

Research Article

Antiulcerogenic activity of husk extract of *Zea mays*

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Background: *Zea mays* husk is used in Ibibio traditional medicine for the treatment of various ailments including diabetes mellitus, malaria and ulcer.

Objective: To investigate the antiulcerogenic potential of husk extract of *Zea mays*.

Methods: Ethanol husk extract of *Zea mays* (187-784 mg/kg) was evaluated for antiulcerogenic activity against indomethacin, ethanol and histamine-induced ulcers in rats.

Results: The husk extract was found to significantly ($p < 0.05 - 0.001$) inhibit ulcers induced by indomethacin, ethanol and histamine in a dose-dependent fashion.

Conclusion: These results suggest that the husk extract of *Zea mays* possess antiulcerogenic potentials which are due to the activities of the phytochemical constituents.

Keywords: *Zea mays*, husk, antiulcer, gastrointestinal system.

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1. Introduction

Zea mays L. (Poaceae) also known as maize or corn, is an annual grass plant cultivated through Nigeria primarily for human consumption and as animal feed. The plant is tall with a fibrous root system and has long narrow leaves on opposite side of the stem and bears ears that are enclosed in modified leaves known as husks (Simmonds, 1979). Besides its nutritive values, maize grains, leaves, cornsilks, stalk, and inflorescence are also used in ethnomedicine for the treatment of several ailments. The corn silk is used as an antidiabetic or diuretic, and decoction of the silk is consumed for the treatment of urinary troubles and gallstones (Foster and Duke, 1990; Gill, 1992; Abo et al, 2008). The ash of the cob is used for the treatment of cough (Gill, 1992) and inflammatory diseases (Okokon et al, 2016). The husks are used for the treatment of pains and arthritis (Owoyele et al, 2010). Warm tea of the husks is used for the treatment of malaria and diabetes in Ibibio

traditional medicine (Okokon et al, 2017a). Also, corn grains and corn husk are also used in the treatment of ulcer traditionally (Jadhav, 2016). The husk extract has been reported to possess some pharmacological properties which include; analgesic, anti-inflammatory (Owoyele et al, 2010), antioxidant (Dong et al, 2014), antidepressant (Okokon et al, 2016) antimalarial and antiplasmodial (Okokon et al, 2017a), hepatoprotective (Okokon et al, 2017b), and nephroprotective (Okokon et al, 2017c) activities. Corn grain have been reported to possess antiulcerogenic effect (Jadhav, 2016). The median lethal dose (LD₅₀) of the ethanol husk extract was determined to be 1874.83 mg/kg (Okokon et al, 2016). Arabinoxylan, which has immunological effects, has been isolated from the husk extract (Ogawa et al, 2005), while eight phenolic compounds (gallic acid, protocatechuic acid, chlorogenic acid, caffeic acid, femlic acid, rutin, resveratrol, and kaempferol) have also been detected in ethanol husk extract of *Zea mays* (Dong et al, 2014). Corn husk has also been reported to be rich in

anthocyanins (Li et al, 2008). Information on the biological activities of the husk extract is scarce. We report in this study the antiulcerogenic activity of the husk extract to confirm its use in the treatment of ulcer in ethnomedicine.

2. Methods

2.1 Collection of plant materials

Fresh husks of *Zea mays* were collected in August, 2017 from Farmland in Uyo in Uyo LGA, Akwa Ibom State, Nigeria. The husks were identified and authenticated as *Zea mays* by a taxonomist in the Department of Botany and Ecological studies, University of Uyo, Uyo, Nigeria. Herbarium specimen (FPH, 614) was deposited at the Faculty of Pharmacy Herbarium, University of Uyo, Uyo.

2.2 Extraction

The plant parts (husks) were washed, cut into smaller pieces and air-dried on laboratory table for 2 weeks. The dried husks were pulverized using electric grinder. The powdered husk was divided into two parts; one part (1.5 kg) was macerated in 50% ethanol for 72 hours. The liquid filtrate obtained was concentrated and evaporated to dryness *in vacuo* at 40°C using rotary evaporator.

