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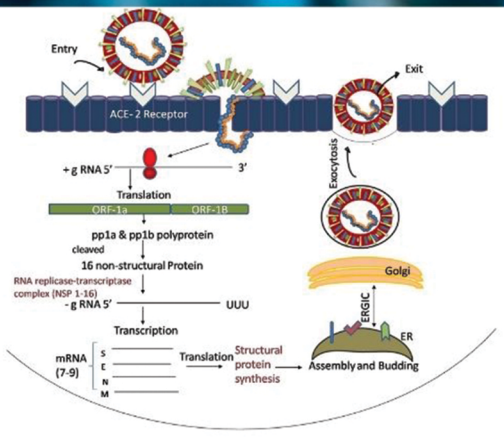

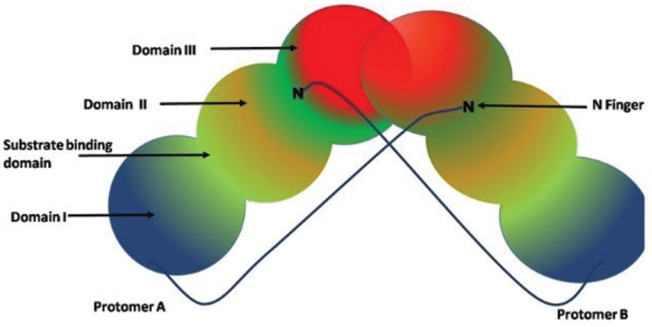

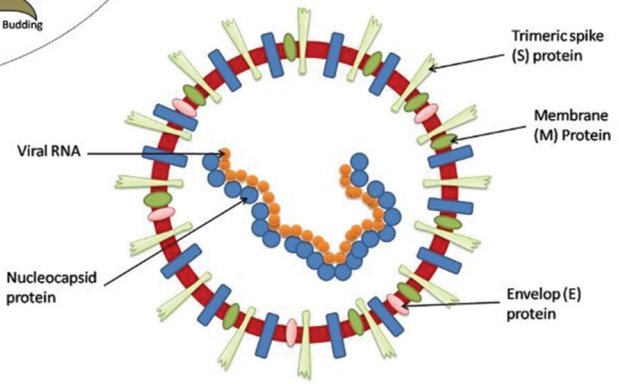

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Evaluation of mechanism(s) of action underlying the antioxidant and antiulcer activity of Sesamum indicum leaves extract in experimental rats

Shivam, Phool Chandra[1], Neetu Sachan[2]

Abstract:

OBJECTIVE: The current study aimed to estimate phytochemical screening, *in vitro* antioxidant activity, and gastroprotective activity of *Sesamum indicum* Linn ethanolic extract.

MATERIALS AND METHODS: The current study was held out by ulceration induced by pylorus ligation and indomethacin-induced ulcer screening models in Wister albino rats. The screening of antiulcer activity of ethanolic extract of *S. indicum* leaves (EESIL) at the different amounts (100, 200, and 400 mg/kg; per orally for 7 days) was compared with omeprazole as a usual antiulcer drug. Additional parameters such as gastric content, pH, total acidity, pepsin activity ulcer score, free acidity, ulcer index (UI), % inhibition of ulcers, mean mucin, pepsin content, and total protein content were observed.

RESULTS: In the pylorus ligation model, the pepsin activity free acidity, pepsin content, UI, total acidity, ulcer score, total protein content, and percentage ulcer inhibition were considerably decreased ($P < 0.05$ and $P < 0.01$), and mean mucin and gastric content pH extensively elevated ($P < 0.05$ and $P < 0.01$) in EESIL tested groups in the comparison of the control group. Doses (100, 200, and 400 mg/kg p.o.) of EESIL showed dose-reliant gastro protective outcomes, a considerable ($P < 0.05$ and $P < 0.01$) decrease in gastric parameters as UI and ulcer score and induction in gastric pH and percentage inhibition of ulcer compared with the control group.

CONCLUSION: Antioxidant, anti-Ulcer, EESIL, and EESIL show antioxidant activity at different concentration. The fallout of the study indicated that the EESIL had improved antiulcer potential due to the decrease in offensive factors and increase in defensive factors.

