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ANTIULCER ACTIVITY OF METHANOLIC FRUIT EXTRACT OF *LAGENARIA SICERARIA*(MOL.)STANDL.

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ABSTRACT

Lagenaria siceraria(MOL) Standl. is a common plant in India.It is considered laxztive,cardiotonic,diuretic,bitter,emetic,lessen inflammation.In the present study methanol extract(ME) of fruit of *Lagenaria siceraria* have been evaluated for antiulcer activity(100,200mg/kg oral).The antiulcer activity was assayed in four experimental models:Pylorus ligation,Ethanol induced,NSAIDs(ASP) induced, and Cold restraint stress(CRS) induced ulcer.Among the methanolic extract shows significant anti ulcer activity.These statement indicate the presence of ulcer healing drugs present in fruit part of *Lagenaria siceraria*.The result shows that methanolic extract shows antiulcer activity may be because of presence of different chemical compounds present in that extracts.

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Key Words

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INTRODUCTION

Lagenaria siceraria (Mol) standl. is one of the excellent fruit for human being made and gifted by the nature having composition of all the essential constituents that are required for normal and good human health [1]. It is climbing herb, 5 angled stem with stout, tendrils 2 fid leaves often 15cm in diameter, cordate, dentate, 5 angular or 5 lobed, hairy on both surfaces, flower large, white, solitary, monocious or dioecious, fruit in large indehiscent, bell shaped, seeds are smooth, 1.6 to 2 cm, white with marginal groove. It is considered as laxative, cardiogenic, diuretic, bitter, emetic, lessens inflammation. These species shows presence of palmitic acid, palmitoleic acid and stearic acid, oleic acid.

According to research and as other species from genus *Lagenaria* shows analgesic, anti-inflammatory, immunomodulatory, antihyperlipidemic, diuretic, antihelminthic and CNS depressant activities on the fruit of *Lagenaria siceraria* [2][3].

MATERIALS AND METHODS

Plant materials and preparation of extracts:

The fruits of *Lagenaria siceraria* were collected from the local market of Lucknow and they were authenticated as *Lagenaria siceraria* (Bottle gourd) by Dr. Syeedha Khatoon, Taxonomist of N.B.R.I (Lucknow) and voucher specimen is submitted in N.B.R.I. for future reference. The fresh ripe fruits were sliced using a home slicer and the slices obtained were shade dried. The dried coarsely powdered plant material was extracted with 99% methanol using rotavapour apparatus (BUCHI). The solvent was evaporated under vacuum which gave semi-solid mass (24.49% w/w). The preliminary phytochemical screening was carried out to detect the chemical constituents of both fresh fruit extract which revealed the presence of flavonoid, steroid, saponins & polyphenols, carbohydrates, proteins. The extracts were stored in tight containers in desiccator.

ANIMALS

Sprague-Dawley rats (140-180gm) were procured from the animal house of National Botanical Research Institute, Lucknow. They were kept in the departmental animal house at $26 \pm 2^\circ\text{C}$ and relative humidity 44-

56%, light and dark cycles of 10 & 14 hr respectively for 1 week before and during the experiments. Animals were provided with standard rodent pellet diet (Amrut, India) and the food was withdrawn 18-24hr before the experiments through water was allowed ad libitum.

EXPERIMENTAL PROCEDURE

Lagenaria siceraria extract (LSE) in doses of 100 & 200mg/kg and H₂ blocker, ranitidine, in the dose of 50mg/kg were administered orally twice daily at 10:00 and 16:00hr respectively, for 10 days for chronic ulcer protective studies. Control group of animals received suspension of 1% carboxymethyl cellulose in distilled water (10ml/kg).

ACTIVITIES STUDIED

For the following activities the animals were divided into four groups, each group containing six animals. Group 1 for control, group 2 for standard and group 3 & group 4 for methanol extract (100 & 200mg/kg).

ANTIULCER ACTIVITY

Aspirin (ASP)-induced ulcers:

ASP in dose of 200mg/kg (20mg/ml) was administered to the animals on the day of the experiment and ulcers were scored after 4hr [4]. The animals were sacrificed and the stomach was then excised and cut along the greater curvature, washed carefully with 5.0ml of 0.9% NaCl. Ulcer index has been calculated by adding the total number of ulcers per stomach and the severity of ulcers per stomach. The total severity of the ulcer was determined by recording the severity of each ulcer after histological confirmation as follows [5]. 0, no ulcer; +, pin point ulcer and histological changes limited to superficial layers of mucosa and no congestion; ++, ulcer size less than 1mm and half of the mucosal thickness showed necrosis; +++, ulcer size 1-2mm with more than two-thirds of the mucosal thickness destroyed with marked necrosis and congestion, muscularis remaining unaffected; +++++, ulcer either more than 2mm in size or perforated with complete destruction of the mucosa with necrosis and hemorrhage, muscularis still remaining unaffected. The pooled group ulcer score was then calculated according to the method of Sanyal et al.