The crude extract (yield 2.83%) was stored in a refrigerator at -4°C until they were used for the experiments reported in this study.

2.3 Animals

Swiss albino male rats (145 - 170g) used for these experiments were gotten from Animal house of Department of Pharmacology and Toxicology, University of Uyo. The animals were housed in standard cages and were maintained on a standard pelleted feed (Guinea feed) and water *ad libitum*.

Permission and approval for animal studies were obtained from the College of Health Sciences Animal Ethics Committee, University of Uyo.

2.4 Evaluation of antiulcer activity

Indomethacin-induced ulcer.

Male adult albino rats were used for the experiment. They were randomly divided into five groups of six rats each. Food was withdrawn 24 hours and water 2h before the commencement of experiment (Alphin and Ward, 1967). Group 1 (control) received only indomethacin (Sigma, 60 mg/kg p.o. dissolved in 5% Na₂CO₃); Groups 2 - 4 were pretreated with *Zea mays* husk extract (187, 374 and 784 mg/kg p.o. respectively) dissolved in distilled water and administered as aqueous suspension; Group 5 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80). One hour later, groups 2-5 were administered with 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 were calculated using standard methods (Zaidi and Mukerji, 1985; Nwafor et al, 2000). Ulcer index represents the degree of lesion or ulceration caused by the ulcerogen, while preventive ratio is the protective potential of the extract/drug.

Ethanol-induced gastric ulceration.

The procedure was similar to that used in indomethacin induced ulceration. The rats randomly assigned into five groups of six rats each based on their body weight. Food was withdrawn 24 hours and water 2h 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 *Zea mays* husk extract (187, 374 and 784 mg/kg p.o. respectively) dissolved in distilled water and administered as aqueous suspension; Group 5 received propranolol (40 mg/kg p.o. dissolved in distilled water). One hour later, groups 2- 5 were administered with 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 in rats.

Adult albino rats of both sexes weighing 120- 170 g were used for the experiment. They were randomized into five groups of six rats each. Food was withdrawn 24 hours and water 2 h before the commencement of experiment (Alphin and Ward, 1967). Group 1 (control) received only histamine acid phosphate (Sigma, 100 mg/kg i.p. dissolved in distilled water)(Maity et al,1995); Groups 2 - 4 were pretreated with *Zea mays* husk extract (187, 374 and 784 mg/kg p.o. respectively) dissolved in distilled water and administered as aqueous suspension; Group 5 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80), 1 hour prior to histamine administration. One hour later, groups 2-5 were administered with histamine acid phosphate (100 mg/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).

2.5 Statistical Analysis

Data are reported as mean + standard error of the mean (SEM) and were analyzed statistically using One-way ANOVA followed by Turkey-Kramer multiple comparison test and values of $p < 0.01$ were considered significant.

3. Results

Indomethacin-induced gastric ulceration.

The extract (p.o.) pretreatment on indomethacin induced gastric ulceration showed a dose dependent reductions in ulcer indices in pretreated groups relative to control. These reductions were statistically significant ($p < 0.05$) compared to control. (Table 1). The ulcerations observed in the stomachs of the extract-pretreated groups were majorly pinpoint wounds and no severe wound was present in the stomach of the animals. Severe wounds were observed in the stomach of the animals in the control group. The effect was lower when compared to that of the standard drug, cimetidine.

Ethanol-induced gastric ulceration.

Pretreatment of rats with husk extract significantly protected the animals from ethanol-induced ulcer

(Table 2). This protection was significant ($p < 0.01$) and dose-dependent as shown in the reduction of ulcer indices relative to control especially in the group treated with the highest dose (784 mg/kg) of the extract. The ulcerative wounds observed in the stomachs of the extract-pretreated groups were majorly pinpoint wounds and no severe wound was present in the stomach of the animals. However, there were severe wounds in the stomachs of the control animals.

Histamine-induced ulceration.

Administration of the husk extract significantly ($p < 0.001$) reduced histamine-induced gastric ulceration in a dose-dependent fashion compared to control (Table 3). Severe wounds were not observed in the stomachs of the extract/drug pretreated groups. The animals in the control group were observed to have severe wounds in their stomachs.