Keywords:

Antioxidant, anti-ulcer, ethanolic extract of *sesamum indicum* leaves, indomethacin, pylorus ligation, ulcer index

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Introduction

Peptic ulcers are pathological lesions in any part of the gastrointestinal system exposed to acid and activated pepsin. Peptic ulcer disease (PUD) is one of the most frequent illnesses in today's world. Due to an difference between protective (mucus, prostaglandins and bicarbonate) and aggressive (acidity and reactive oxygen species [ROS]) factors, it has developed into a widespread global health offender with increasing incidence and pervasiveness.[1] The probable number of about 16,500 deaths occur every year due to PUD.[2] The general signs of gastric ulcers are dyspepsia, including pain, discomfort, bloating, fullness, nausea, heartburn, regurgitation, and whistling in the abdominal region.[3] In the present era, the prevalence of daytime pain remains a common phenomenon along

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with the increased prevalence of night time pain due to lifestyle changes, increased stress, and longer daytime working hours. Currently, most patients with gastric ulcer need long-term treatment with drugs that inhibits gastric acid secretions, such as ranitidine (H_2-receptor antagonist) and pantoprazole (proton-pump inhibitor).[4]

The plant of Sesame (*Sesamum indicum* L. Family: Pedaleaceae) is commonly known as til, beniseed, gingelly, sim-sim, and sesamum. It is a popular oldest oilseed plant used and understood by human beings. Sesame has different local cultivars as well known in the literature, but it is said the genus Sesamum has only one cultivated species.[5] The sesame seed crop is the oldest oilseed crop known to humans for editable oil. The Sesame has various species, and most are wide. Most disseminated varieties of the genus Sesame are spot in sub-Saharan Africa. It was found in multiple types of research that *S. indicum* was cultivated and originated in India. Identifying and formulating phytoconstituents from plants is necessary for treating and managing ulcers. Various herbal medications have been employed in this approach's management and treatment of ulcers over the years.[6] In an exhaustive literature review, sesame leaves were not found to have antiulcer activity. So, we planned to evaluate the mechanism(s) of action underlying the antioxidant and antiulcer activity of *S. indicum* leaves extract in experimental rats.

Materials and Methods

The screening of antiulcer activity was performed in experimental rats, and ethical approval was permitted from the SPS, IFTM University, MBD, Uttar UP, India.

Drugs and chemicals

Ethanol, Petroleum Ether, Diethyl ether, 2, 2-diphenyl-1-picrylhydrazyl (DPPH) (Sisco Research Laboratories Pvt. Ltd.), Ascorbic Acid (Reckon Organic Private Ltd.). This study used different equipment, chemical, and solvents of analytical grade.

Identification and authentication of plant material

Plant authentication was completed by Dr. Ashok Kumar of the Botanical Department, IFTM University, Moradabad, India. The aerial part (leaves) of *S. indicum* was used for the study. The leaves of *S. indicum* were washed and dried in the air and shade. A voucher specimen was submitted to the department for further reference.

Extract preparation

The leaves were adequately cleaned, dried in the shade, and powdered. An electric blender was used for crushing 0.5 kg of air-dried leaves into a homogeneous powder. Pulverized leaves (0.5 kg) were defatted with petroleum ether using a Soxhlet apparatus, and after filtering the resulting slurry, After 24 h, the residue was dried by air. Following that, the defatted residue, dried (400 g from 0.5 kg) was subjected to 15 cycles of constant extraction with 1 L of 95% v/v ethanol using a Soxhlet apparatus at a 60°C-70°C temperature. An oven with dried hot air was used to dry the obtained extract. 400 g of defatted, residue dried yielded 42.3 g of extract. The brownish extract was put into a clean bottle and stored there up until it was needed later in a desiccator.

