

Antiulcer and gastroprotective potential of *Stereospermum suaveolens* in Wistar Rats

Sir,

Peptic ulcer is one of the most frequent disorders of the alimentary tract and, in various countries, its prevalence is estimated at 5–10% of the adult population, still remaining one of the most important problems.^[1] The etiology of peptic ulcer is not clearly known. It results probably due to an imbalance between the aggressive and the defensive factors. Reactive oxygen metabolites, free radicals, nitric oxide and genetic and environmental factors are also thought to play a role in the pathogenesis of ulcers. Although a number of antiulcer drugs, such as H₂ receptor antagonists, proton pump inhibitors and cytoprotectants, are available, all these drugs have side-effects and limitations.^[2] Indian medicinal plants and their derivatives have been an invaluable source of therapeutic agents with fewer side-effects to treat various disorders including peptic ulcer disease (PUD).

Stereospermum suaveolens DC (Bignoniaceae), commonly known as “Patala,” is widely available in India. It mainly contains lapachol, dinatin, β -sitosterol, saponin and palmitic, stearic and oleic acids.^[3] Traditionally, it is mainly used as analgesic, wound healing, antidyspeptic, astringent and liver stimulant.^[4] Some recent literature reviews indicated that many flavonoids and antioxidants possess antiulcerogenic and wound healing activity.^[5] Because phytochemical investigations of the methanolic stem bark extract of *Stereospermum suaveolens* also revealed the presence of flavonoids, phenols, saponins, tannins and alkaloids, an attempt has been made to investigate the antiulcer and gastroprotective activity of the methanolic stem bark extract of *Stereospermum suaveolens* in pylorus-ligated experimental animal models.

Female Wistar albino rats weighing 150–170 g were used for the study. Animals were obtained from the National Institute of Nutrition, Hyderabad, and were kept under standard husbandry conditions and water *ad libitum* throughout the experimental period. The study received approval from the Institutional Animal Ethics Committee. Acute toxicity was tested according to the OECD-423 guidelines and the effective doses of 125, 250 and 500 mg/kg of methanolic stem bark plant extract was selected for the experimental purpose.

Different doses of the methanolic extract was tested for the antiulcer and gastroprotective activity by pylorus-ligated

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experimental animal models on various groups of rats. The rats of group I were not ligated, serving as normal control; rats of group II were ligated but were not treated, serving as experimental control; group III received ranitidine 20 mg/kg and served as standard. The groups IV, V and VI received 125, 250 and 500 mg/kg of methanolic extract by the oral route 2 h prior to the induction of ulcers.

Rats were fasted for 36 h prior to the surgical procedure. Under light ether anesthesia, the abdomen was opened by a small midline incision below the xiphoid process. The pylorus portion of the stomach was identified, slightly lifted out and ligated, avoiding traction to the pylorus or damage to the blood supply. The stomach was then replaced carefully and the abdominal wall closed by interrupted sutures. Animals were sacrificed after 6 h of pylorus ligation.^[6]

The stomach was dissected out as a whole by passing a ligature at the esophageal end and the contents were subjected to centrifugation (3000 rpm for 10 min) for analyzing volume of acid secretion (VAS), pH and free and total acidity. Along with greater curvature, the stomach was opened and pinned on a cork plate and examined for mucosal lesions and severity.^[7] The glandular portion of the stomach was obtained for estimation of reduced glutathione,^[8] superoxide dismutase,^[9] catalase^[10] and lipid peroxidation levels.^[11]

All values were reported as mean $\pm$ SEM. The data were analyzed statistically using one-way analysis of variance (ANOVA) followed by multiple Dennett's test. Statistical significance was set at $P \leq 0.05$.

An effective dose-dependent antiulcer and gastroprotective activity of the methanolic extract of *Stereospermum*

suaveolens was found in the study. Ulcers were produced significantly after 6 h of ligation in the experimental control group. A significant ($*P < 0.05$) increased VAS, free acidity, total acidity, ulcer index and decreased pH was found in the experimental control group as compared with the normal control group, but these parameters were significantly reversed in different doses of the extract-treated group when compared with the experimental control group [Table 1]. The experimental control group animals had ulcers and hemorrhagic streaks, whereas the normal control and standard and extract-treated groups did not show any ulcers and streaks except a couple of red spots in the 125 mg extract-treated group. Similarly, a significant ($*P < 0.05$) increase in lipid peroxidation and decrease in super oxide dismutase, catalase and glutathione level was observed in glandular portions of experimental control group animals when compared with the normal control group, whereas these levels were significantly reversed in the extract- and standard ranitidine-treated groups when compared with that of the experimental control group [Table 2].

