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EVALUATION OF ANTIDEPRESSANT, ANTIDIARRHEAL AND ANTIULCERANT ACTIVITIES OF *HYDNOCARPUS KURZII* LEAF EXTRACTS

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ABSTRACT

Hydnocarpus kurzii commonly known as Chaulmugra, found in hill tract areas, are commonly used for the treatment of leprosy and skin diseases for their high medicinal value. The methanolic leaf extract of *H. kurzii* was subjected to perform anti-ulcerant, anti-diarrheal and anti-depressant investigation in albino rats. Anti-ulcerant activity of *H. kurzii* leaf extracts (150, 300 and 600 mg/kg) was evaluated against ethanol induced gastric mucosal injury using omeprazole (20 mg/kg) as standard. In the histological study of rat's stomach showed significant prevention of gastric haemorrhage and edema with dose 600 mg/kg. The leaf extracts (100, 150 mg/kg) were also subjected to Forced swim test to investigate anti-depressant activity using clonazepam (10 mg/kg) as standard. The test showed considerable anti-depressant activity with 31.77% and 41.74% inhibition of 100 mg/kg and 150 mg/kg doses respectively. Castor oil induced diarrheal models were used to evaluate anti-diarrheal activity of the extracts at doses of 100 and 150 mg/kg using Loperamide (3 mg/kg) as standard. The extracts showed statistically significant ($p^*<0.05$) anti-diarrheal activity with 66.66% and 88.88% inhibition of 100 mg/kg and 150mg/kg doses respectively. These results showed that *H. kurzii* leaf significantly reduces haemorrhage and inflammation of gastrointestinal ulcer by regeneration of mucosal layer and showed potential anti-diarrheal activity.

KEYWORDS: *Hydnocarpus kurzii*, antidepressant, anti ulcerant.

INTRODUCTION

Hydnocarpus kurzii (fam.: Achariaceae) a well known plant with high medicinal uses, has been recognized as an important medicinal plant and has an increasingly high demand worldwide. From its traditional uses in health care and food, extensive phytochemical studies have been reported. Its tribal name is Balgach (Chakma) and Taun Paun (Mogh). *H. kurzii* is a medium-sized evergreen tree, 12-15 m high. It has small yellow color flowers. It is native to South-eastern Asia (particularly Burma called today Myanmar and Thailand). In Bangladesh it is found in the forests of Chittagong, Chittagong Hill Tracts, Cox's Bazar and Moulavi Bazar. Hydnocarpus oil and the crushed seed have long been used in Southeast Asia to treat various skin diseases like scabies, eczema, psoriasis, scrofula, ringworm, and intestinal worms. The active principles of the oil (hydnocarpic and chaulmoogric acids) are strongly antibacterial in nature. For this reason Chaulmoogra is employed in Indian medicine to treat leprosy.[1] In China and Argentina the oil is used against cancer. The oil is used to make soaps with a musk-like odor. The bark contains principles capable of reducing fevers. The bark of the tree is said to be used as a febrifuge. Fruits are fish poison. Seeds are usually applied externally as a dressing for skin diseases combined with walnut oil and pork lard for ringworm; with calomel and sesame oil for leprosy; and with sulfur and camphor for scabies.[2]

This plant was investigated chemically and found that it was composed of mixtures of glycerides, fatty acids like hydnocarpic acid, chaulmoogric acid, gorlic acid, oleic acid and palmitic acid. Pharmacologically it showed thrombolytic, anti-oxidant, cytotoxicity, membrane stabilizing, analgesic, antimicrobial, antibacterial activities.[3,8]

MATERIALS AND METHODS

Drugs and Chemicals

Omeprazole was collected from Beximco Pharmaceuticals Ltd and Loperamide was purchased from Square Pharmaceuticals Ltd, Bangladesh. Clonazepam was used as standard for anti depressant test, was collected from Incepta Pharmaceuticals Ltd, Bangladesh. Castor oil was purchased from WELL's Heath Care, Spain. All the chemicals and reagents were analytical grade.

