Trop J Nat Prod Res, June 2019; 3(6):195-200

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Evaluation of the Spasmolytic and Antiulcer Effect of The Fruit Extract and Fractions of *Cucumis metuliferus*

Ebere E. Okpalaeke, Stella A. Ihim*, Emmanuel I. Peter, Nneoma M. Ofokansi, Chukwuemeka S. Nworu

Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka, 410001, Enugu State, Nigeria.

ARTICLE INFO

Article history:
Received 05 March 2019
Revised 25 June 2019
Accepted 04 July 2019
Published online 09 July 2019

ABSTRACT

The plant *Cucumis metuliferus* (Cucurbitaceae) locally called 'bùurarzaàki' is used by traditional medical practitioners in parts of Plateau state of Nigeria to treat disease such as peptic ulcer, diabetes mellitus, hypertension and HIV/AIDS. This study was undertaken to give credence to the traditional use of *Cucumis metuliferus* in the treatment of peptic ulcers.

The methanol extract of the fruit plant material was fractionated sequentially using n-hexane, ethyl acetate, butanol and water to yield HFCM, EAFCM, BFCM and WFCM fractions, respectively and evaluated for antiulcer properties using experimentally-induced ulcers in mice and rats. *In vitro* antiulcer activity was also evaluated.

Ethanol-induced ulcer was significantly ($p<0.05$) protected by MECM (100, 200 and 400 mg/kg). The extracts MECM (100, 200 and 400 mg/kg), EAFCM (200, 400 mg/kg), and WFCM (200, 400 mg/kg) exhibited dose-dependent and significant ($p<0.05$) protection of rats against indomethacin-induced ulcers. Gastrointestinal propulsion in mice was significantly ($p<0.05$) reduced in a dose-dependent manner with MECM (400 mg/kg) and WFCM (400 mg/kg) showing the highest level of antiperistaltic activity. The contractions evoked by acetylcholine and histamine on the rabbit jejunum were antagonized by the extracts and fractions in a concentration-dependent antispasmolytic manner. Acute toxicity tests showed an oral LD_{50} greater than 5000 mg/kg in mice. Rich varieties of bioactive constituents in MECM include alkaloids, terpenoids, flavonoids, carbohydrates and steroids. These findings demonstrated that the plant possesses pharmacological properties which lend credence to its ethnomedicinal use as an antiulcer and antidiarrhoeal agent.

Keywords: *Cucumismetuliferus*, peptic ulcer, antispasmolytic, antiulcer.

Introduction

Gastrointestinal disorders are part of the most significant causes of morbidity and mortality for the human population. One of such major chronic gastrointestinal disorder affecting a noticeable proportion of about 8 – 10% of people around the globe is peptic ulcer.[1] Peptic ulcer disease refers to a heterogenous group of condition with painful sores or ulcers in the lining of the stomach or the first part of the small intestine, the duodenum, which impairs the quality of life. Every year, peptic ulcer disease affects 4 million people around the world.[2] Peptic ulcers are caused by an imbalance between protective factors in the stomach such as acid-pepsin secretion, integrity of the mucosal barrier, mucus secretion, blood flow, cellular regeneration, prostaglandins, growth factors and endogenous aggressive factors.[3,4]

Although potent anti-ulcer medications are available, majority of them produce several toxicities. In addition, reports on clinical evaluation of these drugs show that there are incidences of relapse, adverse effects and the danger of drug interactions during ulcer therapy thus the need for new and novel alternative molecules which afford better protection and decrease the incidence of relapse.[5-7]

Harnessing the abundance and validating the efficacy of medicinal plants used in folk medicines for the treatment of peptic ulcer is a promising approach to overcoming the limitations of orthodox medicines. Numerous experimental studies have demonstrated that medicinal plants have gastro-protective activity against gastric mucosal injury. The plant *Cucumis metuliferus* (*C. metuliferus*) is a monoecious annual herb belonging to the family Cucurbitaceae. In Nigeria, it is locally called 'bùurarzaàki', 'nòòonon-kuùraà', 'gautar kaji'.[8-10] The plant *C. metuliferus*is used by traditional medical practitioners in certain parts of Plateau state of Nigeria to treat disease such as peptic ulcer, diabetes mellitus, hypertension and HIV/AIDS.[11] 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 anthelmintic properties.[12] The fruit pulp has been reported to increase sperm/semen integrity.[13] Pharmacologically, several effects have been reported such as its haematological effects by increasing the values of blood parameters: packed cell volume, haemoglobin, red blood cell and white blood cell counts;[14] analgesic effects during childbirth using the root;[15] antiviral and anti-leukemic activities;[16] anti-microbial activity against *Salmonella gallinarium in vitro*;[17] reproductive effects;[11] anti-diabetic effects[18,19] and anti-protozoan activity.[20]

However, there is still a paucity of data on the anti-ulcerogenic activity of its fruit extract and fractions in man or animal to support the use of the plants by some traditionalist and locals as a remedy in many gastrointestinal ailments, including its use as anti-ulcer treatment. It is against this background that this research was conducted, aimed at evaluating the anti-ulcer activity of the methanol extract and fractions of the fruit of *Cucumismetuliferus* in experimentally-induced ulcers in rats.