In most of the cases, the etiology of peptic ulcer remains unclear but it may probably result due to damage of the protective gastrointestinal mucosa and decreased levels of defensive mechanisms.^[12] The causes of gastric ulcer after pylorus ligation are believed to be due to stress-induced increase in gastric hydrochloric acid secretion and/or stasis of acid. Increase in gastric motility, vagal overactivity, mast cell degranulation, decreased mucosal blood flow and decreased prostaglandin synthesis are reported to be involved in the genesis of stress-induced gastric ulceration. According to Shay *et al.*, the VAS is also an important factor in the formation of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid. In the present study,

Table 1: Effect of MES in pylorus ligation-induced ulcer model

Treatment groups	VAS (ml)	pH	Free acidity (mEq/L)	Total acidity (mEq/L)	Ulcer index
Normal	0.63 $\pm$ 0.04	4.63 $\pm$ 0.08	16.67 $\pm$ 2.10	33.33 $\pm$ 3.31	0.16 $\pm$ 0.10
Control	4.98 $\pm$ 0.11#	2.41 $\pm$ 0.06#	80.00 $\pm$ 3.65#	151.7 $\pm$ 8.72#	8.08 $\pm$ 0.20#
Ranitidine (20 mg/kg)	0.93 $\pm$ 0.04*	5.06 $\pm$ 0.06*	18.33 $\pm$ 3.07*	48.33 $\pm$ 3.07*	2.00 $\pm$ 0.31*
MES (125 mg/kg)	4.05 $\pm$ 0.06*	3.06 $\pm$ 0.08*	51.67 $\pm$ 3.07*	110.0 $\pm$ 5.16*	4.08 $\pm$ 0.15*
MES (250 mg/kg)	3.18 $\pm$ 0.06*	3.51 $\pm$ 0.06*	35.60 $\pm$ 4.28*	81.70 $\pm$ 4.77*	3.75 $\pm$ 0.21*
MES (500 mg/kg)	2.53 $\pm$ 0.14*	4.40 $\pm$ 0.09*	25.00 $\pm$ 3.59*	56.60 $\pm$ 5.54*	2.25 $\pm$ 0.25*

Values are expressed as mean $\pm$ SEM, $n = 6$, statistics: one-way ANOVA followed by Dennett's test. * $P < 0.05$ treated group vs. pylorus ligation control group; # $P < 0.05$ pylorus ligation control group vs. normal group. MES, methanolic extract of *Stereospermum suaveolens*

Table 2: Effect of MES on the gastroprotective parameters in pylorus ligation-induced ulcer

Treatment groups	LPO (nM/g wet tissue)	SOD (U/min/mg protein)	CAT (U/min/mg protein)	GSH (nM/g wet tissue)
Normal	14.96 $\pm$ 1.71	48.3 $\pm$ 2.21	0.45 $\pm$ 0.010	13.36 $\pm$ 0.44
Control	48.15 $\pm$ 2.15#	9.27 $\pm$ 0.98#	0.19 $\pm$ 0.008#	6.13 $\pm$ 0.30#
Ranitidine (20 mg/kg)	14.12 $\pm$ 0.51*	43.0 $\pm$ 1.45*	0.43 $\pm$ 0.013*	11.61 $\pm$ 0.20*
MES (125 mg/kg)	27.65 $\pm$ 0.89*	31.9 $\pm$ 1.94*	0.36 $\pm$ 0.015*	9.74 $\pm$ 0.09*
MES (250 mg/kg)	21.16 $\pm$ 0.62*	39.45 $\pm$ 2.01*	0.40 $\pm$ 0.005*	11.06 $\pm$ 0.48*
MES (500 mg/kg)	19.98 $\pm$ 0.64*	41.02 $\pm$ 1.56*	0.41 $\pm$ 0.007*	11.55 $\pm$ 0.27*

Values are expressed as mean $\pm$ SEM, $n = 6$, statistics: one-way ANOVA followed by Dennett's test. * $P < 0.05$ treated group vs. pylorus ligation control group; # $P < 0.05$ pylorus ligation control group vs. normal group. MES, methanolic extract of *Stereospermum suaveolens*

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therapeutically equivalent doses of the methanolic stem bark extract produced a significant decrease in all ulcerogenic parameters. Thus, the antiulcer effect of the extract may be involved in counteracting the functions of one or more of the above physical or physiological factors.

Similarly, a role for reactive oxygen metabolites and free radicals has been suggested in the pathogenesis of stress-induced gastric ulcers. Antioxidants are known to protect cellular damage by scavenging the free radical formation, may be due to its possible antioxidant nature.^[13] Increase in malonaldehyde levels results in an increase in the reactive oxygen species, the major radicals being superoxide anion, H₂O₂ and hydroxyl radical. These induce cell degranulation by increasing peroxidation of cell membrane lipids, causing loss of structural and functional integrity of the cell membrane.^[14] Reduced glutathione is also a major facilitator for free radical-mediated lipid peroxidation. Results of the present study also revealed similar alterations in the control group animals. These effects were significantly reversed in the extract-treated group. Thus, it is tempting to suggest that the gastroprotective effect of the extract in pylorus-ligated gastric ulcers could be, in part, also mediated through either a decrease in free-radical generation or its antioxidant activity.

Further pharmacological studies including characterization of the active phytoconstituents responsible for the actual mechanism are required to explore the full therapeutic potential of *Stereospermum suaveolens*.

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