Collection and Preparation of plant extract

The fresh leaves of the plant were collected from Sylhet district of Bangladesh and identified by a taxonomist Hosne Ara, an expert of Bangladesh National Herbarium. A voucher

specimen has been deposited in Bangladesh National Herbarium, Dhaka, Bangladesh under the accession number DACB-41431.

The leaves were washed with water to remove adhering dirt and then cut in small pieces and sun dried for 4-5 days. After that the dried parts were grinded into coarse powder with the help of grinder and stored in an airtight container for further use. The dried plant dust of *H. kurzii* was soaked in a bottle in 1L of Methanol. Then it was kept 8-9 days in room temperature and everyday it was used to shake properly to ensure the maximum amount of constituents present in the grinded plant become soluble into methanol. After 8 days, the whole mixture was done to a coarse filtration by a piece of clean, white cotton material. Then it was filtered through filter paper. The filtrate was then evaporated under reduced pressure to give a dark green viscous mass. The extract was then preserved for the pharmacological study.

Experimental animals

Adult male rats were collected from Jahangirnagar University, Bangladesh. The rats weighed between 130 - 180 g. They were housed in polypropylene cages in groups of six rats per cage and were kept in a room maintained at 25 ± 2◦C with a 12 h light-dark cycle, and were allowed to acclimatize for one week before the experiments. They were given free access to standard laboratory animal feed and water ad libitum.

Experimental Design

Anti ulcer activity

Ethanol induced ulcer[9]

Twenty four experimental animals were randomly selected and divided into six groups denoted as

Group I: Healthy control animals, treated with 85% Distilled water.

Group II: Negative control animals, alcohol induced ulcerated animals treated with saline water 25ml/kg body weight.

Group III: Drug control animals- alcohol induced ulcerated animals treated with Omeprazole (20 mg/kg body weight).

Group IV: Ulcer induced rats treated with plant extract (150 mg/kg body weight).

GroupV: Ulcer induced rats treated with plant extract (300mg/kg body weight) and

Group VI: Ulcer induced rats treated with plant extract (600 mg/kg body weight).

One hour after the drug and extracts treatment, the animals belonging to groups II, III, IV, V and VI were treated with absolute ethanol [5 ml/kg] to induce lesions. The animals were sacrificed after 1 hour and the stomach was opened. The stomachs were excised and inflated by injecting with 0.9% normal saline solution. The excised stomachs were fixed with 10% phosphate buffered solution 15 minutes, and opened along the greater curvature to expose the gastric mucosal layer. Hemorrhagic lesions in the mucosal membrane of the glandular region were observed under a dissecting microscope and were manually scored. After that histological evaluation of gastric lesion were done.

Anti diarrheal activity

Castor oil-induced diarrhea in rats

Castor oil-induced diarrhea was done according to the method of Soba *et al.*[10] and Uddin *et al.*[11]

Sixteen experimental animals were randomly selected and divided into four groups denoted as

Group I: Healthy control animals treated with saline water.

Group II: Drug control animals – castor oil induced diarrheal rats treated with Loperamide (3mg/kg body weight).

Group III: Diarrhea induced animals treated with plant extract (100 mg/kg body weight).

Group IV: Diarrhea induced animals treated with plant extract (150 mg/kg body weight).

All drugs and extracts were given orally to the experimental animals. After one hour, 1 ml castor oil was administered to each of the all animals orally except Group I. The animals were placed in transparent cages to observe the consistency of facial matter (watery, soft or hard) and frequency of defection for four hours. Feces were collected with an absorbent sheet of paper placed below the cages. The total number of diarrheal feces expelled in 4 h was compared with both Group I & Group II.

Anti depressant activity

Forced Swim Test

Antidepressant activity of plant extract was assessed using modified Porsolt test.[12]

Sixteen experimental animals were randomly selected and divided into four groups denoted as

Group-I: Control animals, treated with saline water.

Group-II: Standard control animals, treated with Clonazepam(10mg/kg body weight).

Group-III: Treated with plant extract (100 mg/kg body weight) and

Group –IV: Treated with plant extract (150 mg/kg body weight).

