© 2013 Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas 12 (1): 81 - 91
ISSN 0717 7917
www.blacpma.usach.cl

Artículo Original | Original Article

Anti-ulcer Activity of Sandalwood (*Santalum album* L.) Stem Hydro-alcoholic Extract in Three Gastric-Ulceration Models of Wistar Rats

[Actividad anti-ulcerosa del tallo de Sándalo (Santalum album L.) en extractos hidro-alcoholicos en tres modelos de ulceración gástrica de ratas Wistar]

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Abstract
Sandalwood (*Santalum album* L.) is used in various traditional systems of medicine, like Ayurveda, Siddha and Unani medicine to treat a wide range of ailments. In Unani medicine, Safed Sandal is used to treat gastric ulcers, hence the present study was undertaken to confirm this claim. A limit test as per OECD guidelines was conducted at a dose of 5000 mg/kg to determine the acute toxic dose of Hydro-alcoholic extract from *S. album* stem (SASE). Two test doses of SASE (250 and 500 mg/kg) were subjected to screening of anti-ulcer activity by three *in-vivo* models namely – water immersion - restrain stress, ethanol and indomethacin induced gastric ulceration models in albino wistar rats. A proton-pump inhibitor, Omeprazole 10 mg/kg and H_2 receptor antagonist, Ranitidine 50 mg/kg were employed as standard drugs. The results revealed an increase in gastric protection as a significant decrease ($p < 0.001$) in average number of ulcers, severity of ulcers and cumulative ulcer index was observed in the test groups. Histopathological evidences supported the above findings. The observed anti-ulcer effect of SASE at 500 mg/kg was comparable to that of standard drugs used in the experiments indicating significant anti-ulcer potential especially at higher concentration.

Keywords: Hydro-alcoholic Extract from *S. album* Stem (SASE), anti-ulcer activity.

Resumen
Sándalo (Santalum album L.) se utiliza en diversos sistemas de medicina tradicional, como el Ayurveda, Siddha y Unani para tratar una amplia gama de dolencias. En la medicina Unani, Safed Sandal se usa para tratar úlceras gástricas, por lo tanto, el presente estudio se realizó para confirmar esta afirmación. Una prueba de límite según las directrices de la OCDE se llevó a cabo a una dosis de 5000 mg/kg para determinar la dosis tóxica aguda del extracto hidroalcohólico del tallo de S. álbum (SASE). Dos dosis de prueba de SASE (250 y 500 mg/kg) se sometieron al estudio de la actividad anti-úlcera por tres modelos in vivo, a saber: la inmersión en agua – estrés de restricción, y la ulceración gástrica inducida por etanol e indometacina, en ratas Wistar albinas. Un inhibidor de la bomba de protones, omeprazol 10 mg/kg y el antagonista de los receptores H2, ranitidina 50 mg/kg fueron empleados como fármacos estándar. Los resultados revelaron un aumento de la protección gástrica como una disminución significativa ($p < 0.001$) en el número promedio de úlceras, la gravedad de las úlceras y el índice de úlcera acumulativo se observó en los grupos de prueba. Evidencias histopatológicas apoyaron las conclusiones anteriores. El efecto anti úlcera observado por efecto de SASE a 500 mg/kg fue comparable a la de fármacos estándar utilizados en los experimentos que indican un significativo potencial anti-úlcera, especialmente a mayores concentraciones.

Palabras Clave: Extracto hidro-alcoholico de S. álbum Stem (SASE), actividad anti-ulcerosa.

Recibido | Received: April 6, 2012.
Aceptado en versión corregida | Accepted in revised form: July 17, 2012.
Publicado en línea | Published online: January 30, 2013.
Este artículo puede ser citado como / This article must be cited as: N Ahmed, MS Ali Khan, AM Mat Jais, N Mohtarrudin, M Ranjbar, MS Amjad, B Nagaraju, M Faraz, F Pathan, A Chincholi. 2013. Anti-ulcer Activity of Sandalwood (*Santalum album* L.) Stem Hydro-alcoholic Extract in Three Gastric-Ulceration Models of Wistar Rats. **Bol Latinoam Caribe Plant Med Aromat** 12(1): 81 – 91.

INTRODUCTION

Peptic Ulcer Disease (PUD) encompasses both gastric and duodenal ulcers. Persisting erosions cause damage to the stomach wall becoming perforated and developing peritonitis and massive haemorrhage as a result of mucus, bicarbonate and prostaglandins synthesis inhibition (Wallace, 2008). Several factors influence in the formation of gastric ulcers such as the stomach infection produced by *Helicobacter pylori* (Phillipson *et al*., 2002), the frequent use of non-steroidal anti-inflammatory drugs (NSAIDs) (Bighetti *et al*., 2005) and consumption of alcohol (Bandyopadhyay *et al*., 2002). PUD is a serious gastrointestinal disorder that requires a well targeted therapeutic strategy (Dharmani and Palit, 2006). Nowadays, there are two main approaches for treating peptic ulcer. The first deals with reducing the production of gastric acid and the second by reinforcing gastric mucosal protection (Valle, 2005; Hoogerwerf and Pasricha, 2001). The therapeutic efficacy of commercially available anti-ulcer drugs in the treatment of gastric ulcer is usually accompanied by various side effects (Khan *et al*., 2011), for example, H_2-receptor antagonists (e.g. cimetidine) may cause gyneacomastia in men and galactorrhoea in women (Feldman and Burton, 1990), while proton-pump inhibitors (e.g. omeprazole and lansoprazole) can cause nausea, abdominal pain, constipation and diarrhea (Reilly, 1999; Franko and Richter, 1998). Due to these problems, there is a need to find new anti-ulcer agents that are highly effective with potentially less or no side effects. Medicinal plants have always been the main source of new drugs for the treatment of gastric ulcers (Rates, 2001; Borrelli and Izzo, 2000).

