

## Evaluation of the anti-peptic ulcer activity of the seed extract of sesame (*Sesamum indicum*) in stress induced peptic ulcers in rats

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### ABSTRACT

**Background:** The peptic ulcers can be developed inside the inner lining of the stomach (gastric ulcer) or the small intestine (duodenal ulcer). Around 10% population of the world is suffering from the peptic ulcer disease. From the ancient times there is a reference about herbal extracts like *Sesame indicum* for the treatment of various diseases. The aim of the study is Evaluation of the anti-peptic ulcer activity of the seed extract of sesame (*Sesamum indicum*) in stress induced peptic ulcers in rats.

**Methods:** The study was carried out by stress-induced ulcer model in wistar rats. The antiulcer activity of *S. indicum* (0.5, 1mg/kg p.o. for 7 days) was compared with standard drugs (pantoprazole). The studied parameters were mucin content, gastric volume, pH, total acidity, free acidity, ulcer index, size and number.

**Results:** The low and high dose of *S. indicum* extract significantly reduced gastric mucosal lesion, mucin content, volume of gastric juice, gastric pH, free and total acidity when compared to positive control group. The high dose of *S. indicum* extract showed comparable results in parameters like effect on mucin content, gastric volume, pH, free acidity and total acidity with standard group. The statistical significant changes noted only in ulcer size, number and index.

**Conclusions:** Although the high dose *S. indicum* (1mg/kg) group showed significant gastric protection against ulcer induced by cold restraint method. However, no clear inference can be drawn at this stage and hence there is a need for further extensive research.

**Keywords:** Anti-peptic ulcer effect, Gastric ulcer, *Sesamum indicum*

### INTRODUCTION

Peptic ulcer diseases are a group of heterogeneous disorders, which manifests as a break in the lining of gastrointestinal mucosa bathed by pepsin and acid. Among the diseases of gastro-intestinal diseases, peptic ulcer is the most predominant with a worldwide prevalence of about 40% in the developed countries and 80% in the developing countries. The pathology of the gastric ulcer is lack of equilibrium between gastric aggressive factors and the mucosal defensive factors.<sup>1</sup> The present modality of treatment is the use of histamine H<sub>2</sub>-receptor antagonists, anticholinergic drugs, antacids and PPI's. From olden

days, there have been use of plant sources in the treatment of various disease modalities due to their perceived lower side effects, ease of accessibility and affordability. Plants are some of the most attractive sources for the discovery of new drugs and some have been shown to have promise for the treatment of gastro duodenal ulcer with minimum side effects.<sup>1</sup> Plants with traditional ethno medicinal uses in peptic ulcer management thus need to be screened for potential antiulcer activity. The sesame oil contain the lignans, sesamol, sesamin, pinosresinol and lariciresinol. Sesamol (SES), is a component of traditional health food in various Asian countries. It protects against atherosclerosis, hypertension, and aging. It has also been

explored for wound healing, antioxidant, anti-inflammatory, and free radical scavenging activity.<sup>2</sup>

Presently there are very less studies done on anti-peptic ulcer activity of Sesame oil. Therefore, the aim of the present study is to evaluate the anti-peptic ulcer activity of the seed extract of Sesame (*Sesamum indicum*) in stress induced peptic ulcers in wistar rats.

## METHODS

The study is conducted after the approval issued by Institutional Animal Ethics Committee (IAEC/KMC/13/2016).

### Chemicals/ drugs/ instruments used

Pantoprazole, *S. indicum* seed extract, ketamine, orcinol 1.6%, sulphuric acid 60%, phenolphthalein, topfer's reagent, 0.5% carboxymethyl Cellulose, distilled water, surgical kit, pH meter.

### Plant preparation and extraction

The fresh sesame seeds were purchased from the local market and seeds were grinded to fine powder. The powder is filled in to filter paper bag and placed in the soxhlet apparatus for extraction. The soxhlet apparatus is connected to round bottom flask which is filled by ethanol (90%) solvent and water bath to maintain temperature. The ethanol was boiled at 40 °C for over a period of 24 hours. The extract obtained was 10 % and was stored in desiccator at room temperature.