*Corresponding author. E-mail: ihim.stella@unn.edu.ng
Tel: +2348039576748

Citation: Okpalaeke EE, Ihim SA, Peter EI, Ofokansi NM, Nworu CS. Evaluation of the Spasmolytic and Antiulcer Effect of The Fruit Extract and Fractions of *Cucumismetuliferus*. Trop J Nat Prod Res. 2019; 3(6):195-200. doi.org/10.26538/tjnpr/v3i6.3

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Materials and Methods

Collection and authentication of plant materials

The ripened fruits of *Cucumis metuliferus* were collected from a cultivated in Gwong, Jos North Local Government Area of Plateau State, Nigeria in December, 2015. The whole plant was identified and authenticated by Prof. C. O. Akueshi, of the Department of Botany, University of Jos, Nigeria. A dried voucher specimen was preserved in the herbarium of the Department of Pharmacognosy, University of Jos, Nigeria for future reference with specimen voucher no. UJ/TCG/HSP/07C23.

Preparation of plant material

The fruits were washed, sliced into smaller pieces and air-dried on an aluminum plate maintained at 35^{o}C – 40^{o}C, then pulverized. The fine powder (300 g) was extracted by maceration for 24 h in 2.5 L of 80% methanol with intermittent agitation. The solvent derived extract was concentrated *in vaccuo* using a rotary evaporator at 40^{o}C. The percentage yield of the extract was determined. The dried extract was placed into clean sample bottles and preserved in a refrigerator at -20^{o}C for future use.

Solvent-guided fractionation of MECM and bio-activity guided studies

A portion of the aqueous methanol extract (MECM) (10g) was partitioned using solvents of increasing polarity in the following order: n-hexane, ethyl acetate, butanol and water. The fractionation was achieved by mixing the aqueous methanol extract (10 g) with different solvents (100 mL) separately in a separating funnel and the mixture was shaken vigorously and allowed to stand for 30 min. The fractions were collected and the solvents evaporated to dryness as described earlier. The aqueous extract was freeze-dried. The fractions obtained were HFCM, EAFCM, BFCM and WFCM for n-hexane, ethylacetate, butanol and water fractions, respectively.

Phytochemical analysis

The extracts were subjected to phytochemical analysis according to standard procedures.[21,22]

Experimental Animals

Adult healthy animals of either sex comprising of Wister rats (180 - 200 g), Swiss albino mice (28 - 32 g), guinea pigs (350 - 400 g) or New Zealand rabbits (1.5 - 3.0 kg) were used in the study. The mice and rats were procured from the laboratory animal facility of the Department of Pharmacology, Faculty of Pharmaceutical Sciences, University of Jos, Nigeria. The animals were housed in the institutional facility under standard condition (25 ± 2^{o}C and 12 h light/dark cycle) and were maintained on standard livestock pellet (Vital feeds, Jos, Nigeria). The Guinea pigs and rabbits were sourced locally, maintained on guinea grass (*Panicum maximum*) and acclimatized in the animal facility for two weeks before being used for the experiments. All the animals had access to clean water*ad libitum*. The study was done in accordance to local Institutional Ethical guideline and in line with the European Union Directives for the Protection of Animals used for Experimental and other Scientific Purposes (EU Directive: 2010/63/EU) of 2010.

The acute toxicity (LD_{50}) of the MECM and Fractions

The acute toxicity of MECM was estimated in mice by the oral route using the method of Lorke.[23]The tests involved two phases: the first phase involved determination of the toxic range. The mice were placed in groups and MECM (10, 100, and 1000 mg/kg) was administered by oral gavage (per os) dissolved in distilled water. The treated mice were then monitored for 24 h for mortality. The death pattern in the first phase determined the doses used for the second phase. Since there was no deaths recorded in the first phase, a fresh batch of three mice with 1 animal per group, received 1600, 2900 and 5000 mg/kg of the extract. The mice were observed for lethality and signs of acute intoxication for 24 h. The LD_{50} was then calculated as the geometric mean of the highest non-lethal dose and the least toxic dose.

Anti-ulcer activity tests

The ethyl acetate and butanol fractions (EAFCM and BFCM) were prepared as suspensions in 5% Tween 20 while the methanol extract and water fraction (MECM and WFCM) was prepared in distilled water and tested orally for antiulcer activity, using six gastric ulcer experimental models.

Ethanol-induced gastric ulcer

The anti-ulcerogenic assay was adapted from the method of Robert[24] with slight modification. Briefly, rats were randomized into five groups (n=5) and deprived of food 24 h prior to the experiment. Group I served as the negative control and received 5 mL/kg normal saline. Mice in group II were treated with omeprazole 20 mg/kg and served as the positive control. Mice in groups III, IV and V were administered MECM (100, 200 and 400 mg/kg; *per os*). One 1 h after drug treatment, ethanol (1 mL of 96 %v/v) was administered to the animals orally to induce gastric ulceration. One hour later, all the animals were sacrificed under chloroform anesthesia, [25] the stomachs were excised and opened along with the greater curvature to expose the gastric mucosal layer. In the incised stomach, the mucosa was rinsed slowly with water and the stomach pinned flat on a corkboard and observed using a hand lens. Erosions formed on the glandular portions of the stomach were counted and each given a severity rating on a 0-3 scale based on the diameter of the ulcer (0- no ulceration; 1-ulcers ≤ 1mm; 2- ulcers ≥ 1 mm ≤ 2 mm; 3- ulcers > 3 mm). The total ulcer score for each stomach divided by a factor of 10 was calculated for each animal and expressed as ulcer index (U.I). The degree of ulcer protection was calculated as a percentage with respect to the mean ulcer index of the negative control group. The procedure was repeated for the ethyl acetate (EAFCM), butanol (BFCM) and water (WFCM) fractions at 100, 200 and 400 mg/kg doses.

