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Research article

EVALUATION OF ANTIULCER ACTIVITY OF ETHANOLIC EXTRACT OF *MOMORDICA DIOICA* ON PYLORUS LIGATURE INDUCED AND IBUPROFEN INDUCED ULCER IN ALBINO RATS

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ABSTRACT

Objective: The aim of the present study is to evaluate the anti-ulcer activity of Ethanolic extract of *Momordica Dioica* in pylorus ligation and ibuprofen induced gastric ulcers in rats. **Methods:** Gastric ulcer was induced by giving ibuprofen (200mg/Kg) and by pylorus ligation method. The animals used for the experiment were divided into 4 groups for each model, 6 rats in each group. **In pylorus ligation model**, all groups of rats were pre-treated with test drugs, Group-I (control) received 2% gum acacia-2ml/100g, Group-II (standard) received Ranitidine (60mg/kg.) and group-III, IV were treated with Ethanolic extracts 150mg/kg, 300mg/kg. respectively orally 30mins prior to pylorus ligation. The Antiulcer activity of *Momordica Dioica* was assessed by determining and comparing gastric volume, free acidity, total acidity, pH, percentage of ulcer protection, ulcer index. **In ibuprofen induced ulcer model**, all groups of rats were treated with test drugs for 7 days prior to ibuprofen induced ulcer. Animals were divided into 4 groups and treated with drugs as in above model. After 7 days of treatment, animals were fasted for 24 hrs. Ulcers were produced by giving ibuprofen (200mg/Kg) on the day of sacrifice. The animals were sacrificed 4 hours later and stomachs were open along the greater curvature and ulcers were graded. Percentage of ulcer protection, ulcer index were observed and calculated. **Results:** The extract of *Momordica Dioica* in pylorus ligation model, it decreased the ulcer index (1.66) and there was a decrease in total gastric acid and free acid ($p < 0.0001$), and increases the pH value ($p < 0.0001$) and also reduces the total gastric volume ($p < 0.0003$), increases the percentage of ulcer protection (61.66%). In ibuprofen induced ulcer model, it decreases the ulcer index (10.66) and increases the ulcer protection (72.09%). **Conclusion:** The Ethanolic extract of *Momordica Dioica* was clearly shows a protective effect against total acid, free acid, gastric volume and ulcer index and also increases pH and percentage of protection against ulcers in both models.

Key words: *Momordica Dioica*, Gastric protection, Ibuprofen, Ulcer Index

INTRODUCTION

Peptic ulcer remains a prevalent condition affecting up to 10% of the population and is responsible for considerable morbidity and loss of work time¹ the high incidence and chronicity of the suffering and decreased ability to work associated with it, has made peptic ulcer an important health problem. An ulcer is thought to develop when the equilibrium is disturbed either by enhanced aggressiveness or by lessened mucosal resistance² Drugs that affect acid and enhance defensive mechanisms are available. Of late, the concept is now changing from chemical pH to microbial Hp (pH= acidity, Hp= H.pylori)³ Flood gates of research on Helicobacter pylori actually opened up when Marshall and Warren in 1984 demonstrated the association between this organism with active chronic gastritis and peptic ulcer⁴ Long term use of NSAIDs can also cause gastric ulcer. Treatment cost is estimated more than 2-4\$ billion per year, so most of the ulcers heal by using synthetic drugs. After 6-8 weeks there is a problem of recurrence of side effects. Therefore people prefer natural product drugs for disease treatment. Over 3 quarters of the world population relieved by plants and plant extracts for health care. More than 30% of the entire plant species at one time or other has been used for medicinal purpose⁵ *Momordica Dioica* is an important medicinal plant with potent anti-inflammatory activity. It contains the various chemical classes such as alkaloids, tannins, flavonoids, carbohydrates. *Momordica Dioica* commonly known as teasel gourd and used as vegetable.¹⁵ *Momordica dioica* Roxb belongs to the family Cucurbitaceae⁶ and under the genus *Momordica*, a genus of annual or perennial climbers that contains about 80 species. *Momordica dioica* climber plant commonly known as Teasle Gourd, Kakrol, Kankro, Kartoli, Kantoli, Kantola, Kantroli, Ban karola or Small bitter-gourd is a relatively small oval to ovoid vegetable. It is also called as janglee karela. It is often cultivated for its fruits, which are used as

vegetable. The Fruits are reported to show anti-inflammatory, anti-ulcer, anti-oxidant, and hepatoprotective⁶. Traditionally this fruit was used in ulcer but scientifically not proved. Hence the present study was aimed to investigate the anti ulcer effect of *Momordica Dioica* in experimental animal models

MATERIALS AND METHODS

Experimental animals: Swiss albino rats weighing 150-200g of either sex were used for this experiment, supplied by authentic animal suppliers Sainath Agencies, Hyderabad, AP, and India. They were randomly distributed into groups and housed in cages (6/cage) and kept under standard conditions at 26±2° C and relative humidity 44-56% and 10 hours light: 14 hrs dark cycles each day for 1 week before and during the experiments. All animals were fed the standard rodent pellet diet and *ad libitum*. This study was cleared by the institutional animal ethics committee according to CPCSEA guidelines.