Santalum album (L.) is one of the most important Indian medicinal plants. Traditionally, Sandalwood is used as an astringent, antipyretic, blood purifier, disinfectant in bronchial and genitourinary tract infections, diuretic, expectorant, memory enhancer, and sedative, tonic for heart, liver and stomach. Furthermore, it is used in perfume industry. Various uses mentioned in Ayurveda about sandalwood include its utilization in the treatment of several ailments like bleeding piles, diarrhea with internal bleeding, eye infections, hemorrhage, hiccoughs, inflammation of umbilicous, poisoning, initial phase of pox, urticaria and vomiting (Desai and Hirenath, 1991; Kirtikar and Basu, 1933). It is reported to possess anti-bacterial activity against *Staphylococcus aureus* (Shankaranaryana, 1986) and anti-fungal activity against *Microsporum canis, Trichophyton mentagrophytes* and *T. rubrum* (Chaumont and Bardey, 1989). The essential oil of *S. album* was tested for *in-vitro* anti-viral activity against *Herpes simplex viruses-1 and -2*. It inhibited the replication of these viruses in a dose-dependent manner and was more effective against HSV-1. The oil did not exhibit virucidal and cytocidal activities at the concentrations tested (Benencia and Courrèges, 1999).

The phytochemical and pharmacological investigations proved the presence of antioxidant principles that justify their traditional medicinal values (Scartezzini and Speroni, 2000). *S.album* and other Indian medicinal plants were tested *in-vitro* for their possible regulatory effect on nitric oxide (NO) levels using sodium nitroprusside as NO donor. Most of the plant extracts demonstrated significant direct dose dependant scavenging activity on NO (Jagetia and Baliga, 2004). α-Santalol, an active component of sandalwood essential oil has been studied for skin cancer preventive efficacy in murine models of skin carcinogenesis employing human epidermoid carcinoma A-431 cells. α-santalol at concentrations of 25-75 µl resulted in concentration and time dependant decrease of cell number, which was largely due to cell death. Mechanistic studies showed involvement of caspase-3 activation and poly (ADP-ribose) polymerase cleavage, disruption of the mitochondrial membrane potential and cytochrome-C release into the cytosol, thereby suggesting involvement of both caspase-dependant and independent pathways (Kaur, 2005).

The sandalwood oil at a dose of 200 mg/kg showed highly significant antipyretic effect against yeast induced pyrexia in albino rats; 0.2% of Tween 80 and Paracetamol 100 mg/kg were used as control and standard respectively (Desai and Hirenath, 1991). Santalols have been reported to possess a significant anti-inflammatory property, in several experimental models (Sindhu *et al*., 2010). Experimental assays also revealed the anti-inflammatory effect of sandalwood oil and HESP (Hydrolyzed Exhausted Sandalwood Powder) oil against formalin induced paw oedema in albino rats at a dose of 200 mg/kg, using 0.2% tween 80 as control and phenylbutazone 150 mg/kg as standard. A significant reduction in oedema was observed in case of HESP (Sivaramakrishnan and Shankaranarayana, 1990; Shankaranarayana and Kamala, 1989; Shankaranaryana and Parathasarthi,

1985). Sandalwood oil (8 mg/kg) and HESP (10 mg/kg) produced prolonged decrease in carotid blood pressure, increase in heart rate and respiration in healthy adult mongrel dogs (10-12 kg) anaesthetized with pentobarbitone (35 mg/kg) (Sindhu *et al*., 2010). The sandalwood oil as well as HESP oil was studied for sedative effect on albino mice of either sex at 500/600 mg/kg as well as 600/800 mg/kg respectively using 0.2% Tween 80 as control. Severe depression occurred with death at LD_{50} of 558.0 and 747.6 mg/kg, respectively (Shankaranarayana and Kamala, 1989).

Some clinical studies were also conducted with *S. album*. Kuan- Xiong aerosol containing sandalwood oil along with oils of *Piper longum*, *Dryobalanops aromatica*, *Asarum seiboldi*, and *Alpinea officinarum*. They produced an immediate and quick relief in anginal pain in 69 cases of angina pectoris in comparison with nitroglycerine. Further studies revealed a different mechanism of action from that of nitroglycerine (Guo *et al*., 1983). A polyherbal eye drop preparation containing *S. album* Linn., *Azadirachta indica* A. Juss., *Eclipta alba* Hassk., *Vitex negundo* Linn., *Moringa oleifera* Lam., *Boerhaavia diffusa* Linn., *Rosa moschata* Mill, *Macuillamia rotundifolia* (Michx.) were studied in refractive error or cataract situations for six months. Some improvements were noted in the associated symptoms and subjective improvements of vision were reported by some patients. No side effects of the drug were reported by any patient (Mrinal, 1985).