Table 1: Effect of ethanol husk extract of *Zea mays* on indomethacin-induced ulcer

Treatment	Dose	Ulcer indices	Preventive ratio
	mg/kg		
Control normal Indomethacin	60	11.33 ± 1.85	-
Cimetidine	100	0.64 ± 0.01 ^c	94.35
Crude extract	187	6.66 ± 1.30 ^a	41.21
	374	6.33 ± 0.33 ^b	44.13
	784	1.00 ± 0.01 ^c	91.17

Data are expressed as MEAN ± SEM, Significant at ^a $p < 0.05$, ^b $p < 0.01$, ^c $p < 0.001$, when compared to control. (n=6).

Table 2: Effect of ethanol husk extract of *Zea mays* on ethanol-induced ulcer

Treatment	Dose	Ulcer indices	Preventive ratio
	mg/kg		
Control normal	60	5.78 ± 0.57	-
Propranolol	40	1.16 ± 0.44 ^b	79.93
Crude extract	187	3.00 ± 1.15	48.09
	374	4.00 ± 0.57	30.79
	784	2.66 ± 0.33 ^a	53.97

Data are expressed as MEAN ± SEM, Significant at ^a $p < 0.05$, ^b $p < 0.01$, ^c $p < 0.001$, when compared to control. (n=6).

Table 3: Effect of ethanol husk extract of *Zea mays* on histamine-induced ulcer

Treatment	Dose	Ulcer indices	Preventive ratio
	mg/kg		
Control normal	60	5.33 ± 0.33	-
Cimetidine	100	0.00 ± 0.00 ^c	100
Crude extract	187	2.33 ± 1.45 ^a	56.28
	374	1.33 ± 0.66 ^b	75.04
	784	0.66 ± 0.33 ^c	87.61

Data are expressed as MEAN ± SEM, Significant at ^a $p < 0.05$, ^b $p < 0.01$, ^c $p < 0.001$, when compared to control. (n=6).

4.0 Discussion

Zea mays husk is used traditionally to treat various gastrointestinal disorders including ulcer. For this reason, the antiulcer activity of the husk extract was evaluated using indomethacin, ethanol and histamine-induced ulcer models. 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 (Evbunwa and Bolarinwa, 1990; Nwafor et al, 1996) by inhibiting prostaglandin synthetase through the cyclooxygenase 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).

Suppression of prostaglandins synthesis by indomethacin result in increased susceptibility of the stomach to mucosal injury and gastroduodenal ulceration. The extract was observed to significantly reduce 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. Administration of ethanol has been reported to cause disturbances in gastric secretion, damage to the mucosa, alterations in the permeability, gastric mucus depletion and free radical production (Salim, 1990). This is attributed to the release of superoxide anion and hydroperoxy free radicals during metabolism of ethanol as oxygen derived free radicals has been found to be involved in the mechanism of acute and chronic ulceration in the gastric mucosa (Pihan et al, 1987). It was observed in this study that the extract significantly reduced ethanol induced ulcer. This 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, by the extract 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 may be due to its suppression of histamine-induced vasospastic effect and gastric secretion. Okokon et al, (2017a) reported that the husk extract contains flavonoids, terpenes, saponins, alkaloids and cardiac glycosides among others. Flavonoids 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). 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). However, the husk extract has been reported to contain eight phenolic compounds (gallic acid, protocatechuic acid, chlorogenic acid, caffeic acid, femlic acid, rutin, resveratrol, and kaempferol) with considerable antioxidant potentials (Dong et al, 2014). The antiulcer activity observed in this study maybe due to the antioxidant activities of these phenolic compounds.

5.0 Conclusion

The results of the present study show that *Zea mays* husk extract displays gastroprotective activity as demonstrated by significant inhibition of the formation of ulcers induced through the three different ulcer models. This supports its use in the treatment of gastrointestinal disorders in traditional medicine.

Conflict of Interest declaration

The authors declare no conflict of interest.

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