Each group received a particular treatment i.e. control, standard and extracts of *H. kurzii* leaf respectively.

In this method, rats of either sex were individually forced to swim in an open cylindrical container (diameter 10 cm, height 25 cm) containing 19 cm of water. Treatment was given 60 min prior to study as described by study design. All animals were forced to swim for 6 min and the duration of immobility was observed and measured during the final 4 min interval of the test. Each rat was judged to be immobile when it ceased struggling and remained floating motionless in the water, making only those movements to keep its head above water. A decrease in the duration of immobility is indicative of an antidepressant like effect.

1. Immobility: floating in water without swimming.
2. Swimming: active movements of extremities and circling in the container.
3. Climbing: active movements of forelimbs on the container wall.

Statistical Analysis

The values are represented as mean ± S.E.M, and statistical significance between treated and control groups was analyzed using of One way ANOVA, followed by Dunnett's test where $P<0.05$ was considered statistically significant.

RESULTS

Anti-ulcerant activity

Anti-ulcerant activity of *H. kurzii* leaf extracts (150, 300 and 600 mg/kg) was evaluated against ethanol induced gastric mucosal injury using omeprazole (20 mg/kg) as standard. In the histological study of rat's stomach showed significant prevention of gastric hemorrhage and edema with dose 600 mg/kg.

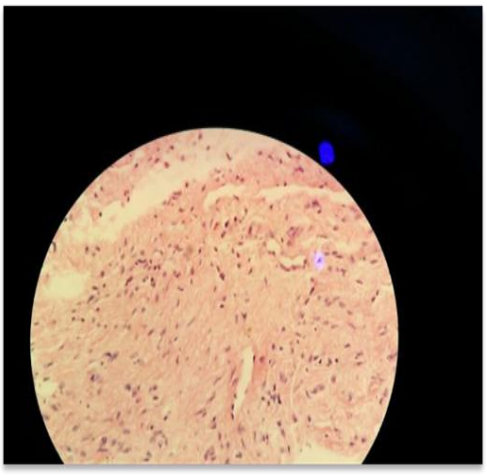

Fig 1: GroupI.

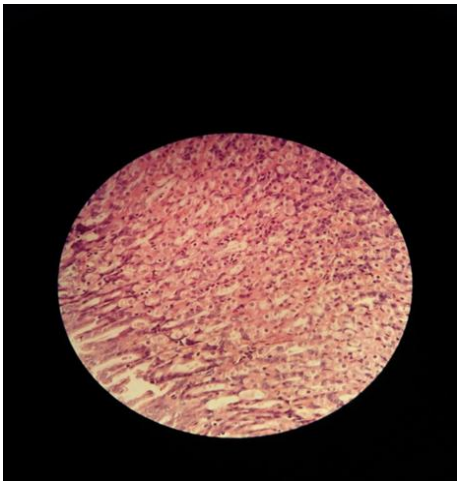

Fig 2: Group II.

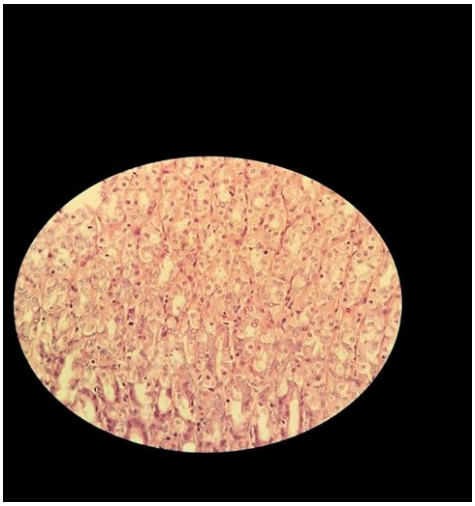

Fig 3: Group III.