Indomethacin-induced gastric ulcer

The effect of MECM and its fractions on gastric ulcer in rats was evaluated by the indomethacin-induced gastric ulcer model. The rats were randomly assigned into five groups (n=5) and pretreated as in the ethanol-induced ulcer. Rats were fastedfor 24 h before treatment. Indomethacin (100 mg/kg) was administered orally 1 h after drug treatment. After 8 h, the animals were sacrificed under chloroform anaesthesia, their stomachs dissected, opened along the greater curvature, rinsed and stretched on cork boards.[26]The degree of ulcer protection was also calculated as in the ethanol-induced model. The procedure was repeated for the ethyl acetate (EAFCM), butanol (BFCM) and water (WFCM) fractions at 100, 200 and 400 mg/kg doses.

Hypothermic resistant stress induced gastric ulcer

Adult swiss albino rats (of either sex) were divided into five groups (n=5) and pretreated as in ethanol-induced ulcer. The rats were then deprived of food for 24 h, but allowed free access to water. One (1) h after oral drug administration, the rats were immobilized individually in retraining cages at a temperature of 4 ± 1^{o}C for 2 h.[27,28] The stomachs were excised, opened along the greater curvature, washed, stretched on cork plates and the inner surface examined for the presence of lesions with a hand lens. The ulcer index per animal was also calculated as in the ethanol-induced ulcer model. The procedure was repeated for the ethyl acetate (EAFCM), butanol (BFCM) and water (WFCM) fractions at 100, 200 and 400 mg/kg doses.

Gastrointestinal Transit time Tests

Swiss albino mice were starved for 24 h prior to the experiment but were allowed unrestricted access to water prior to the experiment. They were randomized into five groups (n=5). Group I served as the negative control and received normal saline (5 mL/kg). Group II served as the positive control and received atropine(10 mg/kg). Groups III, IV and V were treated with various doses of MECM (100, 200 and 400 mg/kg, respectively) per oral. The procedure was repeated for ethyl acetate, butanol and water fractions. One hour after drug treatment, each mouse received 0.5 mL of charcoal meal (5% deactivated charcoal in 10% aqueous tragacanth powder) orally. 30 min later, each animal was anaesthetized with chloroform and the intestine carefully removed and displayed. The intestinal distance moved by the charcoal meal from the pylorus was measured and expressed as a percentage of the distance from the pylorus to the ileocaecal junction for each animal.[29]

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Studies on isolated gut preparations

The effects of MECM on isolated guinea pig ileum and isolated rabbit jejunum preparations were studied. Segments of the tissues, 2-3 cm long were suspended in 50 mL organ bath filled with Tyrode solution of composition (mM/L): NaCl-8.0, KCl-0.2, $CaCl_2$-0.2, $NaHCO_3$-0.1, $NaHPO_4$-0.05, $MgCl_2$ - 0.1 and glucose - 1.0, maintained at 37 ± 1^oC and aerated with air. The preparations were set up under resting tension of 1 g and allowed to equilibrate for 60 min during which the bathing fluid was changed every 15 min. At the end of the equilibration period, the effects of graded concentrations of extracts (MECM, EAFCM, BFCM, and WFCM) on the guinea pig ileum preparation and on the rhythmic movement of the rabbit jejunum preparation were determined. The various doses of the extracts used were 0.01 mg/mL, 0.1 mg/mL, and 1 mg/mL. The effect of the extract on histamine and acetylcholine-evoked contractile responses of guinea pig ileum was also studied. The contact time of activity for each treatment concentration was 15 sec with a tissue recovery period of1 min between drug additions. Responses were determined in triplicate and recorded on a kymograph 10550 through a frontal writing lever.

Statistical Analysis

The results are expressed as mean ±SEM (n =5). Statistical comparisons were performed by one way analysis of variance using GraphPad Prism® 6 software followed by a Duncan's post *hoc* test. Differences between means observations were considered significant at $P < 0.05$.

Results and Discussion

The methanol extract of *Cucumismetuliferus* yielded 26.67% w/w of MECM while the yield of the various solvent fractions (HFCM, EAFCM, BFCM and WFCM) were 3.27% w/w, 6.88% w/w, 11.33% w/w and 74.69 % w/w, respectively. The oral administration of the extract up to 5000 mg/kg did not produce lethality or signs of acute toxicity in mice after 48 h. The phytochemical analysis of MECM shows that it is rich in a variety of bioactive constituents such as alkaloids, terpenoids, flavonoids, carbohydrates and steroids. The fractions showed varying presence of components such as terpenoids, saponins, alkaloids, carbohydrates, flavoniods and cardiac glycosides. The n-hexane fraction only showed the presence of steroid, hence it was not used in the experiment.

Effect of MECM and fractions on ethanol-induced gastric ulcer

In the ethanol-induced ulcer model, the administration of MECM and the fractions of *Cucumismetuliferus*at all doses reduced the ulcer indices of the treated groups. However a higher and significant (P<0.05) ulcer protective effect was recorded for the MECM extract. The ulcer indices at 400 mg/kg dose of MECM was comparable to the standard drug Omeprazole (Figure 1).