S. album is one of the potential anti-ulcer plants used in Unani system of medicine (Jamal *et al*., 2006). Recently a polyherbal preparation, UL-409 containing six medicinal plants namely *Santalum album* L., *Glycyrrhiza glabra* L., *Saussurea lappa* CB Clarke, *Aegle marmelos* Corr., *Foeniculum vulgare* Mill., *Rosa damascena* Mill. at a dose of 600 mg/kg, significantly prevented the occurrence of ulcerations induced by stress, aspirin and alcohol in albino wistar rats (Venkataranganna *et al*., 1998). In another study, UL-409 increased the stomach mucus and decreased the acid volume, the free and total acid contents in rats. Moreover, significantly prevented the occurrence of cold-restraint stress induced ulcerations. Also, significantly inhibited gastric ulceration induced by alcohol and aspirin, as well as cysteamine and histamine induced duodenal ulcers in rats and guinea pigs, respectively. (Mitra *et al*., 1996; Kulkarni and Goel, 1996). Though *S. album* is one of the traditionally used anti-ulcer plants in Unani medicine and a component of certain polyherbal preparations for prevention and healing of gastric ulcers, no attempts were made to assess anti-ulcer potential of Sandalwood alone.

MATERIALS AND METHODS

Extraction of Plant material and Phytochemical Screening

S. album Stem was collected from forest area around Yelhanka Railway Station in January (2011) and authenticated at the Department of Botany, Bangalore University. Approximately 1000 g of *S. album* stem powder was extracted in 40% ethanol in water by soxhletion. The plant material and solvent were taken in 1:5 ratio. *S. album* stem hydro-alcoholic Extract (SASE) was processed at Green Chem Laboratory, Bangalore. The extracted material was delivered as gift sample (Batch No: SWSE/RD/01). SASE was later subjected to preliminary phytochemical screening to identify the presence of phyto constituents (Kokate *et al*., 2007; Khandelwal, 2004; Harborne, 1978).

Experimental Animals

Albino Wistar rats of either sex weighing 150-200 g were housed under standard conditions at 25 ± 5 ºC in a well-ventilated animal house approved by Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA Nº IAEC/37/10) under 12:12 h light - dark cycle. The experimental protocol (IAEC/NCP/37/10) was approved by Institutional Animal Ethical Committee, Nargund College of Pharmacy, Bangalore.

Oral Acute Toxicity Study and Selection of test doses

A safe oral dose of SASE was determined through the acute oral toxic test in rats as described by the Organization of Economic Co-Operation and Development (OECD) as per 423 guidelines (OECD Guidelines for the Testing of Chemicals, 2010). The SASE at a limit dose of 5000 mg/kg was administered orally to three rats and observed for behavioral changes, any toxicity and mortality up to 48 h. The extract was prepared by dissolving the commercial extract in distilled water and the concentration was not to exceed the dose of 1 ml/100 g by weight. The test doses for evaluation of anti-ulcer activity were selected based on the oral acute toxicity testing.

Evaluation of anti-ulcer activity

Acute water immersion restraint stress (CRS) (Kulkarni and Juvekar, 2008)

Low (250 mg/kg p.o.) and high dose (500 mg/kg p.o.) of SASE and Omeprazole 10 mg/kg p.o. were

administered 1 hour prior subjecting the rats to stress (Surendra, 1999). The ulcers were induced in animals by keeping in a plastic restrainer at a temperature of 20˚C, making them immobile and placing vertically with heads facing upwards in holes of stainless steel water bath of dimensions (12.7 cm × 45.7 cm × 45.7 cm) consisting of 12 holes at its top having a diameter of 3 inches, filled with water up to the xiphoid level for a period of 3 hours daily. Same procedure was followed for 10 day. Animals were fasted for 24 hours until the ninth day. On day 10 after subjecting the rats to the stress, stomachs were isolated and cut opened along the greater curvature. The ulcer index and ulcer score were determined. Later, the stomachs were subjected to histopathological examination.

A. Ulcer scoring and ulcer index determination: For ulcer scoring, the stomachs were washed with saline water to look for ulcers in the glandular portion of the stomach. The number of ulcers per stomach was noted and severity of the ulcers was scored microscopically with the help of the hand lens (10 X) and scoring was done as per (Vogel, 2008).

- 0 = no ulcer
- 1 = superficial ulcer
- 2 = deep ulcer
- 3 = perforation

The Ulcer index (U_I) was calculated by the following formula:

$$\mathbf{U_I = U_N + U_S + U_P \times 10^{-1}}$$

- U_N = average number of ulcer per animal
- U_S = average severity score
- U_P = percentage of animal with ulcers

The percentage inhibition was calculated by the following formula:

% Inhibition = [(UI control – UI treated) / UI control] x 100

B. Histopathological studies: The isolated stomachs were kept in formalin solution (15%) then sent to pathologist for histological examination by Haematoxylin and Eosin staining and morphological observations with 100 X and 400 X.

Experimental Design: Briefly, the animals were divided into five groups (n = 6) and treated with the respective test solutions as given below:

Group I: (Normal control): Received distilled water.