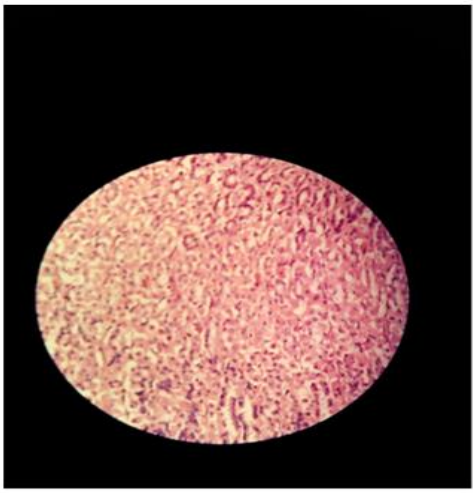

Fig 4: Group IV.

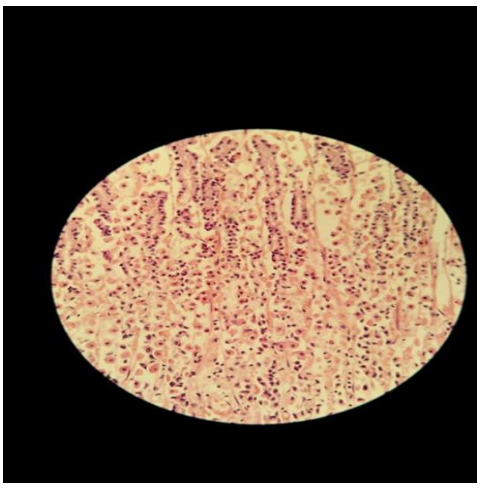

Fig 5: Group V.

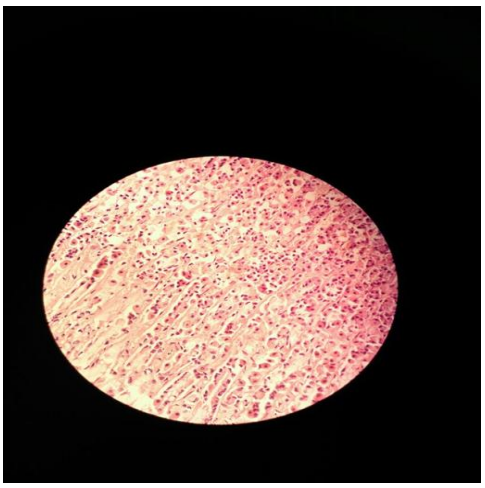

Fig 6: GroupVI.

Anti-diarrheal activity

Castor oil induced diarrheal models were used to evaluate anti-diarrheal activity of the extracts at doses of 100 and 150 mg/kg using Loperamide (3 mg/kg) as standard. The dose showed statistically significant (p*<0.05) anti-diarrheal activity with 66.66% and 88.88% inhibition of 100 mg/kg and 150mg/kg doses respectively. These results showed sufficient anti-diarrheal activity.

Table 1: Effect of *H. kurzii* leaf extracts on Castor oil induced diarrheal rats.

Group	Dose	No. of wet feces in 4h	% inhibition
Normal control	5 ml/kg	2.25±0.5527	
Standard	3 mg/kg	0.75±0.2886*	66.6666*
Leaf extract	100 mg/kg	0.75±0.5527*	66.6666*
Leaf extract	150 mg/kg	0.25±0.2886*	88.8888*

Each value represents Mean ± SEM , n= 4

*significant as compared to control (p< 0.05)

Anti depressant activity

The leaf extracts (100, 150 mg/kg) were also subjected to Forced swim test to investigate Anti-depressant activity using clonazepam (10 mg/kg) as standard. The test showed considerable anti-depressant activity by decreasing immobility time with 31.77% and 41.74% inhibition of 100 mg/kg and 150 mg/kg doses of leaf extracts respectively.

Table 2: Effect of *H. kurzii* leaf extracts on Immobility time of rats in Forced swim test.