Effect of MECM and fractions on indomethacine-induced mucosal ulcer

The result showed a significant (P<0.05) inhibition of gastric mucosal lesions induced by indomethacin in a dose-dependent manner. Only MECM at all doses tested (100, 200 and 400 mg/kg) showed significant protection when compared to the negative control group (27.8%, 36.89% and 69.67%, respectively). EAFCM and WFCM (200 and 400 mg/kg) also produced potent inhibitions compared to the negative control except the 100 mg/kg dose which was high but not significant (P>0.05) (Figure 2).

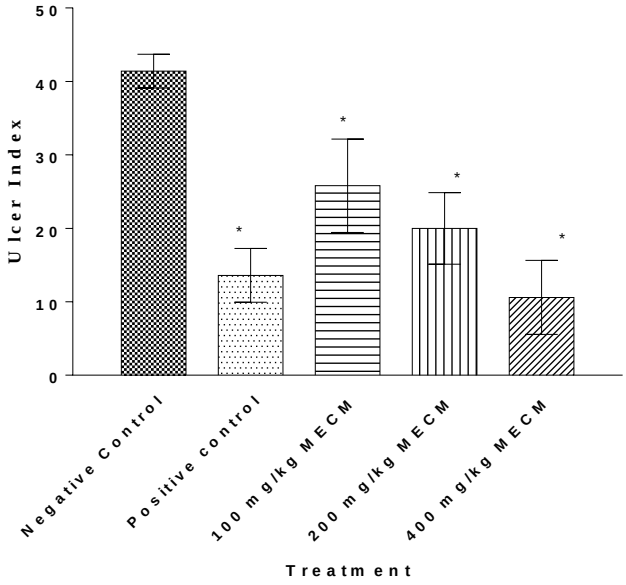

Figure 1: Effect of Methanol Extract (MECM) of *Cucumis metuliferus* on Ethanol-induced Ulcers in Rats. * Significant at $P < 0.05$, Treatment versus Negative control; n = 5.

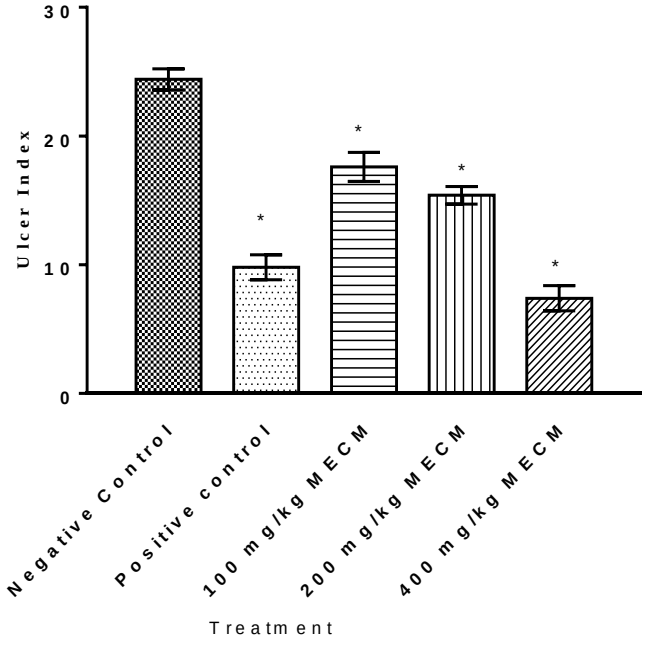

Figure 2: Effect of Methanol Extract of *Cucumismetuliferus*on Indomethacin-induced Ulcers in Rats. * Significant at $P < 0.05$, Treatment versus Negative control; n = 5.

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

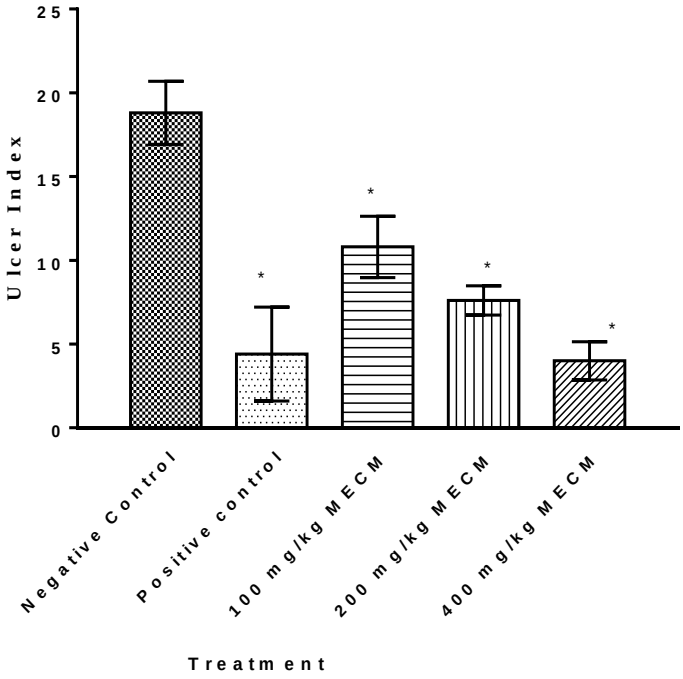

Figure 3: Effect of Methanol Extract of *Cucumismetuliferus*on Hypothermic Restraint Stress-induced Ulcers in Rats. * Significant at $P < 0.05$, Treatment versus Negative control; n = 5.