Group II: (Negative control): Received stress three hours a day for a period of 10 days.

Group III: (Standard drug + Stress). Received standard drug Omeprazole 10 mg/kg p.o. one hour before three hours of stress for a period of 10 days.

Group IV: (Test drug Dose I + Stress). Received test drug (SASE 250 mg/kg) one hour before three hours of stress for a period of 10 days.

Group V: (Test drug Dose II + stress). Received test drug (SASE 500 mg/kg) one hour before three hours of stress for a period of 10 days.

Acute Ethanol (Et-OH) induced ulcer

(Majumdar, 1999)

Animals were treated with distilled water, Omeprazole, SASE 250 mg/kg and 500 mg/kg orally for 10 days and kept for 24 hours fasting until the ninth day. Animals were treated with test extract and standard drug, Omeprazole (10 mg/kg p.o.) one hour before ethanol administration on 10^{th} day. Ethanol (60%) was administered to every animal at a dose of 1 ml/200 g by weight on day 10. One hour later all the animals were sacrificed, the stomachs were isolated and ulcer index, ulcer score was determined and histopathological studies were performed as mentioned earlier. Briefly, the animals were divided into five groups (n = 6) and treated with the respective test solutions as given below:

Group I: (Normal control): Received distilled water.

Group II: (Negative Control): Received Ethanol 1 ml/200 g by weight on day 10.

Group III: (Ethanol + Omeprazole): Received Omeprazole 10 mg/kg for 10 days and Ethanol 1 ml/200 g by weight on day 10.

Group IV: (Ethanol + Test drug Dose I): Received Test drug (SASE 250 mg/kg p.o.) for 10 days and Ethanol 1 ml/200 g by weight on day 10.
Group V: (Ethanol + Test drug Dose II). Received Test drug (SASE 500 mg/kg p.o.) for 10 days and Ethanol 1 ml/200 g by weight on day 10.

Indomethacin (IND) induced ulcer in rats
(Vogel, 2008; Majumdar, 1999)
S. album Stem Extract (SASE 250 mg/kg and 500 mg/kg) and Ranitidine were administered once daily until day 10. Indomethacin was administered on day 10 for the induction of ulcers in all groups except the normal control. On day 10, one hour after having received the test and standard drug, the animals were administered Indomethacin (20 mg/kg) *per os*. Animals were sacrificed by cervical dislocation immediately one hour after treatment with Indomethacin. Stomachs were isolated for ulcer scoring and histopathological examination. Briefly, the animals were divided into five groups (n = 6) and treated with the respective test solutions as given below:

Group I: (Normal control): Received distilled water.
Group II: (Negative control): Received Indomethacin 20 mg/kg on day 10.
Group III: (Indomethacin + Ranitidine): Received Ranitidine 50 mg/kg for 10 days and Indomethacin 20 mg/kg on day 10.
Group IV: (Indomethacin + Test drug Dose I): Received SASE 250 mg/kg for 10 days and Indomethacin 20 mg/kg on day 10.
Group V: (Indomethacin + Test drug Dose II): Received SASE 500 mg/kg for 10 days and Indomethacin 20 mg/kg on day 10.

Statistical Analysis
The values are expressed as Mean ± SEM. The data was analyzed by One- way ANOVA followed by Dunnett's multiple comparison test using GraphPad Prism Version 5.04. The significance of difference was accepted at $p < 0.001$.

RESULTS
The percentage yield of extract was found to be 5%. Preliminary phytochemical screening reveals the presence of secondary metabolites like alkaloids, anthraquinone glycosides, saponins, tannins and terpenes. Acute toxicity testing revealed that SASE up to a dose of 5000 mg/kg is safe, as there were no mortalities or signs of toxicity in the limit test. Hence for the screening of anti-ulcer activity, two SASE doses 250 and 500 mg/kg in the range of 1/20 – 1/10 were selected. The anti-ulcer potential of SASE was assessed by a physical stress model - water immersion restraint stress model and two chemically induced gastric ulcer models (i) Ethanol, a common and intense gastric mucosa eroding agent and (ii) Indomethacin, a Non-Steroidal Anti-Inflammatory Drug (NSAID) was employed as an agent to assess effect of extract against drug induced acute gastric ulcers. In all the three models, both the test groups showed marked decrease ($p < 0.001$) in average number of ulcers per animal and ulcer index when compared to the negative control, indicating high degree of anti-ulcer activity **[results indicated in Tables 1-3 and Figure 1]**.

Table 1
Results of Water immersion restraint stress induced gastric ulceration model

Groups	Normal control	Vehicle + CRS	Omeprazole + CRS	SASE extract (250 mg/kg)	SASE extract (500 mg/kg)
Ulcers per animal ± SEM	-	18.66 ± 2.48***a	0.66 ± 0.33***b	6.66 ± 1.68***b	5.66 ± 2.34***b
Severity of ulcer	-	7.16 ± 1.27***a	0.50 ± 0.34***b	3.16 ± 0.54***b	2.50 ± 0.34***b
% of ulcers	-	100	34	66.7	52
Ulcer index	-	12.58	3.51	7.64	6.1

Note: Data was analyzed by One way ANOVA followed by Dunnett's multiple comparison test. ***P < 0.001 (n = 6). [a]when compared with normal control group, [b] when compared with negative control group.