Cold-restraint stress (CRS)-induced ulcers:

Rats were deprived of food, but not water, for about 18hr before the experiment. On day six, the experimental rats were immobilized by strapping the fore and hind limbs on a wooden plank and kept for 2hr, at temperature of 4-6 C[6]. Two hours later, the animals were sacrificed by cervical dislocation and ulcers were examined on the dissected stomachs as described above.

Pylorus ligated (PL)-induced ulcers:

Drugs were administered for a period of 5 days as described above and the rats were kept for 18hr fasting and care was taken to avoid coprophagy. Animals were anaesthetized using pentobarbitone (35mg/kg, i.p.), the abdomen was opened and pylorus ligation was done without causing any damage to its blood supply. The stomach was replaced carefully and the abdomen wall was closed in two layers with interrupted sutures. After 4hr, stomachs were dissected out and cut open along the greater curvature and ulcers were scored by a person unaware of the experimental protocol in the glandular portion of the stomach as mentioned in aspirin induced ulcers.

ETHANOL (EtOH)-induced ulcers:

The gastric ulcers were induced in rats by administering 100% EtOH (1ml/200g, 1hr)[7] and the animals were sacrificed by cervical dislocation and stomachs were incised along the greater curvature and examined for ulcers. The ulcer index was scored, based upon the product of length and width of the ulcers present in the glandular portion of the stomach (square millimeter per rat).

STATISTICAL ANALYSIS

All the data were presented as means \pm S.E.M. and analyzed by Neuman-keuls test and unpaired student t test for the possible significant interrelation between the various groups. A value of $p < 0.005$ was considered statistically significant.

RESULT

Effect of LSE at dose of 100-200mg/kg, twice a day for 5 days prevented the acute gastric ulcer in a dose related manner. The range of percent protection were Ethanol 42.66-60.83% ($p < 0.001$), ASP 53.77-68.36% ($P < 0.001$), PL 56.16-63.73% ($p < 0.001$), CRS 59.65-64.40% ($p < 0.001$)

respectively. The percent protection of ranitidine ranged from 64.61-79.42% ($p < 0.001$) respectively in various gastric ulcer models. Secretion of mucus & bicarbonate barrier, which is regarded as first line of defense against potential ulcerogens. In chronic ulcers induced by ASP, LSE reduced ulcer index significantly with decreased perforation after 10 days treatment.

DISCUSSION & CONCLUSION

The present study showed that the methanolic extract of *Lagenaria siceraria* possess gastroprotective activity as evidenced by its significant inhibition in the formation of ulcers induced by various physical & chemical agents. Pylorus ligation induced ulcers are due to autodigestion of the gastric mucosa & break down of the gastric mucosal barrier[8]. Synthetic NSAIDs like Aspirin cause mucosal damage by interfering with prostaglandin synthesis, increasing acid secretion and back diffusion of H^+ ions[9]. The incidence of ethanol induced ulcer is predominant in the glandular part of stomach was reported to stimulate the formation of leukotriene C_4 (LTC₄), mast cell secretory products [10] and reactive oxygen species[11] resulting in the damage of rat gastric mucosa.[12]. Aspirin-induced depletion of gastric wall mucosa been prevented by LSE.

Stress plays an important role in etiopathology of gastric –duodenal ulceration. Increase in gastric motility, vagal over activity[13]; mast cell degranulation; decreased gastric mucosal blood flow[13] and decreased prostaglandin synthesis[14] are involved in genesis of stress induced ulcers. Complex neurochemical mechanisms are involved in the organism's biological response to noxious stimuli like stress. The pathologic alteration occurs with the changes in the synthesis, actions and degradation of hormones, neurotransmitter and neuromodulator. The central nervous system plays an important role in stress ulceration and regulation of plasma corticosterone[14]. As etiopathogenesis of these ulcer models are different, mechanism of LSE should then include number of predisposing factors. On the other hand, the mucosal protection induced by non-prostanoid compounds was perhaps mediated through the mobilization of endogenous prostaglandins[15].

Gastric ulcer is often a chronic disease and it may persist for 10-20 years characterized by repeated episodes of healing and re-exacerbations. LSE significantly healed the penetrating ulcers induced by ASP after 10 days treatment. The more work is required for the clear understanding of mechanism of action with chemically identified active principles. However, in the present study the plant shows a potent antiulcer activity, which justifies the ethanomedical claims.

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TABLE-1- Effect of *Lagenaria siceraria* extract (LSE, Twice daily for 10 days) on ETHANOL (EtOH) INDUCED

Treatment (mg/kg)	Ulcer index	Percentage protection
Control	10.29±.024	-
100	5.9±.057*	42.66
200	4.03±.075*	60.83
Standard	3.7±.071*	64.61

One way ANOVA Followed by NEWMAN-KEULS TEST Values are mean±S.E.M. for six rats

*p<0.001 when compared to control group.