### Experimental animals

The animals were taken from central animal house - male/female albino rats of Wistar strain, weight - 200-250gm. The animals were housed under standard condition, housed individually with normal water and food granules, 12:12 hours light dark cycle, 50% humidity and 28°C temperature and provided with standard food granules and water ad libitum.

### Animal grouping and treatment

#### Ulcer inducing method

The procedure for inducing ulcers is with the stress-induced ulcer model, which include animals being fasted for a period of 18-24 hours prior to the experiment. Ulcers are then induced by placing animals individually in a restricted cage for 8 hours and in restraint cold ventilated refrigerator at a temperature of 2-3°C for 2-4 hours.<sup>1</sup>

#### Drug dosing

- Group I - Negative control, 0.9% normal saline - no ulcers induced x 7 days

- Group II - Positive control 0.9% saline + ulcer induced rats x 7 days
- Group III - Standard - pantoprazole 30mg/kg x 7 days
- Group IV - Test 1 - sesame extract 0.5mg/kg x 7 days
- Group V - Test 2 - sesame extract 1mg/kg x 7 days

Day 1 - The ulcers were induced by the Stress-Induced Ulcer Model. From Day 3 - 9: Standard and test drugs are given via oral route via a feeding tube and animals are dosed once a day, with 0.5% carboxy methyl Cellulose (vehicle) for 7 days, with the dosage mentioned above. On day 10 - the animals are euthanized using ketamine, the abdomen is dissected then the stomach was removed for the assessment of gastric mucosal damage.

**Table 1: Animals were divided in to 5 treatment groups 6 rats in each group.**

Group no.	Group name	Drugs to be administered	No. of rats
I	Negative Control	0.9% Normal saline	6
II	Positive Control	0.9% Normal saline + ulcer induced rats	6
III	Standard	Pantoprazole(30mg/kg)	6
IV	Test dose 1	<i>S. indicum</i> extract (0.5mg/kg) for 7 days	6
V	Test dose 2	<i>S. indicum</i> extract (1mg/kg) for 7 days	6
Total rats			30

All drugs are given via oral route via a feeding tube and animals are dosed once a day, with 0.5% carboxy methyl Cellulose (vehicle)

### Measurement of ulcer

The stomach was dissected along the greater curvature and fixing on a board or transparent glass examination can be carried out with hand lens macroscopically and by a tracing on the transparent paper and the paper on to graph sheets and size of ulcers and the ulcer index was calculated as per the method of Rao et al.<sup>3</sup>

Ulcer index = Ulcer size X ulcer number

### Mucin content determination: (Winzler method)

Diluted sample orcinol (1.6%) and sulphuric acid (60%) are added, vortexed and boiled for 10 min mixtures are cooled in ice-cooled water to stop reaction and absorbance studied at 425nm.

### Measurement of volume of gastric juice

Gastric juice from the stomach will be drained into a centrifuge tube after the animals were sacrificed. The tube will be centrifuged at 3000rpm for 10 minutes and the Centrifuged sample will be decanted and analysed for the volume of gastric juice.<sup>3</sup>

**Measurement of pH of gastric juice**

pH of the centrifuged sample of gastric juice is measured using a digital pH Meter, type DPH-100 (Dalal instruments).

**Measurement of free and total acidity**

The free and total acidity is measured by titrating 0.1 ml of gastric juice with 0.01 NaOH using toppers reagent and phenolphthalein as INDICATORS (HAWK, 1965). Orange yellow and point with toppers reagent is for the free acid content and the pink endpoint with phenolphthalein gives a measure of total acid content. Acidity is expressed as mEq/L per 100 grams body weight.

**Statistical analysis**

The results will be analyzed using one way ANOVA in SPSS 21 Software for Microsoft. The statistical significant value for any measure was set to  $p < 0.05$  at a confidence interval of 95%. The results expressed are in mean  $\pm$  standard error mean.

