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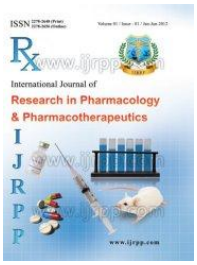

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Anti-Ulcer activity of *Simarouba glauca* against Ethanol and Indomethacin induced ulcer in rats

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Abstract

Simarouba glauca a member of the Simaroubaceae family, is used in antimicrobial and insecticidal activity, antidysentric, antiherpetic, antihelminthic and antiprotozoal activities, but according to the best of our knowledge there is no scientific detailed report on antioxidant, haemolytic and thrombolytic activities. The purpose of the present study is to investigate the acute oral toxicity and anti-ulcer profile of the Chloroform Extract of *Simarouba glauca* (CSG) extract in albino rats. No toxicity of extract up to 2000 mg/kg body weight orally as per OECD guidelines No.423. CSG at the doses of 200 and 400 mg/kg body weight orally was administered to evaluate anti-ulcer activity by using Ethanol and indomethacin, induced gastric ulcer models in Albino rats. Chloroform extract of *Simarouba glauca* dose dependent inhibition in ethanol induced gastric lesions, causing 82.63 % protection at 400 mg/kg, and 53.48 % protection at 200 mg/kg, CSG dose dependent inhibition in indomethacin induced gastric lesions, causing 62.65 % protection at 400 mg/kg and 54.86 % protection at 200 mg/kg, All the results are found to be statistically significant ($p \leq 0.05$). Hence we suggest that Chloroform Extract of the leaves of *Simarouba glauca was* able to decrease the acidity and to increase the mucosal defense in the gastric areas, thereby justifying its use as an antiulcerogenic agent.

Keywords: *Simarouba glauca,* Anti-ulcer activity, Ethanol, Indomethacin.

INTRODUCTION

Peptic ulcers are open sores that develop on the inside lining of esophagus, stomach and the upper portion of small intestine.

The most common symptom of a peptic ulcer is abdominal pain.

Peptic ulcers include:

- Gastric ulcers that occur on the inside of the stomach
- Esophageal ulcers that occur inside the hollow tube (esophagus) that carries food from throat to stomach
- Duodenal ulcers that occur on the inside of the upper portion of small intestine (duodenum)

In recent years, focus on medicinal plant research has increased and several studies had shown immense potential of medicinal plants. Herbal medicines derived from plant extract, are increasingly being recognized in treating various clinical diseases.

Simarouba glauca, (Family: Simaroubaceae) Simarouba is a medium-sized tree that grows up to 20 meter high, with a trunk 50 to 80 cm in diameter. It produces bright green leaves 20 to 50 cm in length, small white flowers, and small red leaves. It is indigenous to the Amazon rainforest and other tropical areas in Mexico, Cuba, Haiti, Jamaica, and Central America. From the source of literature documentation and relevant traditional approaches on plant drugs, the present investigation was carried out to know the anti-ulcer profile of the Chlroform extract of *Simarouba glauca* (CSG).

MATERIALS AND METHODS

Plant material

S.glauca leaves were collected from distinct region of Kerala state, India.

Preparation of plant material

Fresh leaves were collected and dried at room temperature. Dried leaves were powdered mechanically. Powdered leaves were then packed in Soxhlet apparatus and extraction was done. 80 gm of dry powder was subjected to Soxhlet extraction with 200 mL chloroform extraction was carried out for 3 hrs, 3 cycles and temperature was maintained at 75°C. Colour of extract was green. The extracts is then concentrated and dried under reduced pressure. The solvent free semisolid mass thus obtained is dissolved in tween 80 and used for the experiment.

Animals Used

Albino rats (180–220 g) of either sex were maintained in a 12 h light/dark cycle at a constant temperature 25◦C with free access to feed and water. All animals were fasted prior to all assays and were divided into different experimental groups each of 6 rats. Moreover the animals were kept in specially constructed cages. All experiments were carried out according to the guidelines for care and use of experimental animals and approved by Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

Acute toxicity study

The acute toxicity of Chloroform extract of *Simarouba glauca* leaves was determined as per the OECD guideline no.423 (Acute Toxic Class Method). It was observed that the test extract was not lethal to the rats even at 1800 mg/kg dose. Hence, $1/10^{th}$ (200 mg/kg) and $1/5^{th}$ (400 mg/kg) of this dose were selected for further study.