Treatment	Dose (mg/kg)	Duration of immobility (sec)
Negative control		80.25±18.3507
Standard (Clonazepam)	10	121.25±32.9051
Leaf extract of *H. kurzii*	100	105.75±35.2274
Leaf extract of *H. kurzii*	150	46.75±14.8501

Each value represents Mean ± SEM , n= 4

DISCUSSION

Anti ulcerant Study

The etiology of peptic ulcer is unknown in most of the cases, yet it is generally accepted that it results from an imbalance between aggressive factors and the maintenance of mucosal integrity through the endogenous defense mechanisms.[13] The causes of gastric ulcer pyloric ligation are believed to be due to stress induced in gastric hydrochloric acid secretion or stasis of acid and the volume of secretion is also an important factor in the formation of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid.[14] The results revealed that ethanol acid administration in the negative control group resulted in massive ulcer formation in comparison with the normal healthy group. However, pre-treatment with omeprazole at the dose of 20mg/kg and methanolic extract of *H. kurzii* at doses 150mg/kg showed slight activity, 300mg/kg showed moderate activity and 600mg/kg showed significant inhibition. Among the test drugs the best result was obtained at an optimum dose of 600mg/kg which was potentially effective as compared with standard drug omeprazole. In the present study, the histopathological examination of the stomach disclosed that oral administration of the plant part suppressed the massive degeneration and accumulation of inflammatory cells in the gastric mucosal layer after ethanol acid challenge. The suppressive effects were observed at all doses of the test drugs.

In this study the extract showed protection against characteristic lesions produced by ethanol acid administration. This antiulcer effect of methanolic extract of *H. kurzii* may be due to both reductions in gastric acid secretion and gastric cytoprotection. Further studies needed for exact mechanism. However, the present investigation concluded that reduced ethanol acid induced ulcer in a dose dependent manner and at the higher dose the effect is similar to that of reference drug.

Anti diarrheal Study

Diarrhea is usually considered a result of altered motility and fluid accumulation within the intestinal tract. One of the main aim of the present study was to evaluate the anti diarrheal activity of the methanolic leaf extract of *H. kurzii* on castor oil induced diarrhea. Castor oil is composed of high content of the hydroxylated unsaturated fatty acid like ricinoleic acid[15] Ricinoleate(90%) of castor oil is the causative agent for diarrhea production.[16] Endogenous prostaglandin is also stimulated by ricinoleate.[17] Prostaglandins (mainly PgE) possess good diarrheogenic properties in experimental animals as well as in human beings. The inhibitors

of prostaglandins biosynthesis may reduce castor oil-induced diarrhea.[18] Most of the anti-diarrheal agents act by reducing the gastrointestinal motility and/or the secretions. Inhibitors of prostaglandin biosynthesis decrease castor oil induced diarrhea.[19] The methanolic extract of the plant showed statistically significant anti diarrheal activity ($p^* < 0.05$) with 66.66% and 88.88% at 100 mg/kg and 150 mg/kg o in rats. Tannins, flavonoids, alkaloids, saponins and steroids of plant extracts have been reported to possess anti-diarrheal activity.[20,21] The leaves of *H. kurzii* possess anti diarrheal property on the basis of these bioactive compounds.

Anti depressant Activity

Depression is an important psychiatric disorder that affects individuals' quality of life and social relations directly. The leaf extract showed antidepressant activity by decreasing the immobility time in forced swim test in rats at 100 mg/kg and 150 mg/kg with 31.77% and 41.74% inhibition respectively which means it has sufficient antidepressant activity. Antidepressants that selectively inhibit norepinephrine uptake reduce immobility and selectively increase climbing without affecting swimming. On the other hand serotonin reuptake inhibitors also reduce immobility but increase swimming instead of climbing.[22] The results of modified forced swim test of the extract didn't show any statistically significance but may increase the consciousness and motility in depression.

CONCLUSION

Medicinal plants being as an important natural resource and potentially safe drugs can play an important role in assuaging human health by contributing herbal medicines. In present study of methanolic extract of *H. kurzii* was subjected to anti ulcer, anti depressant and anti diarrheal test to validate the traditional use and to find out new therapeutic activity. Therefore, further chemical and pharmacological studies on *H. kurzii* will be designed to isolate new bioactive compounds and their exact mode of action and toxicity profile to eventually find the new lead compound.

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