**RESULTS**

The high dose of *S. indicum* extracts (group-5) significantly reduced gastric mucosal lesion (Table 2),

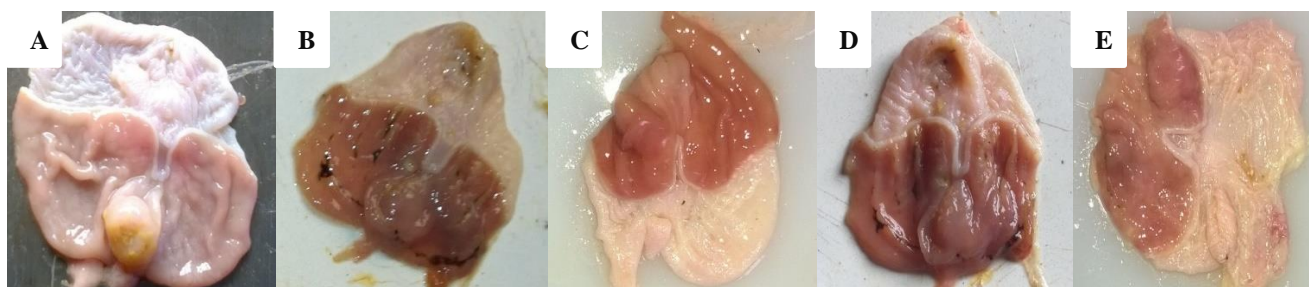
mucin content (Table 3), volume of gastric juice (Table 3), gastric pH (Table 3), free and total acidity (group-3) when compared to positive control group.

**Table 2: Effect of *S. indicum* on gastric ulcer.**

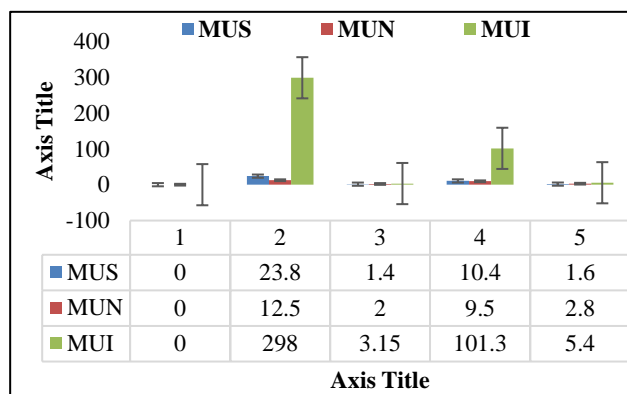
Group	Mean ulcer Size (mm)	Mean ulcer number	Mean ulcer index
Group I	-	-	-
Group II	23.8 $\pm$ 0.47 <sup>c-e</sup>	12.5 $\pm$ 0.76 <sup>c-e</sup>	298 $\pm$ 19.5 <sup>c-e</sup>
Group III	1.4 $\pm$ 0.3 <sup>b,d</sup>	2 $\pm$ 0.4 <sup>b,d</sup>	3.15 $\pm$ 0.6 <sup>b,d</sup>
Group IV	10.4 $\pm$ 0.4 <sup>b,c,e</sup>	9.5 $\pm$ 0.4 <sup>b,c,e</sup>	101.3 $\pm$ 0.7 <sup>b,c,e</sup>
Group V	1.6 $\pm$ 0.3 <sup>b,d</sup>	2.8 $\pm$ 0.65 <sup>b,d</sup>	5.4 $\pm$ 1.4 <sup>b,d</sup>

Values are mean  $\pm$  SEM (n=6). Values are statistically significant at \* $P < 0.05$  using one way ANOVA followed by Tukey's test. b:  $p < 0.05$  vs positive control, c:  $p < 0.005$  vs standard, d:  $p < 0.05$  vs test 1, e:  $p < 0.05$  vs test 2

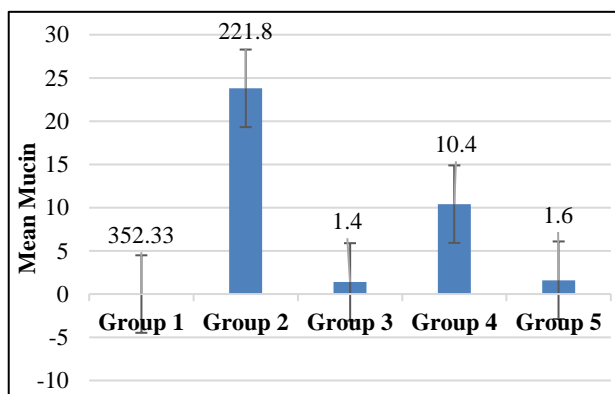
The low dose test group (group-4) showed significantly reduced gastric mucosal lesion (Table 2), mucin content (Table 3), volume of gastric juice (Table 3), gastric pH (Table 3), free and total acidity (group-3) when compared to positive control group. When compared with the standard group it showed significant changes only in ulcer size, number and index but not in other laboratory parameters.