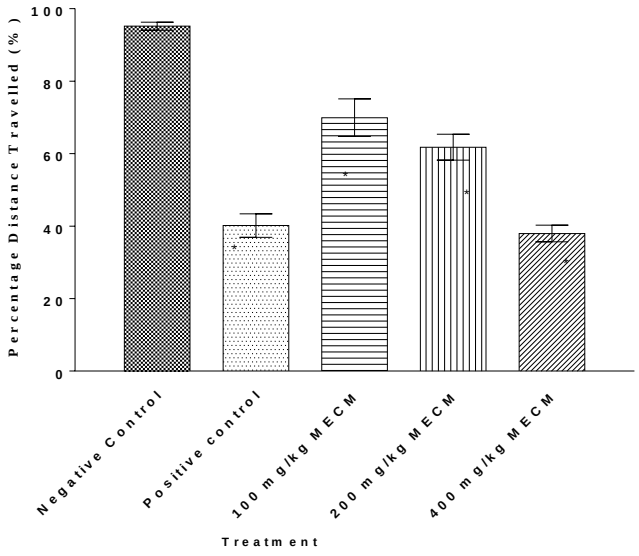

Figure 4: Effect of Methanol Extract of *Cucumismetuliferus*on Gastrointestinal Transit time in Mice. * Significant at $P < 0.05$, Treatment versus Negative control; n = 5.

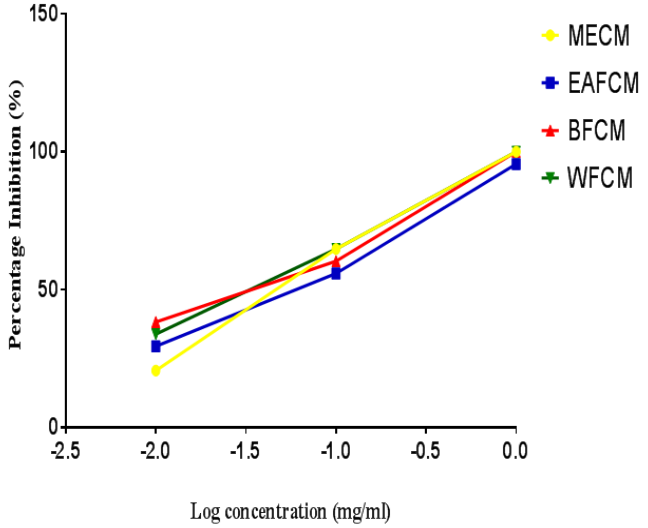

Figure 5: Effect of methanol extract and fractions on contractile response induced by histamine on guinea pig ileum. MECM – Methanol crude extract of *Cucumismetuliferus*; EAFCM – Ethyl Acetate Fraction; BFCM – Butanol Fraction; WFCM – Water Fraction.

Effect of MECM and fractions on hypothermic restraint stress induced ulcer

MECM and its fraction conferred some degree of protective effects against ulcers induced by stress cold restraint as shown by the reduced ulcer indices in the treated group of animals. Significant ($P<0.05$) gastro-protective effect was shown by MECM and all its fractions when compared to the control group except EAFCM at 100 mg/kg dose. The inhibition produced by 400 mg/kg dose of MECM (78.72%) was comparable to the ulcer inhibition produced by the standard drug Omeprazole (76.60%) (Figure 3).

Effect of MECM and fractions on gastrointestinal propulsions

Administration of the extracts reduced the gastrointestinal propulsion in mice ($P<0.05$) in a dose-dependent manner. In the control group, the charcoal meal plug traversed 57.80% of the length of the intestine while BFCM (400 mg/kg) traversed 41.80%, MECM (400 mg/kg) traversed 60.11%, EAFCM (400 mg/kg) traversed 23.98% and WFCM (400 mg/kg) traversed 61.68%. MECM and WFCM showed the highest levels of antiperistaltic activity and reduced the distance traversed by the charcoal meal significantly (Figure 4).

Effect of MECM on isolated smooth muscle preparations

The methanol extract did not show inherent spasmogenic effect on the isolated guinea pig ileum. Increasing concentrations of the extracts and fractions did not elicit contractile response on the isolated guinea pig ileum but produced a dose-related inhibition of the contractile response to histamine and acetylcholine (Figure 5). On the isolated rabbit jejunum, the methanol extracts and fractions showed a concentration-dependent antispasmolytic effect.

Investigations into the pathogenesis of peptic ulcer have revealed that whenever there is a shift in balance between protective factors in the stomach such as acid-pepsin secretion, integrity of the mucosal barrier, mucus secretion, blood flow, cellular regeneration, prostaglandins, growth factors and endogenous aggressive factors.[3,30] Therefore diverse therapies are aimed at augmenting mucosal defense or inhibiting gastric secretions.[31] The evaluation of medicinal plants as a means of identifying potential lead gastro-protective compounds is now a priority.[32] This study was undertaken to investigate the claim that the fruits extract of *C. metuliferus*is effective in the management of gastrointestinal dysfunctions especially peptic ulcer disease. Multiple

aetiologic factors abound in ulcer pathogenesis and the ability of the extract to protect against indomethacin-induced gastric erosion points to its potential to inhibit one or more inciting stimuli in ulcerogenesis.[33] The extract and fractions protected rats against gastric ulcers induced by indomethacin and ethanol, inhibited gastrointestinal motility by reducing small intestinal propulsion and exhibited spasmolytic effects by inhibiting jejunal contractions and antagonizing the contractions of the isolated intestinal tissues evoked by acetylcholine and histamine.