TABLE-2- Effect of *Lagenaria siceraria* extract (LSE, Twice daily for 10 days) on ASPRIN (ASP) INDUCED

Treatment (mg/kg)	Ulcer index	Percentage protection
Control	12.33±.06	-
100	5.7±0.07*	53.77
200	3.9±0.07*	68.36
Standard	3.3±0.06*	73.26

One way ANOVA Followed by NEWMAN-KEULS TEST Values are mean±S.E.M. for six rats

*p<0.001 when compared to control group

TABLE-3- Effect of *Lagenaria siceraria* extract (LSE, Twice daily for 10 days) on PYLORUS LIGATION (PL)

Treatment (mg/kg)	Ulcer index	Percentage protection
Control	18.475±0.07	-
100	8.1±0.02*	56.16
200	6.7±0.03*	63.73
Standard	3.8±0.07*	79.42

One way ANOVA Followed by NEWMAN-KEULS TEST Values are mean±S.E.M. for six rats

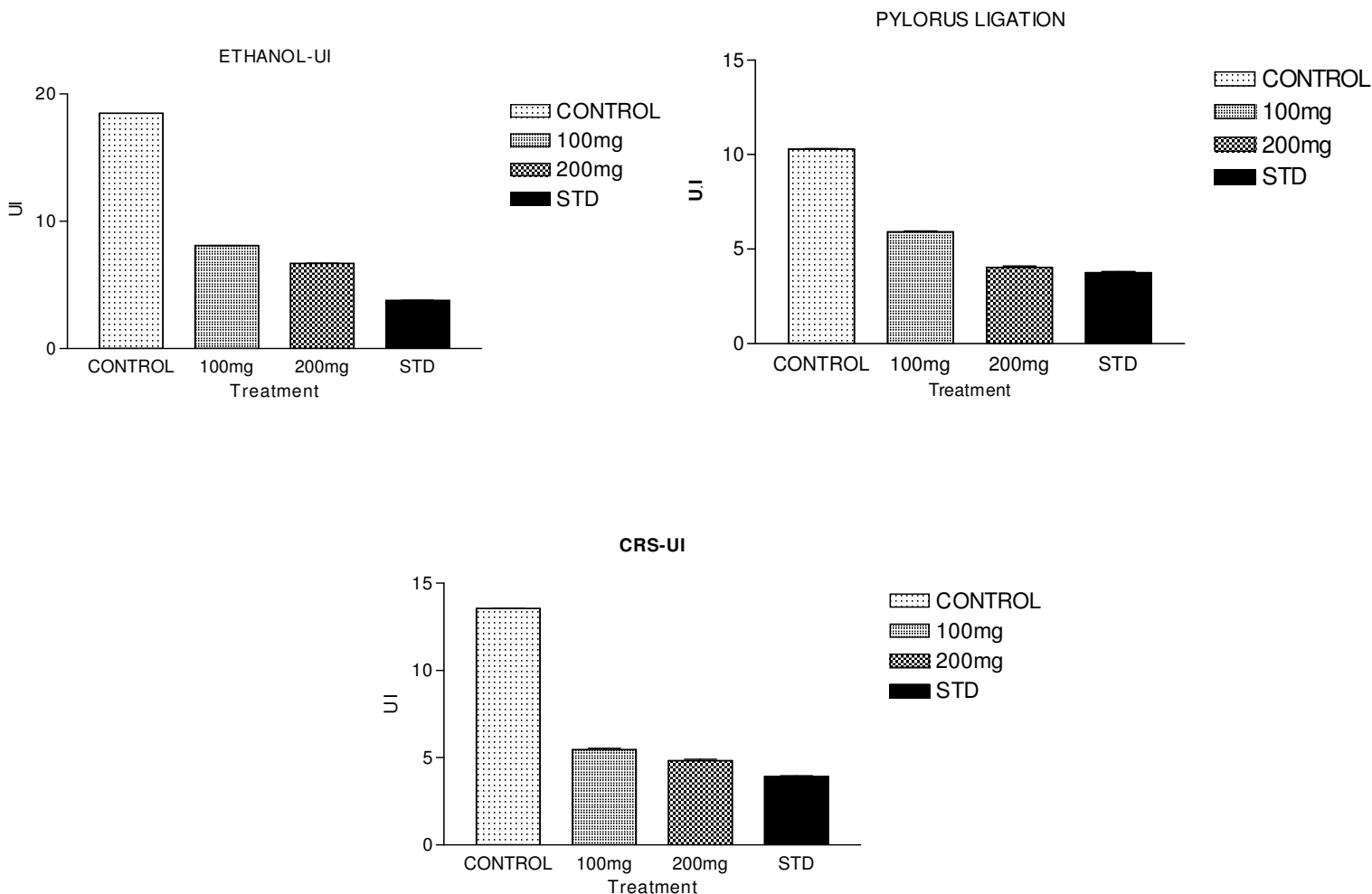
* $p < 0.001$ when compared to control group.

TABLE-4-Effect of *Lagenaria siceraria* extract(LSE, Twice daily for 10 days) on cold restraint stress(CRS)

Treatment(mg/kg)	Ulcer index	Percentage protection
Control	13.54±0.01	-
100	5.46±0.07*	59.65
200	4.82±0.08*	64.40
Standard	3.9±0.06*	71.19

One way ANOVA Followed by NEWMAN-KEULS TEST Values are mean±S.E.M. for six rats

* $p < 0.001$ when compared to control group.



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