**Figure 1 (A to E): Dissected part of the stomach on day 10<sup>th</sup> showing ulcers in each treatment group. A) Negative control group, B) Positive control group, C) Standard group, D) Test 1 group, E) Test 2 group.**



**Figure 2: Mean ulcer- size/ number/ index.**



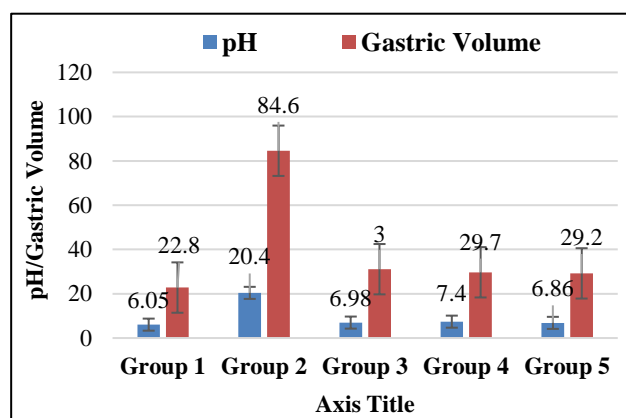
**Figure 3: Mean mucin content.**

**Table 3: Effect of *S. indicum* on Mucin Content, pH and Vol. of Gastric Juice**

Group	Mucin	pH	Volume of gastric juice (ml)
Group I	352.33±3.8 <sup>b-e</sup>	4.49±0.04 <sup>b</sup>	2.02±0.07 <sup>b-e</sup>
Group II	221.8±1.7 <sup>c-e</sup>	2.56±0.03 <sup>c-e</sup>	7.27±0.12 <sup>a,c-e</sup>
Group III	331.1±3.7 <sup>b</sup>	4.56±0.73 <sup>b</sup>	3.07±0.07 <sup>a,b</sup>
Group IV	340.5±2.1 <sup>b</sup>	4.6±0.06 <sup>b</sup>	3.7±0.10 <sup>a,b</sup>
Group V	315±8.8 <sup>b</sup>	4.1±0.16 <sup>b</sup>	4.2±0.29 <sup>a,b</sup>

Values are mean±SEM (n=6). Values are statistically significant at \*P<0.05 using one way ANOVA followed by Tukey's test. a: p<0.05 vs negative control b: p<0.05 vs positive control, c: p<0.005 vs standard, d: p<0.05 vs test 1, e: p<0.05 vs test 2

The high dose of *S. indicum* extract (group-5) showed comparable results in parameters like effect on mucin content, gastric volume, pH, free acidity and total acidity with the standard group (Table 3, 4 and 5). The statistical significant changes noted only in ulcer size, number and index (Table 2).

**Figure 4: Mean pH and gastric volume.****Table 4: Effect of *S. indicum* on free acidity and total acidity.**

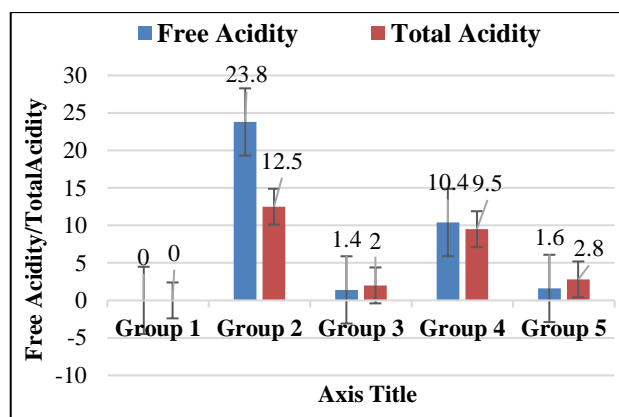
Group	Free acidity (mEq/L/Hr/100gm)	Total acidity (mEq/L/Hr/100gm)
Group I	6.05±0.05 <sup>b-e</sup>	22.8±1.4 <sup>b-e</sup>
Group II	20.4±0.09 <sup>c-e</sup>	84.6±0.37 <sup>c-e</sup>
Group III	6.98±0.08 <sup>a,b,d</sup>	31.1±0.37 <sup>a,b</sup>
Group IV	7.4±0.13 <sup>a,b,c,e</sup>	29.7±0.54 <sup>a,b</sup>
Group V	6.86±0.08 <sup>a,b,d</sup>	29.2±0.51 <sup>a,b</sup>