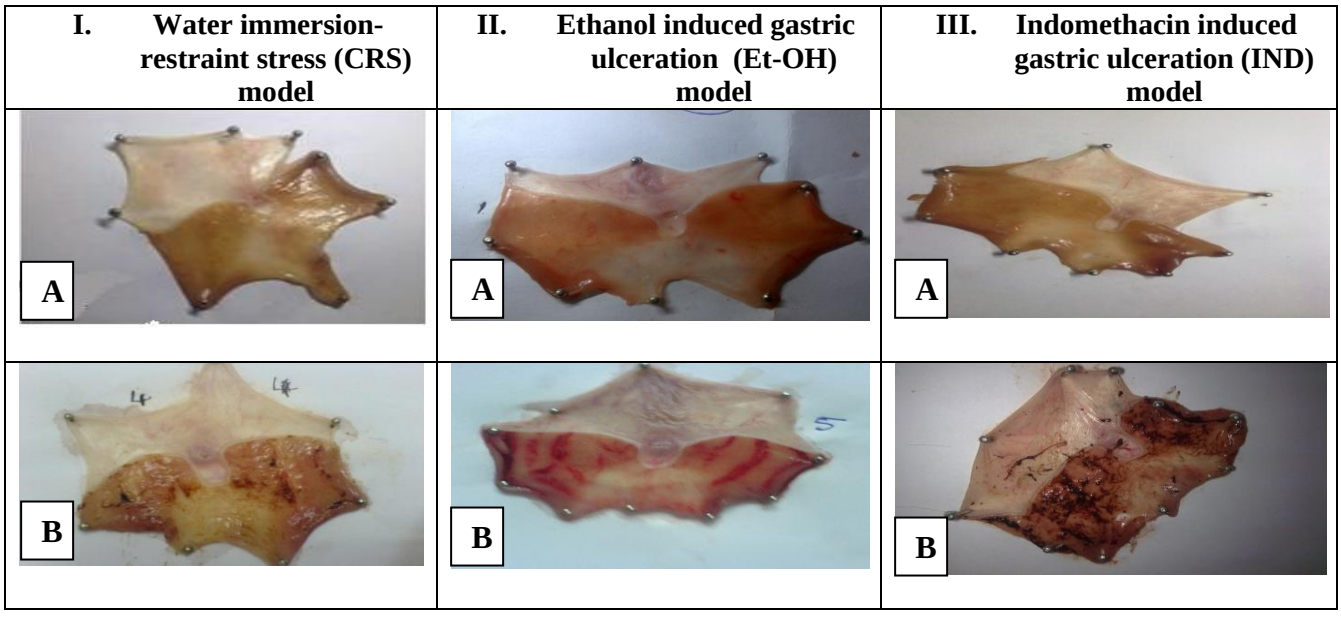
Table 2
Results of Ethanol induced gastric ulceration model

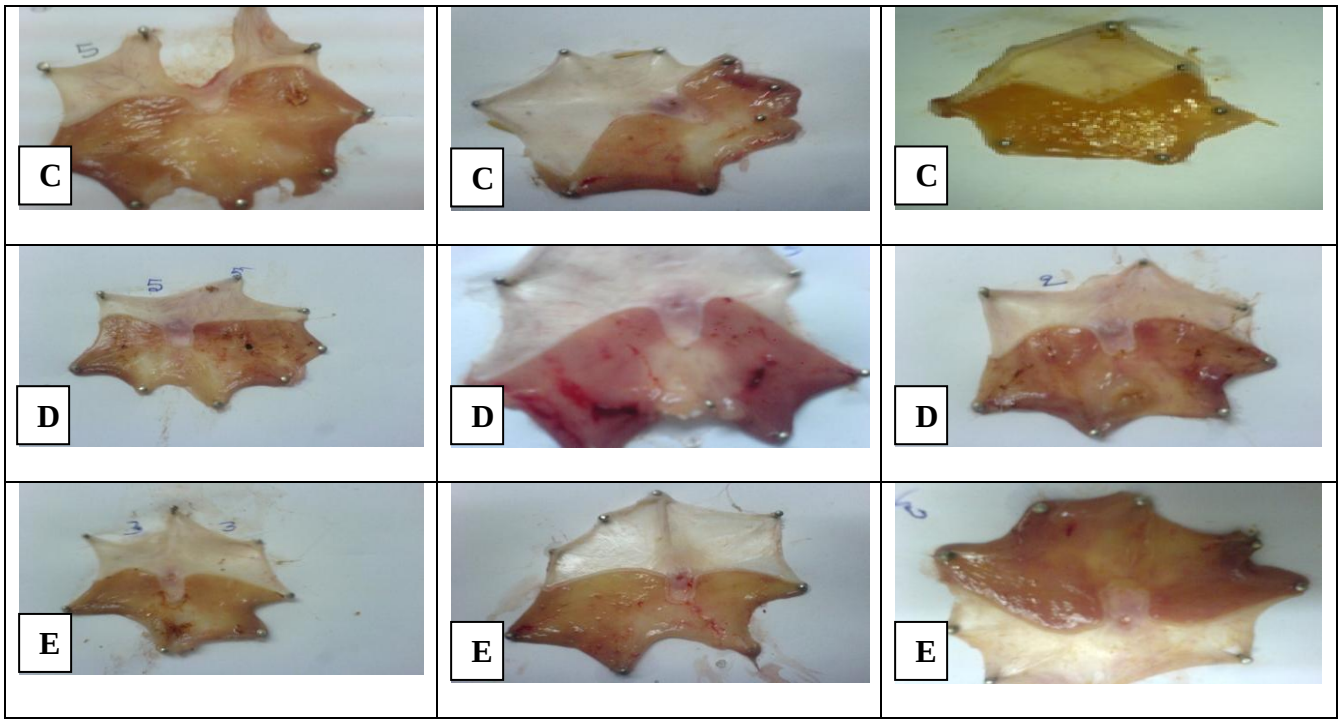
Groups	Normal control	Vehicle + Ethanol	Omeprazole + Ethanol	SASE extract (250 mg/kg)	SASE extract (500 mg/kg)
Ulcers per animal ± SEM	-	21.50 ± 2.12***a	2.66 ± 0.49***b	4.16 ± 0.87***b	2.83 ± 0.60***b
Severity of ulcer	-	12.83 ± 1.27***a	0.66 ± 0.21***b	2.66 ± 0.42***b	1.50 ± 0.34***b
% of ulcers	-	100	66.3	100	83.4
Ulcer index	-	13.43	7.02	10.63	8.78