Plant material: Fresh green fruits of *Momordica Dioica* popularly known as spine gourd were obtained in sufficient quantity from local forest in Eluru, A.P in March 2013. They were carefully washed to remove dust particles and other foreign materials and cut into small pieces dried in shaded areas. The dried pieces of fruit make a fine powder with grinder.

Preparation of alcohol extract: The dried fine powder of the *Momordica Dioica* powder was weighed on balance 30g. and taken into the sac like cloth material and placed in the Soxhlet basket. 300 ml of ethyl alcohol was taken as solvent into the Soxhlet flask. Cold tap water must flow through the inlet and outlet of the condenser. The Soxhlet apparatus kept running for 24hours for proper extraction. The extract laden solvent falling from the Soxhlet basket is dark in color and it becomes clearer, that indicates the extraction process is finished. At the end of the extraction process the solvent is

then evaporated⁷, total yields was 5gm, percentage yield was 16.6% as mg per gm dried powder. The extract 600mg was suspended in 2ml of 2% Gum acacia and administered according to dose mentioned as below by oral route.

Experimental design: The animals used for the experiment were divided into 4 groups for each model, 6 rats in each group.

In Pylorus ligation model: All groups of rats were pre-treated with test drugs, Group-I (control) received 2% gum acacia-2ml/100g, Group-II (standard) received Ranitidine (60mg/kg)⁸ and group-III, IV were treated with Ethanolic extracts 150mg/kg, 300mg/kg respectively orally 30mins prior to pylorus ligation. After giving drugs all groups of animals were anesthetized with ether and lower abdominal wall was opened and pyloric end was ligated. Then abdominal wall was closed with interrupted sutures. During this procedure strict aseptic conditions were maintained to prevent infections. After 4 hours of pylorus ligation, animals were sacrificed and stomach was opened along with the greater curvature and total gastric contents were collected and centrifuged. The Antiulcer activity of *Momordica Dioica* was assessed by determining and comparing gastric volume, free acidity, total acidity, pH, percentage of ulcer protection, ulcer index.

In the Ibuprofen induced ulcer model, all groups of rats were treated with test drugs for 7 days prior to ibuprofen induced ulcer. Animals were divided into 4 groups and treated with drugs as in above model. After 7 days of treatment, animals were fasted for 24 hrs. Ulcers were produced by administration of ibuprofen (200mg/Kg)⁹. The animals were sacrificed after 4 hours administration of ibuprofen and stomachs were open along the greater curvature and ulcers were graded. Percentage of ulcer protection ulcer index were observed and calculated.¹⁰

Gastric juice collection: gastric juice was collected and filtered through glass wool in a

measuring cylinder. The gastric contents were centrifuged at 3000rpm for 5 min, and the supernatant was used for the estimation of total acidity (pH). The volume of gastric juice was expressed as ml/100g of body weight.¹¹

Estimation of total acidity: 1 ml of supernatant was diluted to 10 ml of distilled water. The solution was titrated against the 0.05 ml/L NaOH using phenolphthalein as an indicator. Titration was continued until the color changed to light pink. The volume of NaOH required was noted and was taken as corresponding to the total acidity. Acidity was expressed as Total acidity = (volume of NaOH × Normality × 100)/ 0.1(mEq/L).¹²

The ulcer score was determined by using a 10 × magnifying hand lens. The scoring of severity of ulceration was as follows: 1 mm (pin point)= 1; 1-2 mm=2; >2 mm=3; >3 mm=4. The mean ulcer score was determined by dividing the total ulcer indices in a group by the total number of animals in that group. Ulcer score = total ulcer index (UI) in a group/ total number of animals in that group. The curative ratio of an ulcer was determined by subtracting the test ulcer score from the control ulcer score divided by the control ulcer score. The result was multiplied by 100.¹³

Statistical analysis: The results obtained were expressed as Mean±SEM and were analyzed by the application of One-way Analysis of Variance (ANOVA)

RESULTS

Pylorus ligation method: Extract of *Momordica Dioica* (150mg/Kg, 300mg/Kg) treated animals has shown significant reduction in Ulcer Index, Volume of Gastric juice (p<0.001), total acid and free acid (p<0.001) and also it increases the pH (p<0.001), percentage protection (61.66%) when compared with the control group. Standard drug treatment with ranitidine (60mg/Kg) also showed significant reduction in Ulcer Index, Volume of Gastric juice, total acid and free acid and also increases in pH and percentage of protection (92.37%).

Table 1: Effect of *Momordica Dioica* on pylorus ligation ulcer model (n=6, Mean±SEM)

Group	Treatment	Dose	Gastric contents (Mean±S.E.M)				Ulcer index	% of ulcer protection
			Vol. of gastric juice	Total acid	Free acid	pH		
1	Control-2% GA	2ml/100g	4.70±0.34	94.33±3.59	32.33±1.56	2.03±0.12	4.33	0%
2	Standard-Ranitidine	60mg/kg	2.98±0.15** *	53.33±4.07**	19±1.36*	4.79±0.14**	0.33	92.37%
3	Test-T ₁ -extract	150mg/kg	4.15±0.27*	79.83±4.14*	27.83±0.98*	3.46±0.26*	2.8	35.33
4	Test-T ₂ -extract	300mg/kg	3.18±0.21**	63±2.54**	25.50±1.89*	3.98±0.13**	1.66	61.66

*P<0.05, **P<0.01, ***P<0.001 compared to Control.