Preliminary phytochemicals

The preliminary phytochemical screening of ethanolic extract of *S. indicum* leaves (EESIL) was performed to identify different active phytochemicals.[7]

In vitro study

2, 2-diphenyl-1-picrylhydrazyl assay

The free radical scavenging action for EESIL was estimated with DPPH assay method.[8]

4 Hydroxyl radical scavenging activity.

Specific to the potent ROS in the living system is the hydroxyl radical. Damage to cells is brought on by the hydroxyl ion's reaction with polyunsaturated fatty acid molecules found in cell membrane phospholipids.[9]

Phenolic content in extract

Using a colorimetric assay known as the Folin-Ciocalteu method, the total phenolic amount was evaluated. An aliquot of extract (0.3 mL) of bark or leaf was employed in conjunction with the Folin-Ciocalteu phenol reagent (2.25 mL). The solution was kept into 2.25 mL of 6% sodium carbonate and let to remain for 5 min at the room temperature. It was then allowed to stand for 90 min. At 725 nm, the combination's absorbance was gauged. The findings were reported as mg Gallic acid equivalent (GAE) per gram of isolate depending on a standard calibration curve of gallic acid (0–200 mg/mL).[10]

Flavonoid content in extract

The overall flavonoid concentration was determined using the aluminum colorimetric technique with a few alterations using quercetin as the reference. For a calibration curve, a quercetin concentration range was produced (0–200 mg/mL). In a nutshell, 0.1 mL of 10% aluminium chloride, 80% methanol, 1 M potassium acetate, and distilled water were added to and combined with 0.5 mL of standard and 0.5 mL of extract in distinct test tubes. The same process was used to create a blank, but 0.5 mL of distilled H_2O was taken in place of standard or sample, and quantity of aluminum chloride was also deducted. For 30 min, all tubes were incubated at the room temperature.[10]

Experimental animals

The animal house of the School of Pharmaceutical Sciences, IFTM University, in Moradabad, India, provided 93 adult albino rats of either sex, weighing 160–180 g. The study protocol, reference number 2019/837/MPH/10, dated December 15, 2019, was approved by Institutional Animal Ethics Committees, and Committee for the Purpose of Control and Supervision of Experiments on Animals guidelines were followed throughout the experiment and maintenance. Every animal was housed in a standard husbandry environment with access to food, water, and libations.

Acute oral toxicity study

Prior to the experiment, three adult female albino rats were famished for the whole night. According to Organisation for Economic Co-operation and Development (OECD) Guideline 425, each animal received varying doses of the ethanolic extract of *S. indicum* (50–2000 mg/kg), and their behavior was observed persistently for 1 h, then at semi-intervals for 4 h for any gross change in behavior, and now for another 72 h for any death, followed by 14 days for any mortality.[11] Changes in skin, fur, mucus membrane (nasal), eyes, and autonomic salivation, lacrimation, sweat, dilation of blood vessels, urine incontinence, and feces), as well as central nervous system (tiredness, gait, tremors, and convulsion) modifications are evaluated once daily in the cage. *S. indicum* leaf extract has been demonstrated to be safe up to a level of 2,000 mg/kg of body weight. The quantities selected for antiulcer testing were 100, 200, and 400 mg/kg, respectively.[11]

Grouping of animals and antiulcer study treatment plan

Albino rats were employed in all experimental designs; they were split into five groups of six. The animals were allowed free access to water throughout a 24-h fasting prior to the testing. Simple distilled water was provided to Group I animals as a vehicle control; EESIL was given to Groups II, III, and IV at scaled doses (100, 200, and 400 mg kg^{-1} for 7 days (once daily), respectively; and 5th Group animals were given omeprazole 20 mg/kg as a control group.

Pylorus ligation induced ulcers

The grouping of animals for the antiulcer activity for this model is shown in Table 1. Six animals each made comprised each of the four groups from which the animals were separated. Saline (1 ml/kg, p. o.) was given to the I Group as a control. The II, III, and IV Groups were given 100, 200, and 400 mg kg^{-1}, p. o. of EESIL, respectively. Omeprazole (20 mg/kg, p. o.) was given to the last group. Before pylorus ligation, the animals fasted for 36 h.[12] A small incision was made beneath the xiphoid process to reveal the animal's abdomen while it was being lightly sedated with ether. To preserve its blood supply, the stomach's pyloric area was slightly raised and ligated. Carefully repositioning the stomach, the abdominal wall was stitched shut.[13]

Table 1: Grouping of animals for antiulcer activity

Groups	Sample size
Control	6
EESIL 100 mg/kg	6
EESIL 200 mg/kg	6
EESIL 400 mg/kg	6
Omeprazole 20 mg/kg (p.o.)	6