Values are mean±SEM (n=6). Values are statistically significant at \*P<0.05 using one way ANOVA followed by Tukey's test. a: p<0.05 vs negative control b: p<0.05 vs positive control, c: p<0.005 vs standard, d: p<0.05 vs test 1, e: p<0.05 vs test 2

## DISCUSSION

The result of this study revealed that sesame extract accelerated the gastric healing in stress induced ulcer when

dosed for a period of 7 days and the rate of healing is comparable to the standard drug pantoprazole.

**Figure 5: Mean free and total acidity.**

The evidence is based on the changes noticed in the gastric mucosa, gastric pH, mucin content, gastric volume, free acidity and total acidity.

The high dose sesame group (1mg/kg) showed the significant reduction in the gastric mucosal damage when compared with the control and standard pantoprazole group (30mg/kg). All other parameters like mucin content, gastric pH, volume, free and total acidity were comparable.

Group 3 (pantoprazole 30mg/kg) and group 4 low dose sesame 90.5mg/kg) showed the significant difference in all the parameters when compared with group I and II.

These ulcers occur following severe stress. The causes are as follows: Psychological stress, physiological stress which occurs in conditions like shock, severe trauma, extensive burn (Curling's ulcer), septicaemia, cushing's ulcer.<sup>4</sup>

The pathology of the stress ulcer is not clear, the possible hypotheses for genesis of stress ulcers is Ischaemic hypoxic injury to the mucosal cells and depletion of the gastric mucus barrier rendering the mucosa susceptible to attack by acid-peptic secretions.<sup>4</sup>

In the present study the ulcer induction was done using restraint cage and placing the rats in cold ventilated freezer for 2 hours. Edward et al, studied the Synergism between cold and restraint for rapid production of stress ulcers in rats and they observed that restraint and exposure to cold acted synergistically to produce gastric ulcers.<sup>5</sup>

Sesame (*Sesamum indicum*) belongs to family Pedaliaceae with the chemical compositions of lignans, sesamol, sesamin, pinoresinol and lariciresinol. Sesamol (SES), is a component of traditional health food in various Asian countries. It protects against atherosclerosis, hypertension, and aging. It has also been explored for wound healing,

antioxidant, anti-inflammatory, and free radical scavenging activity.<sup>6</sup>

*Sesamum indicum* contains phenols, flavonoids, anthocyanins, cyanogenic glycosides, polyacetylene alkaloids and peptides, the plant also contains vitamins like riboflavin, nicotinic acid tocopherol, pantothenic acid, thiamine, niacin, and trace amount of ascorbic acid.<sup>7</sup>

Several flavonoids prevent gastric mucosal lesions produced by various models of experimental ulcer and protect the gastric mucosa against various necrotic agents.

They are the most important plant constituents associated with anti-ulcer activity and also stabilize membranes and this may be the mechanism by which they inhibit ulcer induction.<sup>8</sup>

Sesame was shown to have the anti-ulcer and anti-secretory properties of the hexane extract of *Sesamum indicum* several studies have been conducted on extract of sesame on ethanol, NSAID's and water immersion induced ulcer model and have been observed positive results.<sup>9</sup>

In the present study it is observed that the extract of sesame attenuated the gastric mucosal damage by its antioxidant and free radical scavenging property, so this model (cold restraint) can confirm the gastro-protective property.

## CONCLUSION

Although the high dose sesame (1mg/kg) group showed significant gastric protection against ulcer induced by cold restraint method. However no clear inference can be drawn at this stage and hence we consider the work for further extensive research.

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*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Animal Ethics Committee (IAEC/KMC/13/2016)*

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