Table 3
Results of Indomethacin induced gastric ulceration model

Groups	Normal control	Vehicle + Indomethacin	Ranitidine + Indomethacin	SASE extract (250 mg/kg)	SASE extract (500 mg/kg)
Ulcers per animal ± SEM	-	14.66 ± 1.22***a	3.20 ± 0.66***b	5.83 ± 0.65***b	3.83 ± 0.54***b
Severity of ulcer	-	7.00 ± 0.44***a	0.88 ± 0.30***b	2.66 ± 0.33***b	1.66 ± 0.55***b
% of ulcers	-	100	52	83	63
Ulcer index	-	14.66	5.05	9.1	7.1

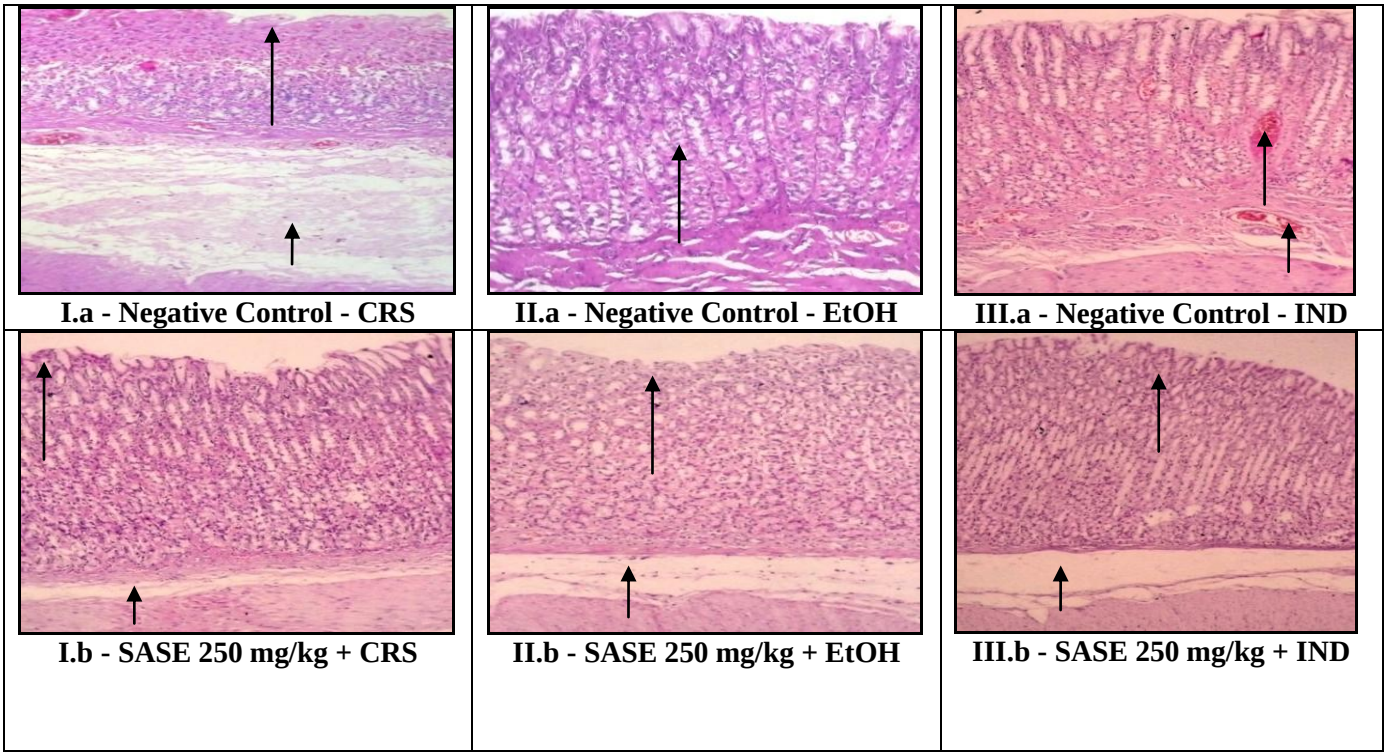
Figure 1
Stomachs of rats subjected to several gastric ulceration models