EESIL=Ethanolic extract of *Sesamum indicum* leaves

The therapy was given orally shortly after the pylorus was ligated. During the postoperative phase, the animals were denied food and drink, and after 6 h of pylorus ligation, the rats were shocked with an excess dose of ether anesthesia. A glass container was used to collect the secretions once the stomach was opened. The content's volume was calculated, and it was centrifuged for 10 min at 2000 rpm. The pH, free acidity, total acidity, and pepsin concentration of the supernatant were determined using aliquots (1 ml each). On the other hand, the precipitate was utilized to calculate total proteins. Individually, stomach was checked for lesions in the foregut and categorized based on severity.[14]

The number of ulcers was tallied, and each ulcer was given a score based on its appearance: perforation, deep ulcers, and hemorrhagic streaks (3). An ulcer index (UI) was generated from each animal's ulcer score. Using the formula below, the UI in the pylorus-ligated stomach was determined.

Where U_I; U_P (percentage of animals with ulcers), U_N (average number of ulcers related to one animal); and U_S (average severity score). The percentage inhibition of ulceration was calculated and compared with control.

The percentage of ulcer protection was evaluated by the following formula:

$$\% \ Protection = \left[\frac{Control \ mean \ UI - Test \ mean \ UI}{Control \ mean \ ulcer \ index} \right] \times 100$$

NSAIDs (indomethacin) induced gastric ulcer

Animals were given a single dosage of indomethacin (20 mg/kg BW) orally 1 h after the last administration of the test substance. Nonsteroidal anti-inflammatory drugs (NSAIDs) were administered to the rats for 6 h before they were euthanized by an anesthetic overdose and dissected, then the stomach was removed.[15] The stomach was opened along its larger curvature and cleaned with a solution of serum physiological solution (0.9% NaCl). The mucosa was

then exposed to determine the volume of gastric content, gastric content pH, and UI.[16]

Histopathological examination

The experimental rats' stomach tissues were removed, conserved in a 10% buffered formalin solution in labeled bottles, and processed for histopathological assessment. Tissue encased in paraffin wax was sectioned into 5 mm thick sections, stained with eosin and hematoxylin, mounted on glass slides, and viewed using an inverted digital microscope.[17]

Statistical analysis

The mean and standard error of the mean were used to express assessments of observed data. The one-way Analysis of variance was used to evaluate the means. $P < 0.05$ was used to determine the statistical significance.

Results

Preliminary phytochemicals

The EESIL was screened for various phytochemical tests per the reported methods. It was found that EESIL contains different phytochemicals such as carbohydrates, flavonoids, glycosides, amino acids, steroids, alkaloids, protein, and tannins.

In vitro study (antioxidant assays)

2, 2-diphenyl-1-picrylhydrazyl activity

The antioxidant action of EESIL has been estimated by the DPPH radical scheme using ascorbic acid as a reference substance. The concentration of the solution prepared ranges from 20 µg/ml to 100 µg/ml. DPPH is a highly stable free radical substance. The antioxidant activities of standard (ascorbic acid) and EESIL are explained in terms of inhibition (%). The highest inhibition percentages of ascorbic acid and EESIL are 80.45%–65.65% at 100 µg/ml. The extract's IC_{50} value was determined to be 67.57 µg/ml [Figure 1].

Hydroxyl radical scavenging activity

The antioxidant activity of EESIL has also been evaluated by a 4-hydroxyl radical scavenging assay using ascorbic acid as a reference or standard substance. The test substances' concentration ranges from 250 µg/ml to 1000 µg/ml. The antioxidant activity of standard and EESIL in terms of inhibition (%) in 1000 µg/ml concentrations, ascorbic acid and EESIL have the highest inhibition percentages of 85.43% and 69.46%, respectively. The IC_{50} for extract was found as 64.41 µg/ml [Figure 2].

Total phenolic and flavonoid content determination

We looked into the ethanolic extract of *S. indicum's* total flavonoid and phenolic content. *S. indicum* leaves extract was discovered to have 58.498.4 mg/g of GAE g^{-1} (D. W.), and 67.37 mg/g ± 12.4 mg/g of rutin equivalent (RE) g^{-1} (D. W.), respectively.