In this study, the extracts of *Cucumismetuliferus* potently inhibited ethanol-induced ulcers in rats. Ethanol has been identified as a major risk factor for the development of gastric ulcers.[34] Ethanol-induced gastric mucosal lesions are known to be caused by direct toxic action of ethanol, reduction in bicarbonate secretion and depletion of gastric wall mucous.[35] Ethanol is known to increase the release of histamine, influx of calcium ions, generation of free radicals through lipid peroxidation while reducing endogenous glutathione and prostaglandins.[36] This action destroys the protective mucosal layer and renders cells of the stomach lining exposed to the proteolytic and hydrolytic actions of gastric acid.[34] This inhibition of ethanol-induced gastric mucosal lesion therefore indicates the cytoprotective potential of the methanol extract of *Cucumismetuliferus*and its fractions. It may be possible that the extract and its fractions act by promoting or augmenting any of the mucosal defense factors. Further studies are required to investigate the precise mechanism.

The methanol extract and fractions of *Cucumismetuliferus* showed significant (p<0.05) protection of rats against indomethacin-induced ulcers. Indomethacin and related non-steroidal anti-inflammatory drugs (NSAIDs) are known to induce gastrointestinal ulceration by inhibiting the biosynthesis of prostaglandins which are important in the gastrointestinal mucosal repairs,[37] suppressing acid secretions, stimulating gastric mucus and bicarbonate secretion as well as augmenting and maintaining mucosa blood flow thus offering gastroprotective effects.[38]Consequently, the potential of the extract and its fractions to significantly protect the animals against ulcer induced by indomethacin signifies possible cytoprotective activity. Although further studies are required to further elucidate the mechanism.[39,40]

Hypothermic restraint stress induced ulcers are associated with histamine released during stress resulting in increased gastric acid secretion and decreased mucus production,[41] thus a decrease in pH.[42] MECM and its fractions showed significant (p<0.05) protection against stress ulcers. Some studies have suggested the leukotriene-C4 (LTC4) a lipoxygenase derived metabolite of arachidonic acid acts on the gastric microvasculature constricting sub-mucosal venules with subsequent statis of blood flow and plasma leakage from vascular beds causing mucosal injury thus playing a prominent role in stress-induced ulcers.[43]

Studies on gastrointestinal motility showed that MECM as well as its fractions inhibited peristaltic propulsive movement indicating a dose-dependent inhibition of gastrointestinal motility. Wound healing is hastened and ulcer pains reduced with reduced gut movement.[44]Thiscorrelates with the results noted in the *in vitro* studies. The results of the isolated intestinal tissues studies reveals that neither MECM nor its fractions relaxed or contracted the guinea pig ileum but potently and significantly inhibited the spasmogens– acetylcholine and histamine- induced contractions in a concentration-dependent pattern suggesting a non-specific spasmolytic effect.[32] This is a desirable property of a putative antiulcer agent.[44] Acetylcholine and histamine have been implicated in the pathogenesis of ulcer as both neurotransmitters stimulate and regulate gastric acid secretion,[45] therefore inhibition of their activity is important to providing beneficial effect in anti-ulcer therapy by reducing gastric acid secretion. Although the MECM antagonized the contractile responses to the spasmogens on isolated tissues, conclusion may not be drawn from this in associating the anti-ulcer properties of *Cucumismetuliferus*to the inhibition of these spasmogens which are important in ulcer pathology.

Lastly, MECM and its fractions also antagonized the spontaneous rhythymicpendular contractions of the isolated rabbit jejunum and this is consistent with the reduction elicited in the gastrointestinal motility model and could be found useful in the management of peptic ulcer.[46] Overall, MECM showed better antiulcer effect than the other fractions.

The plant extract could generally be regarded as safe since the LD_{50} value suggests remote risk of acute intoxication at a single dosing.[23] The anti-ulcer effect of the extract and fractions could result from the presence of one or several phytochemicals in the plant as it appears to possess non-specific gastro-protective activity against ulcers induced by different ulcerogens acting through different mechanisms. The extracts of *Cucumismetuliferus*contains flavonoids, terpenoids, alkaloids, carbohydrates and steroids Previous studies have associated some of these bioactive constituents with cytoprotectiveand anti-ulcer effects. Flavonoids which occur in relative abundance in this plant have been demonstrated to antagonize the effects of histamine which is a major mediator in ulcerogenesis.

Conclusion

The methanol fruit extract of *Cucumismetuliferus* and its fractions protected rats against ulcers induced by several ulcerogens*in vivo* and *in vitro.* We therefore postulate that the non-specific cytoprotective effect of the plant may be due to its potential to augment mucosal defense mechanism. Efficacy claims in the traditional use of this plant could be proven with this study. Further studies will be required to elucidate the precise constituent responsible for the anti-spasmodic activity of *Cucumismetuliferus.*

Conflict of Interest

The authors declare no conflict of interest

Author's Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this work will be borne by them.

Acknowledgements

The authors wish to acknowledge the use of the laboratory facility of the Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, University of Jos.

