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ANTI-ULCER PROPERTIES OF ALKALOIDS ISOLATED FROM THE FRUIT PULP OF *CUCUMIS METULIFEROUS* (CURCUBITACEAE)

S. Omale*², N. N. Wuyep¹ and A. Auta² N. N. Wannang¹

Department of Pharmacology, Faculty of Pharmaceutical Sciences, University of Jos¹, Jos, Nigeria

Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, University of Jos², Jos, Nigeria

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Correspondence to Author:

Simeon Omale

Lecturer, Department of Pharmacology,
Faculty of Pharmaceutical Sciences,
University of Jos, Jos, Nigeria

ABSTRACT

Anti-ulcer properties of the alkaloids isolated from the fruit of *Cucumis metuliferus* was investigated in mice. Ethanol-induced gastric lesion was used to assess the anti-ulcer activity. In this study, there was a significant ($p < 0.05$) decrease in haemorrhages and ulcerations of the gastric mucosa at 500 and 1000 mg/kg of the alkaloid compared with control. The activity of the extract is comparable to that of the standard control group administered ranitidine (1 mg/kg). The alkaloids of *C. metuliferus* showed a demonstrable potential as an anti-ulcer agent that could be used for the treatment of peptic ulcer disease.

INTRODUCTION: *Cucumis metuliferus* belongs to the family Cucurbitaceae a monoecious, climbing, annual herb with staminate flowers that can be grown practically anywhere provided the season is warm^{1, 2}. The climbing plant grows and flowers with subsequent fruiting as from July to September while the fruit ripened from October to December³. The fruits have spiny thorns, ovoid in shape about 8-10 cm long and 4-5 cm in diameter, it turns from complete green to yellow or orange colour when ripped. The white flat seeds are embedded in the spongy mesocarp which is sweet, bland or bitter in taste¹. The plant has two species identified by their taste, the sweet and bitter species. The bitter form contains cucurbitans (triterpenoids) which is a highly toxic compounds⁴. The non bitter form has been found to be less toxic and have been variously used and cultivated for their medicinal and food values⁵.

Cucumis metuliferus has been variously claimed to cure diseases such as peptic ulcer, hypertension, diabetes, HIV/AIDS by traditional medical practitioners in

Plateau state Nigeria. It has been reported that the seeds and fruits of the plant are eaten raw as food supplement and that it is highly valued for its antihelmintic properties⁶. The fruit pulp has been reported to increase sperm/seminal integrity¹.

Peptic ulcer is a condition in which there exists a discontinuity in the entire thickness of the gastric or duodenal mucosa that persists as a result of acid and pepsin in the gastric juice. This is as a result of imbalance between defensive factors that protects the mucosa and the offensive factors that disrupt this important barrier⁷. The anti-ulcerogenic activities of many plant product has been reported to be due to an increase in mucosal defensive factors rather than decrease in offensive factors⁸.

The anti-ulcer property of the crude extract was established in our laboratory⁹. The aim of this work is therefore, to evaluate the anti-ulcer property of isolated alkaloids from the fruit of *Cucumis metuliferus*.

METHODS:

Plant collection: The ripped fruits of *Cucumis metuliferous* were collected from cultivated field in Abbatoir, Jos South Local Government Area of Plateau state Nigeria in November, 2007. The fruits were identified and authenticated by D.L. Wonang of the Department of Botany, University of Jos, Jos, Nigeria.

Plant preparation: The greenish mesocarp and the pulp content were separated from the seeds, homogenized and passed through sieve size 0.25 mm after thorough stirring. The juicy content was then spread in trays and dried in a drying cabinet at a temperature of about 58°C until dried. The dried pulp content and the yellowish fibrous portion were then reduced to fine particle size using mortar and pestle.

The alkaloidal constituent of the powder of *Cucumis metuliferous* was isolated according to the standard methods^{10, 11}. The isolated alkaloid was stored in air tight container in a refrigerator until required for use.

Anti-ulcer study: Twenty adult mice weighing between 18 – 25 g were obtained from animal house of the Department of Pharmacology, University of Jos, Nigeria. After adaptation for three weeks, the animals were divided into four groups of five animals each.