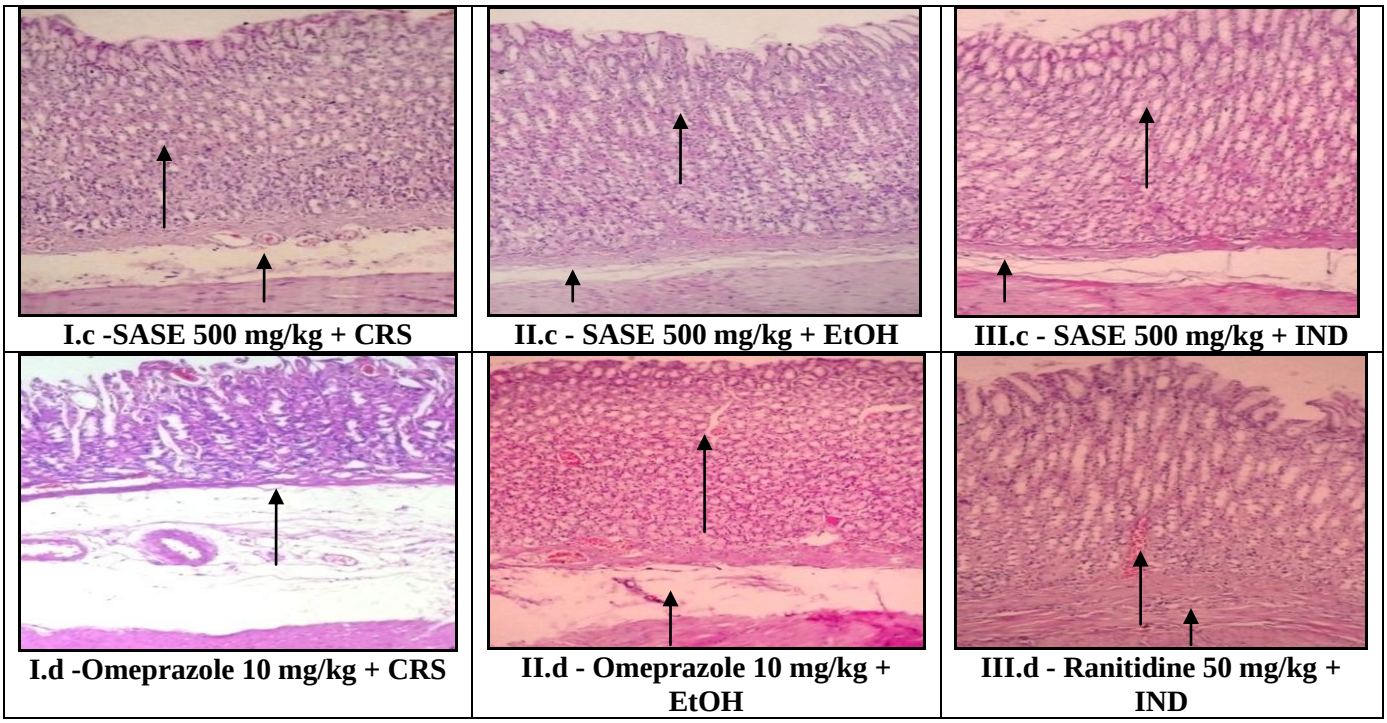




Note: A: Normal Control (Distilled water), B: Negative Control (CRS, Et-OH and IND) C: Standard (Omeprazole 10 mg/kg in CRS and Et-OH induced gastric ulcer models and Ranitidine 50 mg/kg in IND model, D: SASE 250 mg/kg (Test Dose – I), E: SASE 500 mg/kg (Test Dose - II).

Figure 2
Histological slides of stomachs of rats subjected to various treatments





I.c -SASE 500 mg/kg + CRS | **II.c - SASE 500 mg/kg + EtOH** | **III.c - SASE 500 mg/kg + IND**

I.d -Omeprazole 10 mg/kg + CRS | **II.d - Omeprazole 10 mg/kg + EtOH** | **III.d - Ranitidine 50 mg/kg + IND**