References

1. Klein-Junior LC, Gandolfi RB, Santin JR, Lemos M, Cechinel FV, Andrade SF. Antiulcerogenic activity of extract, fractions, and some compounds obtained from *Polygolacyparissias* St Hillaire&Moquin (Poligalaceae). NaunynSchmiedebergs Arch Pharmacol. 2010; 381:121-126.
2. Zelickson MS, Bronder CM, Johnson BL,Camunas JA, Smith DE, Eawlinson D, Von S, Stone HH, Taylor SM. Helicobacter pylori is not the predominant etiology for peptic ulcers requiring operation. Am Surgeon J. 2011; 77:1054-1060.
3. Freitas CS, Baggio CH, Finau J, Anginoni M, Pizzolatti MG, Santos AR, Marques MA. Inhibition of H+/K+ ATPase in the gastroprotective effect of Baccharisillinita DC. J Pharm Pharmacol. 2008; 60:1105-1110.
4. Gosh S and Kinnear M. Peptic ulcer disease. In: clinical pharmacy and therapeutics. Roger W(Ed) (3rd Ed).Churchill living stone; 2003. 143-161 p.
5. Howden CW, Jones DB, Peace PK, Burget DW, Hunt RH. The treatment of gastric ulcer with antisecretory drugs: relationship of pharmacological effect to healing rates. Dig Dis Sci. 1988; 33:619-624.
6. Akah PA, NnaetoOluchi, Nworu CS, Ezike AC. Medicinal plants used in the traditional treatment of peptic ulcer diseases: a case study of *Napoleonavogelii* Hook and Planch (Lecythidaceae). Res JPharmacol. 2007; 1(3):67-74.
7. Akah PA, John-Afica L, Nworu CS. Gastroprotective properties of *Ocimumgratissimum*L. against experimental ulcers in rat. IntJ Pharmacol. 2007; 3(5):461- 467.