In-vivo anti-ulcer activity study

Effect of the ethanolic extract of Sesamum indicum leaves on gastric ulceration in pylorus ligation model

In rats with their pyloruses tied off, the secretion of gastrointestinal content, stomach pH, total acidity, pepsin activity, UI, free acidity, ulcer score, percent ulcer inhibition, pepsin content, mean mucin, and total protein content are presented in [Tables 2-4]. The stomach content, UI, pepsin activity, free acidity, pepsin content, total acidity, and total protein content all considerably decreased when matched to first group ($P < 0.05$ and $P < 0.01$). In contrast, the pH of gastric content, mean mucin, and percentage ulcer inhibition were increased significantly ($P < 0.05$ and $P < 0.01$). The EESIL (100, 200, and 400 mg kg^{-1}) showed inhibition percentages of 25.5, 47.0, and 66.5, respectively, while the conventional medication, omeprazole, showed an inhibition percentage of 77.5. With omeprazole, EESIL at 400 mg/kg showed antiulcer action.

Effect of the ethanolic extract of Sesamum indicum leaves on gastric ulceration in NSAIDs-induced ulcer model

In the indomethacin-induced model, the gastric content, pH, ulcer score, and index are observed and shown in Table 5.

Histopathological studies

Pylorus ligation model

The control group has diffuse mucosal ulcers and severe inflammatory cell penetration in the mucosa and submucosa, as indicated in the histological examinations. There was diffuse mucosal ulceration with necrosis and acute inflammatory cells, and necrosis was present in some of the glands. In the group that received a low dose of EESIL (100 mg/kg), the gastric mucosa is seen to have an intact epithelium, propria, lamina, and muscularis mucosa. Moderate mononuclear inflammatory infiltration is evident in the epithelial cells, and the submucosa displays edema with few congested vascular spaces. The gastric mucosa with integral muscularic mucosa, epithelium, and lamina propria were present in group that received a medium dose (200 mg/kg). The group given a high dose of EESIL (400 mg/kg) has intact lamina propria, gastric epithelium, and muscularis mucosa. Mild mononuclear inflammatory infiltration and a few congested vascular areas interfere with epithelial cells. Gastric mucosa with intact muscularis mucosa, lamina propria, and epithelium is seen in the standard group treated with omeprazole (20 mg/kg) section investigated. Mononuclear inflammatory infiltration and crowded vascular spaces are detected interfering with

Table 2: Effect of ethanolic extract of *Sesamum indicum* leaves on gastric content, gastric pH, acidity and pepsin activity in pylorus ligation model

Treatment	Dose (mg/kg)	Gastric content (mL)	Gastric pH	Acidity (mEq/l)		Pepsin activity (mL/h)
				Free	Total	
Control	1 mL	8.35±0.08	2.70±0.28	6.17±0.71	7.34±0.11	3.90±0.04
EESIL	100	8.35±0.02$^{\#}$	3.15±0.07$^{*\#}$	5.34±0.11	7.10±0.50$^{\#\#}$	3.08±0.06$^{*\#}$
EESIL	200	7.30±0.05*	4.07±0.03**	5.25±0.01	6.14±0.05*	2.95±0.05*
EESIL	400	7.00±0.05**	5.21±0.02***	4.81±0.08*	3.46±0.01**	2.18±0.14**
Omeprazole	20	6.35±0.08**	5.85±0.07***	4.49±0.01*	2.18±0.08**	1.46±0.01**

$^{*}P$<0.05 and $^{**}P$<0.01 against control group, $^{\#}P$<0.05 and$^{\#\#}P$<0.01 against standard group (Omeprazole). Values represent mean±SEM, n=6. Statistical analysis was performed using one-way ANOVA followed by Tukey Kramer Multiple Comparison Test. EESIL 100 mg/kg, EESIL 200 mg/kg, 400 mg/kg and Omeprazole 20 mg/kg. EESIL=Ethanolic extract of *Sesamum indicum* leaves

Table 3: Effect of ethanolic extract of *Sesamum indicum* leaves on ulcer score, ulcer index and percentage inhibition of ulceration in pylorus ligation model

Treatment	Dose (mg/kg)	Ulcer score	Ulcer index	Percentage inhibition of ulcers
Control	1 mL	3.33±0.12	12.65±0.20	-
EESIL	100	3.21±0.15	11.50±0.05$^{\#\#}$	25.5±0.5
EESIL	200	2.89±0.11*	8.56±0.08$^{**\#}$	47.0±2.0
EESIL	400	2.01±0.13**	2.71±0.26***	66.5±2.2
Omeprazole	20	1.18±0.12***	1.77±0.21***	77.5±2.5