The animals were fasted with free access to water for twenty four hours to ensure empty stomach. The animals were pretreated with 1 ml of ethanol in water (50% v/v) orally to induce gastric ulceration. Thirty minutes after, the animals in group 1 were administered 1 ml/kg of distilled water, group 4 received 100 mg/kg of ranitidine as standard drug while group 2 and 3 received 500 and 1000 mg/kg of the alkaloid respectively. All administration was done orally using intubation tube. The animals were sacrificed by cervical dislocation one hour post administration of alkaloids. The abdomen was incised

to expose the stomach which was then incised along their greater curvature and gently rinsed with normal saline. The stomach was placed on a glass and the number and severity of the ulcerations were examined using hand lens according to the method of Alphin and Wart, (1967) to the following scale¹²;

Greater than 3 mm	:	3
Less than 3 mm	:	2
Haemorrhaged ulcer	:	1.0
Pinpoint ulcer	:	0.5

Ethical Consideration: Ethical clearance and approval for this study was obtained from the University of Jos Animal Ethics Committee. The study was carried out according to the guidelines on laboratory animal care outlined by the committee.

Statistical Method: All results were expressed in mean \pm SEM and tests of significant differences between the means were carried out using the student t-test and a probability value of $p < 0.05$ was considered to be statistically significant.

RESULTS AND DISCUSSIONS: Alkaloids of *Cucumis metuliferous* produced a dose dependent decrease in the number and severity of gastric ulcerations. There was a significant ($p < 0.05$) decrease in the gastric lesions of the treated group compared with the control group.

The results showed a significant decrease in the number and severity of gastric ulcerations at 500 and 1000 mg/kg compared with the control, which was administered distilled water (table 1). There was also significant dose dependent decrease in the haemorrhage and pinpoint ulceration induced by ethanol in the treated group (see **table 1**).

TABLE 1: EFFECTS OF THE ISOLATED ALKALOIDS OF CUCUMIS METULIFEROUS ON GASTRIC MUCOSAL LESION ON MICE

Treatment	Mean Ulcer Score \pm SEM			
	>3mm	<3mm	P. point	H. ulcer
Control distilled water 1ml/kg	1.2 \pm 0.74	0.8 \pm 0.2	8.2 \pm 2.33	1.0 \pm 0.0
Alkaloids 500 mg/kg	0.8 \pm 0.80	0.8 \pm 0.37	3.8 \pm 2.48*	0.8 \pm 0.41
Alkaloids 100 mg/kg	0.6 \pm 0.40*	1.2 \pm 0.49	0.8 \pm 0.80*	0.2 \pm 0.20*
Ranitidine 100 mg/kg	0.0 \pm 0.0*	1.4 \pm 0.40	2.8 \pm 1.20*	0.0 \pm 0.00*

* $p < 0.05$; n = 5

Ethanol induce ulcers in the gastric mucosa either by decreasing mucosal blood flow, depletion of gastric wall mucous content or decreased prostaglandins¹³⁻¹⁶. Ethanol has also been reported to cause gastric mucosal lesions through vasoconstriction and release of vasoactive substances such as histamine, and the production of free radicals which causes a discontinuity to the mucosal cell membrane^{15, 17}.

Free radical scavengers protect the gastric mucosa against alcohol induced gastric ulceration^[18]. Any- ulcer drugs such as ranitidine a H₂ receptor antagonist have been found to reduce mucosa lesions by inhibiting the basal acid production or secretions¹³. While some drugs that offer gastric mucosa protection by either potentiating mucosal defensive mechanism, mucous secretion, production of prostaglandins, increasing mucosal blood flow or decreasing production and or secretion of gastric acid¹³.

The isolated alkaloids of *Cucumis metuliferous* decreased ethanol induced gastric ulceration. Tepermans and Sopper (1990) reported a similar effect in the reduction of gastric acid histamine content in experimental animals administered with isolated flavonoids of *Cucumis metuliferous*¹⁹. Wannang *et al.*, (2009) reported that the pulp extracts of *Cucumis metuliferous* increases mucosal integrity and reduces the volume of gastric acid in mice. The result of this current study showed that the anti-ulcer properties of *Cucumis metuliferous* could be related probably in parts to its alkaloidal constituents.

CONCLUSION: The isolated alkaloids of *Cucumis metuliferous* has demonstrable dose dependent anti-ulcer properties and offered gastric mucosal protection in mice.

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