ANTI-ULCER ACTIVITY

Ethanol induced gastric ulcer

Animals were randomly divided into four groups each of 6 rats. Group I treated with 6% v/v aqueous tween 80 (10 ml/kg p.o), Group II & III treated with Chloroform extract of *Simarouba glauca* (200 and 400 mg/kg p.o) respectively for 14 days and Group IV treated with Omeprazole (20 mg/kg p.o) were administered 30 min prior to induction of gastric ulcer. On the 14^{th} day, Gastric ulcers were induced with ethanol at a dose of 8 ml/kg administered to all groups by orally. The animals were anaesthetized 6 h with ether and stomachs were incised along the greater curvature and the ulcer index for each rat was taken as the mean ulcer score.

Indomethacin induced gastric ulcer

Animals were divided into four groups each of six rats. Group I treated with 6% v/v aqueous tween 80 (10 ml/kg p.o), Group II & III treated with Chloroform extract of *Simarouba glauca* (200 and 400 mg/kg p.o) respectively for 14 days and Group IV treated with Omeprazole (20 mg/kg p.o) were administered 30 min prior to induction of gastric ulcer. On the 14^{th} day, Gastric ulcer were induced with indomethacin (40 mg/kg p.o) administered to all groups after fasting for 24 h. The animals were sacrificed 4 h after treatment with the ulcerogenic agent to assess the antiulcer activity and ulcer index were examined on the dissected stomachs as described below.

Measurement of ulcer index

The stomachs were excised and were examined for hemorrhagic lesions in glandular mucosa. Immediately after the animals were sacrificed, their stomachs were dissected out, cut along the greater curvature and the mucosa were rinsed with cold normal saline to remove blood contaminant, if any.

The sum of the length (mm) of all lesions for each stomach was used as the ulcer index (UI), and the percentage of inhibition (% *I*) was calculated by using the following formula:

$$\% I = \frac{(USc - USt)}{USc} \times 100$$

Where USc = ulcer surface area in control and
USt = ulcer surface area in treated animals.

Statistical analysis

The data were expressed as mean ± standard error mean (S.E.M).The Significance of differences among the group was assessed using one way and multiple way analysis of variance (ANOVA). The test followed by Dunnett's test p values less than 0.05 were considered as significance.

RESULTS

Acute toxicity study

Acute toxicity study in which the animals treated with the Chloroform Extract of *Simarouba glauca* at a higher dose of 1800 mg/kg did not manifest any significant abnormal signs, behavioral changes, body weight changes, or macroscopic findings at any time of observation. There was no mortality in the above-mentioned dose at the end of the 14 days of observation.

Effect of Chloroform Extract of Simarouba glauca on gastric ulcer induced by Ethanol

The Chloroform Extract of *Simarouba glauca* showed significant anti-ulcer effect against ulcers induced by Ethanol in a dose dependent manner. In ethanol induced ulcer model, Chloroform Extract of *Simarouba glauca* at a dose of 200 and 400 mg/kg body weight showed protective effect of 53.48 and 82.63%, respectively, whereas Omeprazole showed protection index of 83.85% at a dose of 20 mg/kg body weight (Table -1).

Effect of Chloroform Extract of Simarouba glauca on gastric ulcer induced by Indomethacin

The Chloroform Extract of *Simarouba glauca* showed significant anti-ulcer effect against ulcers induced by *Indomethacin* in a dose dependent manner. In Indomethacin induced ulcer model, Chloroform Extract of *Simarouba glauca* at a dose of 200 and 400 mg/kg body weight showed protective effect of 54.86 and 62.65%, respectively, whereas Omeprazole showed protection index of 75.79 % at a dose of 20 mg/kg body weight (Table -2).