$^{*}P$<0.05, $^{**}P$<0.01 and $^{***}P$<0.001 against control group, $^{\#}P$<0.05 and $^{\#\#}P$<0.01 against standard group (Omeprazole). Values represent mean±SEM, n=6. Statistical analysis was performed using one-way ANOVA followed by Tukey Kramer Multiple Comparison Test. EESIL 100 mg/kg, EESIL 200 mg/kg, 400 mg/kg and Omeprazole 20 mg/kg. EESIL=Ethanolic extract of *Sesamum indicum* leaves

Table 4: Effect of ethanolic extract of *Sesamum indicum* leaves on mean mucin, pepsin content and total protein content in pylorus ligation model

Treatment	Dose (mg/kg)	Mean mucin (µg/g)	Pepsin content (µmole/mL)	Total protein content (µg/mL)
Control	1 ml	0.085±0.05	36.67±0.22	133.96±2.1
EESIL	100	0.085±0.05$^{\#}$	31.47±0.01$^{*\#\#}$	121.21±0.48$^{*\#\#}$
EESIL	200	0.130±0.01$^{\#}$	25.73±0.25$^{**\#}$	82.19±0.36$^{***\#}$
EESIL	400	0.960±0.01*	23.05±0.56$^{**\#}$	63.97±0.21$^{***\#}$
Omeprazole	20	1.040±0.05*	15.47±0.01***	55.64±0.70***

$^{*}P$<0.05, $^{**}P$<0.01 and $^{***}P$<0.001 against control group, $^{\#}P$<0.05 and $^{\#\#}P$<0.01 against standard group (Omeprazole). Values represent mean±SEM, n=6. Statistical analysis was performed using one-way ANOVA followed by Tukey Kramer Multiple Comparison Test. EESIL 100 mg/kg, EESIL 200 mg/kg, 400 mg/kg and Omeprazole 20 mg/kg. EESIL=Ethanolic extract of *Sesamum indicum* leaves

Table 5: Effect of ethanolic extract of *Sesamum indicum* leaves on gastric content, gastric pH, ulcer score and ulcer index in nonsteroidal anti-inflammatory drugs -induced model

Treatment	Dose (mg/kg)	Gastric content (mL)	Gastric pH	Ulcer score	Ulcer index	Percentage inhibition of ulcers
Control	1 mL	7.50±0.11	2.30±0.28	4.23±0.12	13.25±0.30	-
EESIL	100	7.35±0.12	2.95±0.15$^{\#}$	3.45±0.25$^{*\#}$	10.40±0.05$^{*\#\#}$	24.5±0.5
EESIL	200	7.01±0.15**	3.07±0.03***	2.05±0.15***	7.66±0.08$^{**\#\#}$	44.0±1.7
EESIL	400	6.09±0.16***	4.98±0.12***	1.45±0.13***	2.89±0.66$^{***\#}$	68.5±2.42
Omeprazole	20	6.12±0.18***	5.79±0.17***	1.18±0.13***	1.67±0.21***	87.5±2.3

$^{*}P$<0.05, $^{**}P$<0.01 and $^{***}P$<0.001 against control group, $^{\#}P$<0.05 and $^{\#\#}P$<0.01 against standard group (Omeprazole). Values represent mean±SEM, n=6. Statistical analysis was performed using one-way ANOVA followed by Tukey Kramer Multiple Comparison Test. EESIL 100 mg/kg, EESIL 200 mg/kg, 400 mg/kg and Omeprazole 20 mg/kg. EESIL=Ethanolic extract of *Sesamum indicum* leaves

epithelial cells. The submucosa consists of connective tissue stroma with dilated and congested vascular spaces. The muscularis propria appears unremarkable [Figure 3].

