992). Ethanol also produces mucosa damage by direct necrotizing action which in turn reduces defensive factors, secretion of bicarbonate and production of mucus (Rujjanawate *et al.,* 2005). The protective effect of extract against ethanol-induced gastric lesions may in part be due to reduced leukotriene activity produced.

5.0 Conclusion

Conclusively, the results of the study showed that the aqueous extract of the roots of *Leptadenia hastata* display gastroprotective activity as demonstrated by the significant inhibition of the formation of ulcers induced through different ulcer models. Hence, the extract can be used as an alternative to the orthodox anti- ulcer drugs or as an add-on therapy.

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