Stomachs of negative control group in all sets of experiments showed degenerated epithelial cells, inflammatory cells aggregation, necrosis and ulceration in mucosa **[Long arrows in Fig. 2: I, II and III.a]**. Congested vascular spaces, mixed inflammatory infiltration (macrophages and neutrophils) and moderate to severe oedema were observed in sub-mucosa **[Short arrows in Fig. 2: I and III.a]**. Stomachs of animal receiving SASE 250 mg/kg revealed ulceration **[Long arrows in Fig. 2: I and II.b]** and erythrocytes (heamorrhage) with inflammatory cells **[Long arrow in Fig. 2: II.b]** in mucosa of Ethanol-induced ulcers model while it remained unaffected in Indomethacin induced ulcers model **[Long arrow in Fig. 2: III.b]**; Sub-mucosa showed mild-moderate oedema and scattered mononuclear inflammatory infiltration **[Short arrows in Fig. 2: I, II and III.b]**. Mucosa in stomachs treated with SASE 500 mg/kg and standard drugs (Omeprazole 10 mg/kg and Ranitidine 50 mg/kg) was intact though few scattered lymphocytes **[Long arrows in Fig. 2: I, II and III.c and I, II and III.d]** were present indicating inflammation in all the experimental models. Sub-mucosa in SASE 500 mg/kg treated group was found to be normal in Ethanol and Indomethacin induced ulcers **[Short arrows in Fig. 2: II and III.c]**, whereas in Water immersion – restraint stress model, mild oedema, congested vascular spaces and scattered chronic inflammatory infiltrations were observed **[Short arrow in Fig. 2: I.c]** which were common in sub-mucosa of standard group (Omeprazole 10 mg/kg and Ranitidine 50 mg/kg) in all the models **[Short arrows in Fig. 2: II and III.d]**. Inflammatory signs were evident in standard groups. SASE 500 mg/kg, produced significant gastric-ulcer preventive effect that was more pronounced than the standards in several evaluated parameters.

DISCUSSION

Stress induced gastric ulcer is a method used to evaluate effect of drugs on gastric secretion. Stress induced ulcers are probably mediated by histamine release with enhancement in acid secretion and a reduction in mucus production (Peters and Richardson, 1983). Based on the observations, the protective action of *S. album* at 250 mg/kg and 500 mg/kg doses against stress induced gastric ulceration could be due to its anti-histaminic and anti-secretory effects. Ethanol induced gastric lesion formation may be due to stasis in gastric blood flow, which contributes to the development of the hemorrhagic and necrotic aspect of tissue injury (Surendra, 1999; Soll, 1990; Shay *et al*., 1945). Indomethacin is a known prominent inhibitor of prostaglandin synthesis that in turn damages the mucosal barrier, the damage in the mucosal barrier

causes permeation of sodium ions from the mucosa into the lumen (Vedavyasa, 1999). It is reported that leukotriene antagonists (5-lipoxygenase inhibitors) are capable of inhibiting both alcohol and NSAID - induced gastric ulceration in rats (Parnaham and Brune, 1987). Therefore the protective effect produced by *S. album* against Ethanol and NSAID-induced gastric ulceration could also be due to inhibition of 5-lipoxygenase pathway.

In a bioassay-guided fractionation study, six sesquiterpenes, (Z)-2 beta-hydroxy-14-hydro-beta-santalol (1), (Z)-2 alpha-hydroxy-albumol (2), 2R-(Z)-campherene-2,13-diol (3), (Z)-campherene-2beta,13-diol (4), (Z)-7-hydroxynuciferol (5), and (Z)-1beta-hydroxy-2-hydrolanceol (6), together with five known compounds, (Z)-alpha-santalol (7), (Z)-beta-santalol (8), (Z)-lanceol (9), alpha-santaldiol (10), and beta-santaldiol (11) were isolated from *S. album.* The crude extracts as well as the isolated compounds showed antibacterial activity against *H. pylori*. Especially, compounds 7 and 8 have strong anti-*H. pylori* activities against a clarithromycin-resistant strain (TS281) as well as other strains (Ochi *et al*., 2005). Sandalwood extract contains more than hundred constituents of tannins category (Sindhu *et al*., 2010**).** Tannins are used in medicine primarily because of their astringent property. They react with the proteins of the tissue layers (Samuelsson, 1999). Tannins tan the outermost layer of the mucosa and render it less permeable and more resistant to chemical and mechanical injury or irritation (Asuzu and Onu, 1990).

Oral treatment of *S. album* Stem hydro-alcoholic Extract (SASE) demonstrated good level of gastric protection in rats by effectively inhibiting physically (Stress) and chemically (both Local Irritant and Drug - NSAID) induced gastric ulceration. The property can be attributed to the wide range of phytochemicals present in the herbal extract and the action may be related to other beneficial effects, discussed earlier in the paper, particularly the phytochemicals like α- and β-santalols and six new sesquiterpenes that demonstrated anti-*H.pylori* activity and tannins could be responsible for anti-ulcer effect observed in the experiments. Results of present and previous studies by Kulkarni and Goel (1996), Mitra *et al*. (1996) and Venkataranganna *et al*. (1998) highlight that *S. album* can be used to treat PUD resulting from various factors (diverse etiology) as it exhibits multiplicity in mechanism of action. From high efficiency of *S.album*, alone in all the three experimental models of present investigation and previous reports on efficacy of UL-409 (an anti-ulcer polyherbal preparation), it can be concluded that *S. album* could be the main ingredient or one of the important components of UL-409 making remarkable contribution to its therapeutic potential. Thus, the present study provides scientific evidence to the traditional gastro-protective action of *S. album*.

ACKNOWLEDGMENTS

The authors wish to thank Dr. A. Vamseedhar (MD-Pathology, Sree Siddhartha Medical College), for assisting in histopathological part of the project and the management of Nargund College of Pharmacy for providing necessary facility to conduct animal experiments.

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