NSAIDs induced ulcer model

The control group has diffuse mucosal ulcers and severe inflammatory cell penetration in the mucosa and submucosa, as revealed in the histological investigations. There was diffuse mucosal ulceration with necrosis and acute inflammatory cells, and necrosis was observed in some of the glands. In the group that received a low dose of EESIL (100 mg/kg), the muscularis mucosa, lamina propria, and intact epithelium of the stomach are visible. Moderate mononuclear inflammatory infiltration is evident in the epithelial cells, and the submucosa displays edema with few congested vascular spaces. Gastric mucosa with intact lamina propria, muscularic mucosa, and epithelium was seen in the group given a dose (200 mg kg^{-1}). The gastric mucosa in the group tested with EESI (400 mg kg^{-1}) has intact

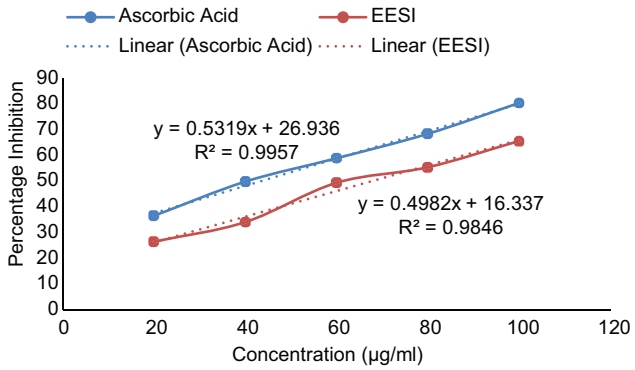

Figure 1: Effect on percentage inhibition of Ascorbic Acid and EESI. EESI = Ethanolic extract of *Sesamum indicum*

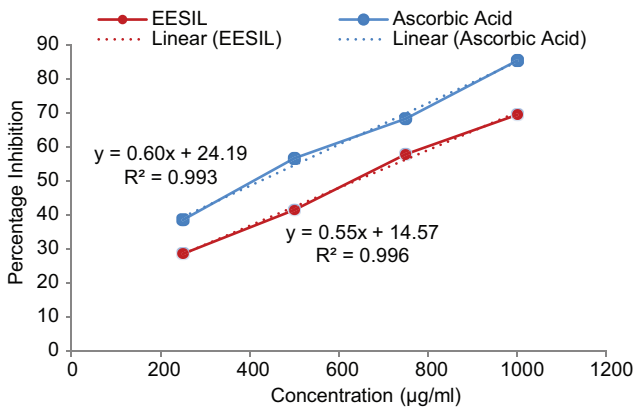

Figure 2: Effect on percentage inhibition of Ascorbic Acid and EESI. EESI = Ethanolic extract of *Sesamum indicum*

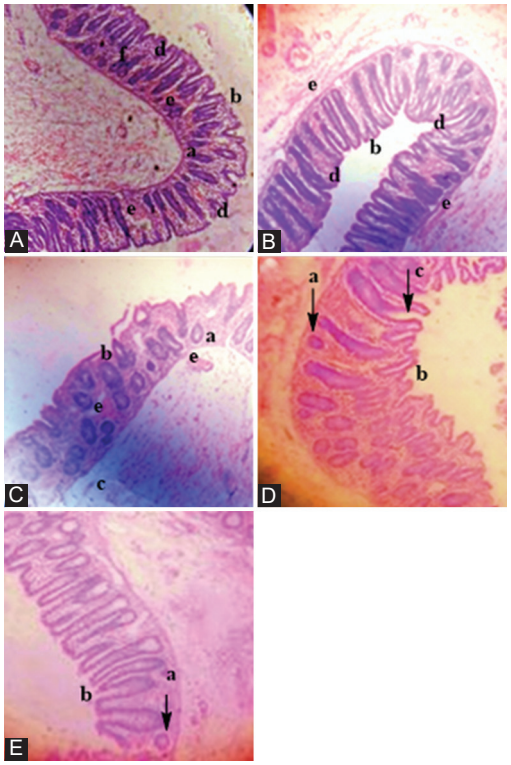

Figure 3: Histopathological Pictures of stomach tissue of Wister Rats of Pylorus Ligation model. Histological sections were stained with H and E (×100). (A) The Control Group, (B) EESIL 100 mg/kg, (C) EESIL 200 mg/kg, (D) EESIL 400 mg/kg, (E) Omeprazole 20 mg/kg. (a) Gland Cells, (b) Epithelial cell, (c) wide edema and leucocytes infiltration of sub mucosa, (d) confluent necrosis on margin zone, (e) hemorrhage, (f) erosion in the upper half of mucosa. EESIL = Ethanolic extract of *Sesamum indicum* leaves