8. Burkill HM. Useful Plants of West Tropical Africa. Vol.1 (2nded). Royal botanic gardens, London; 1985. 570-605 p.
9. Anon A. Mienkie Welman National Herbarium, Pretoria 2009. http://www.plantzafrica.com/planted /cucumismet.htm. Accessed on 15th March 2016.
10. Jimam NS, Wannang NN, Anuka JA, Omale S, Falang JD, Adolong AA. Histopathologic effects of *Cucumismetuliferus* E. Meyer (Cucurbitaceae) fruits in albino rats. IntJ Pharm Sci Res. 2011; 2(8):2190-2194.
11. Wannang NN, Jiman NS, Gyang SS, Saleh G. Effects of *Cucumismetuliferus* E. Meyer ex. naud. (Cucurbitaceae) fruit extract on some male reproductive parameters in adult rats. Afr J Pharm Pharmacol. 2008; 2(3):48-51.
12. Cheiji R. Encyclopedia of medicinal plants. MacDonald 15 BUO, 1984; 356:10541-10545.
13. Wannang NN, Jimam NS, Omale S, Aguiyi JC. Effects of *Cucumismetuliferus* (Cucurbitaceae) fruits on enzymes and haematological parameters in albino rats.AfrJ Biotech. 2007; 6(22):2515-2518.
14. Usman JG. Phytochemical screening and antibacterial effects of *Cucumismetuliferus* (Jelly Melon) E. Meyer. Ex naudin (Cucurbitaceae) fruits against fowl typhoid. A dissertation submitted to the school of postgraduate studies, University of Maiduguri, in partial fulfilment of the requirement for the degree of master of science in Pharmacology 2014. 155 p.
15. Roodt V. Common wild flowers of the Okavango Delta; medicinal uses and nutritional value. 1998. The shell Field Guide Series: Part II.
16. Moore PS and Pizza C. Observations on the inhibition of HIV-1 reverse transcriptase by catechins. Biochem J. 1992; 288:717-719.
17. Usman JG, Sodipo OA, Kwaghe AV, Sandabe UK. Uses of Cucumismetuliferus.A review. Cancer Biol. 2015; 5(1):24-34.
18. Jimam NS, Wannang NN, Omale S, Gotom B. Evaluation of the hypoglycemic activity of *Cucumismetuliferus* (Cucurbitaceae) fruit pulp extract in normoglycemic and alloxan-induced hyperglycemic rats. J Young Pharm. 2010; 2(4):384-387.
19. Gotep J. Glycosides fraction extracted from fruit pulp of *Cucumismetuliferus* E. Meyer has antihyperglycemic effect in rats with alloxan induced diabetes. J Nat Pharmacol. 2011; 2:48-51.
20. Abubakar A, Iliyasu B, Ojiegbu FN, Igweh AC, Shamaki BU, Dung EC, Domtur LL, Okogun JI, Gbodi TA, Ogbadoyi EO. Evaluation of the antitrypanosomal activity of *Cucumismetuliferus* pulp extract in rabbits.J Med Plant Reseserv. 2011; 5(11):2136-2142.
21. Harborne JB. Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis (3rd ed.) London: Chapman & Hall 1998.
22. Evans WC. Trease and Evans Pharmacognosy (16th ed) Edinburgh: WB Saunders 2009.
23. Lorke D. A new approach to practical acute toxicity testing.Arch Toxicol. 1983; 54:275–287.
24. Robert A, Nezamis JE, Lancaster C, Hanchar AJ, Klepper MS. Cytoprotection by prostaglandins in rats. Prevention of gastric necrosis produced by alcohol, HCl, NaOH, hypertonic NaCl and thermal injury.Gastroenterol. 1979; 77:433-443.
25. Morimoto Y, Shimohara K, Oshima S, Sukamoto T. Effects of the new anti- ulcer agent KB- 5492 on experimental gastric mucosal lesions and gastric mucosal defensive factors, as compared to those of terpenone and cimetidine. Jap J Pharmacol. 1991; 57:495-505.
26. Urishidani T, Kasuya Y, Okabe S. The mechanism of aggravation Indomethacin-induced ulcer by adrenalectomy in rats.Jap J Pharmacol. 1979; 29:775-780.
27. Al-Mashhadani WM, Karim KH, Al- Taie RI, Al-Zahawi HM. Nifedipine versus cimetidine in prevention of stress–induced gastric ulcers in rats. Eur J Pharmacol. 1991; 192:117-121.
28. Akah PA and Nwafor SV. Studies on the anti-ulcer properties of *Cissampelosmucronata* leaf extract. Indian J Exp Bio. 1999; 37:936-938.
29. Nwafor PA, Okwuasaba FK, Binda LG. Anti-diarrhoeal and anti-ulcerogenic effects of methanol extract of *Asparagus pubescens* root in rats. J Ethnopharmacol. 2000; 72:21-427.
30. Venkataranganna MV, Gopumadhavan R, Sundaram R,Mitra SK. Evaluation of possible mechanism of anti-ulcerogenic activity of UL-409 an herbal preparation. J Ethnopharmacol. 1998; 63:187-192.
31. Afifi FU, Khalit E, Tamini SO, Disi A. Evaluation of gastroprotective effects of Laurusnobilisseeds on ethanol-induced gastric ulcer in rats. J Ethnopharmacol.1997; 58:9-14.
32. Nwafor SV and Akah PA. Effect of methanol leaf extract of *Cissampelosmucronata* A Rich against Indomethacin-induced ulcer.Indian J Exp Bio. 2003; 41:181-183.
33. Awaad AS, El-Meligy RM, Soliman GA. Natural products in the treatment of ulcerative colitis and peptic ulcer. J Saudi Chem Soc. 2013; 17(1):101-124.
34. Sener G, Paskaloglu K, Ayanoglu-Dülger G. Protective effect of increasing doses of famotidine, omeprazole, lansoprazole, and melatonin against ethanol-induced gastric damage in rats. Ind J Pharmacol. 2004; 36:171.
35. Marhuenda E, Martin MJ, Alarcon L. Antiulcerogenic activity of aescine in different experimental models. Phytother Res. 1993; 7:13-16.
36. Galvin GB and Szabo S. Experimental gastric mucosal injury: Laboratory models reveal mechanism of pathogenesis and new therapeutic strategy. Fed Am SocExp Bio J. 1992; 6:825-831.
37. Banoob DW, McCloskey WW, Webster W. Risk of gastric injurywith enteric-coated versus nonenteric coasted aspirin. Ann Pharmacother. 2002; 36:163-166.
38. Wightkin WT: Stress ulcer: Pathophysiology and prevention. Am J Hosp Pharm. 1980; 37:1651–1655.
39. Coblijn UK, Goucham AB, Lagarde SM, kuiken SD, Van-Wagensveld BA. Development of ulcer disease after Roux-en -Y gastric bypass, incidence, risk factors, and patient presentation: A systematic review. Obes Surg. 2014; 24:299-309.
40. Yedgar S, Krimsky M, Cohen Y, Flower RJ. Treatment of inflammatory diseases by selective eicosanoid inhibition: A double-edged sword?.Trends Pharmacol Sci. 2007; 28:459-64.
41. Jia YT, Wei W, Ma B, Xu Y, Liu WJ, Wang Y, Lv KY, Tang HT, Wei D, Xia Z . Activation of p38 MAPK by reactive oxygen species is essential in a rat model of stress-induced gastric mucosal injury. J Immunol. 2007; 179:7808-7819.
42. Murakami M, Lam SA, Inada M. Pathophysiological and pathogenesis of acute gastric mucosal lesions after hypothermic restraint stress in rats. Gastroenterol. 1985; 88:660-665.
43. Hua XY, Dahlen Se, Lundberg JM, Hedqvist P. Leukotrienes C4, D4 and E4 causes widespread and extensive plasma extravasation in guinea pig. Naunyn-Schmiedebergs.Arch Pharmacol. 1985; 330:136-142.
44. Mersereau WA and Hinchey EJ. Relationship between myoelectric and mechanical activity in the genesis of ulcers in Indomethacin-insulin treated rats. Dig Dis Sci. 1988; 33:200-208.
45. Hoogerwerf WA and Pasricha PJ. Agents Used for Control of Gastric acidity and treatment of peptic ulcers and gastroesophageal reflux disease. In: J.G.Hardman, L.E.Limbird, A.G.Gilman(Eds.) .Goodman &Gilman.s The Pharmacological Basis of Therapeutics., (10th Ed). McGraw-Hill, New York, 2001. 1005-1020 p.
46. Brunton LL. Agents for control of gastric acididty and treatment of peptic ulcer. In: The pharmacological basis of therapeutics. (9th Ed). In: Hardman LE, Limbird JG, Molinoff PB, Ruddon RW, Gilman AG (Eds). McGraw-Hill New York, 1996. 901-915 p.