Ibuprofen induced ulcer model: Extract of *Momordica Dioica* (150mg/Kg, 300mg/Kg) treated animals has showed significant reduction in Ulcer Grades (p<0.001), Ulcer Index (10.66) with high dose (300mg/Kg) and increase in

percentage of protection (72.09%) when compared to control group. Standard drug treatment with ranitidine (60mg/Kg) also showed significant reduction in Ulcer Index and increase in percentage of protection (95.65%).

Table: 2. Effect of *Momordica Dioica* in Ibuprofen induced ulcer model

Groups	Treatment	Dose	Ulcer grade (Mean±SEM)	Ulcer index	% of ulcer protection
1	Control-2% GA	2ml/100g	33.33±3.33	38.2	0
2	Standard-ranitidine	60mg/kg	1.66±1.66***	1.66	95.65
3	Test-T ₁ -extract	150mg/kg	26.66±2.10*	27.99	26.72
4	Test-T ₂ -extract	300mg/kg	10±4.47*	10.66	72.09

*P<0.05, **P<0.01, ***P<0.001 compared to Control.

DISCUSSION

In spite of tremendous development in the field of synthetic drugs during recent era, they are found to have some or other side effects, whereas plant products or homeo drugs still hold their own unique place by the way of having no side effects. Peptic ulcer disease is a chronic inflammatory disease characterized by ulceration in the upper GI.¹⁴ The pathophysiology of ulcers is due to an imbalance between aggressive factors (acid, pepsin, H.pylori and NSAIDs) and local mucosal defensive factors (mucous, bicarbonate, blood flow and prostaglandins). The integrity of gastro duodenal mucosa is

maintained through a hemostatic balance between these aggressive and defensive factors. The major cause of gastric ulcer is the chronic use of NSAIDs. Therapeutic & adverse effects of NSAIDs have been attributed to the ability of these drugs to inhibit the action of cyclooxygenase (COX). COX is responsible for the synthesis of prostaglandins that normally inhibit acid secretion, as well as having a protective effect on gastric mucosa. Infection of the stomach mucosa with H.pylori—a gram negative spiral shaped bacterium is now generally considered as the major cause of gastro

intestinal ulcers. Treatment includes H₂-receptor antagonists (Cimetidine), proton pump inhibitors (Omeprazole) and cytoprotectives (Misoprostol). Antacids like Aluminium hydroxide & magnesium hydroxide are used often to neutralize excess gastric acidity in the stomach. Due to problems associated with recurrence after treatment, there is a need to seek an alternative drug against gastrointestinal ulcers.¹⁵ The present investigation demonstrated the efficacy *Momordica Dioica* of plant extract against gastric ulceration induced by two experimental models viz. Pylorus ligation induced gastric ulceration and Ibuprofen induced ulceration.

In pylorus ligation model, the plant extract of *Momordica Dioica* produces a decrease in the ulcer number, total gastric volume, total acid, and free acid and increases the pH and percentage of ulcer protection (61.66%) and in standard drug (Ranitidine) treated animals the percentage of ulcer protection (92.37%) when compared with control group (0%). High dose of extract (300mg/Kg) more active than low dose (150mg/Kg) but less active than standard drug (Ranitidine).

In Ibuprofen induced ulcer model, the plant extract of *Momordica Dioica* produces a decrease in the ulcer number and increase in percentage of ulcer protection (72.09%) and with standard drug the percentage of ulcer protection (95.65%) when compared to control group (0%). High dose of extract (300mg/Kg) more active than low dose (150mg/Kg) but less active than standard drug (Ranitidine).

The anti ulcer property of *Momordica Dioica* in both the experimental models explained above, is due to presence of flavonoids, terpenoids, tannins, and triterpenes. The triterpenes are known as an anti-ulcer agent and their action has been mentioned to be due to activation of cellular proteins, reduction of mucosal prostaglandin metabolism, cytoprotective actions and reduction of gastric vascular permeability and remaining compounds have been shown to scavenger free

radicals.¹⁶⁻¹⁸ The results in the present study seem to provide support for the use of *Momordica Dioica* as an anti-ulcer drug in folk medicine. Therefore, also in view of its large use in India further investigations are needed to know about its anti-ulcer activity in human beings.

CONCLUSION

The present study indicates that the plant *Momordica Dioica* has potential anti-ulcer activity against pylorus ligation and Ibuprofen induced ulcers in experimental animals. So this activity of plant probably due to the compounds present such as Flavonoids and triterpenes. So the plant *Momordica Dioica* uses for both Ayurvedic and Modern drug development areas because of its phyto-medicinal uses but it needs further clinical trials before complete trust and usage.

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