Table 1: Effect of Chloroform Extract of *Simarouba glauca (*CSG) *in* ethanol (8 ml/kg) induced gastric ulcer in rats

Group	Design of Treatment	Ulcer Index (U.I)	Percentage Inhibition
I	Control (6% v/v aqueous tween 80, 10 ml/kg b.w) p.o	26.14 ± 0.18	---
II	CSG (200mg/kg body wt.) p.o	12.16 ± 0.10*	53.48 %
III	CSG (400mg/kg body wt) p.o	4.54 ± 0.48**	82.63 %
IV	Omeprazole (20mg/kg b.w) p.o	4.22 ±0.78**	83.85 %

Data are indicating as mean ± S.E.M. Statistical analysis was done by one-way ANOVA followed by Dunnett's multiple comparison test. $^{*}P < 0.01$ and $^{**}P < 0.001$ as compared to control (n = 6 in each group).

CSG = Chloroform Extract of *Simarouba glauca.*

Table-2: Effect of Chloroform Extract of *Simarouba glauca (*CSG) in Indomethacin (40 mg/kg) induced gastric ulcer in rats

Group	Design of Treatment	Ulcer Index (U.I)	Percentage Inhibition
I	Control (6% v/v aqueous tween 80, 10 ml/kg b.w) p.o	16.44 ± 0.78	---
II	CSG (200 mg/kg body wt) p.o	7.42 ± 0.56*	54.86 %
III	CSG (400 mg/kg body wt) p.o	6.14 ± 0.12**	62.65 %
IV	Omeprazole (20 mg/kg body wt) p.o	3.98 ± 0.11**	75.79 %

Data indicating as mean ± S.E.M. Statistical analysis was done by one-way ANOVA followed by Dunnett's multiple comparison test. $^{*}P < 0.01$ and $^{**}P < 0.001$ as compared to control (n = 6 in each group).
CSG = Chloroform Extract of *Simarouba glauca*.

DISCUSSION & CONCLUSION

The anti-ulcer effect of *Simarouba glauca* was tested against gastric lesions induced by ethanol, the experimental model related to lesion pathogenesis with production of reactive oxygen species. Reactive oxygen species are involved in the pathogenesis of ethanol-induced gastric mucosal injury *in vivo*. *Simarouba glauca* prevented the mucosal lesions induced by ethanol. Results in the present study also indicate similar alterations in the anti-oxidant status after ethanol induced ulcers. The gastric mucosal protection against ethanol can be mediated through a number of mechanisms that include enhancement of the gastric mucosal defense through increase in mucus and/or bicarbonate production, reducing the volume of gastric acid secretion or by simply neutralizing the gastric acidity.

CSG may either reduce the gastric acid secretion or enhance the barrier defense of the mucosal wall. CSG dose dependent inhibition in ethanol induced gastric lesions (Table -1).

Their anti-ulcerogenic potency was tested against indomethacin-induced ulcer. Indomethacin is a cyclooxygenase inhibitor which suppresses gastroduodenal bicarbonate secretion, reduces endogeneous prostaglandin biosynthesis and disrupts the mucosal barrier as well as mucosal blood flow in animals. It is also well known that prostaglandins synthetized in large quantities by the gastrointestinal mucosa can prevent experimentally induced ulcers by ulcerogens. Thus, when the ulcers lesions are induced by indomethacin, the cytoprotective effect of the anti-ulcer agent can be mediated through endogeneous prostaglandins. The results obtained show that the mean ulcer index was significantly reduced in the Chloroform extracts from the leaves of *Simarouba glauca* treated groups, compared to their respective controls. *Simarouba glauca* extracts may be stimulate the secretion of prostaglandins or possess prostaglandins like-substances (Table -2).

The Chloroform extracts of *Simarouba glauca* at a dose of 400 mg/kg showed similar activity to that of omeprazole. The gastro protective effect of omeprazole is mediated through block of acid secretion by inactivation of H+/K+-ATPase. This study reveals that the Chlroform extracts from the leaves of *Simarouba glauca* are potent inhibitors of gastric mucosal lesions caused by ethanol, indomethacin, pylorus ligation and cold-restraint stress in rats.

Further, our results fortify the pharmacological importance of CSG as an anti-ulcer agent. Etiology of ulcers produced in different ulcer models is diverse. Since CSG has been found effective in various models depicting its anti-ulcerogenic activity, CSG and its active constituents may emerge as more effective therapeutic agents to counter peptic ulcer incidence.

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