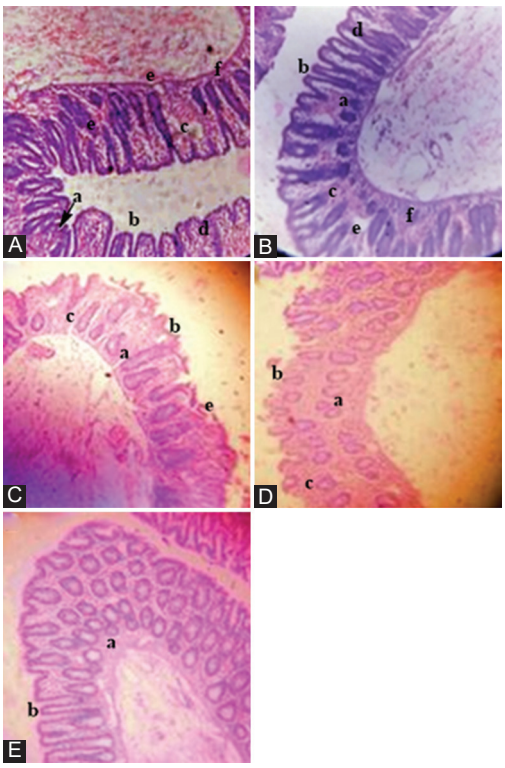

Figure 4: Histopathological Pictures of stomach tissue of Wister Rats of Indomethacin induced ulcer model. Histological sections were stained with H and E (×100). (A) The Control Group, (B) EESIL 100 mg/kg, (C) EESIL 200 mg/kg, (D) EESIL 400 mg/kg, (E) Omeprazole 20 mg/kg. (a) Gland Cells, (b) Epithelial cell, (c) Wide edema and leucocytes infiltration of sub mucosa, (d) confluent necrosis on margin zone, (e) hemorrhage, (f) erosion in the upper half of mucosa. EESIL = Ethanolic extract of *Sesamum indicum* leaves

epithelium, lamina propria, and muscularis mucosa. Mild mononuclear inflammatory infiltration and a few congested vascular areas clash with epithelial cells. In the section under investigation, the control group receiving omeprazole (20 mg kg^{-1}) demonstrated stomach mucosa with intact muscularis mucosa, lamina propria, and epithelium. Mononuclear inflammatory infiltration and clogged vascular spaces are detected interfering with epithelial cells. The connective tissue stroma of the submucosa has dilated and crowded vascular areas. The muscularis propria appears to be indistinguishable [Figure 4].

Discussion

The gastroprotective efficacy and antioxidant impact of *S. indicum* extract were examined in experimental rats with

pyloric ligation and indomethacin-induced gastric ulcers, as well as the putative underlying processes involved in their actions. Before evaluating pharmacological activity, preliminary phytochemicals analysis of test extracts (EESIL) was performed. PUD is a frequent gastrointestinal illness. Antiulcer medications include a lot of adverse side effects.[18] Several plants have been shown to be effective in treating gastroduodenal diseases in clinical trials. A stress-induced increase in stomach acid (Hydrochloric acid) secretion is the cause of a gastric ulcer, which promotes ulceration by exposing the stomach's unprotected lumen to the accumulated acid.[19]

As evidenced by pylorus ligation ulcers, autodigestion of the stomach mucosa and degeneration of the gastric mucosal wall result in superior gastrointestinal damage, with lesions, hemorrhage potentially catastrophic rupture, and ulcers. Stomach ulcers are caused by the stomach's pyloric blockage, which causes gastric acid accumulation. Agents that lower stomach acid output while increasing mucus secretion can help prevent ulcers from developing due to this surgery. Omeprazole, like ranitidine, is an antiulcer medication that inhibits stomach secretion and pepsin activity via an anti-secretary mechanism. Auto-digestion and stomach wall breakdown are caused by the digestive effects of retained gastric fluids (including pepsin and gastric acid), disruption of gastric blood flow, and enhanced construction of free radicals.[20] Drugs that cause a decrease in gastric juice output and an increase in mucus production can help to avoid gastric ulcers induced by pyloric ligation.[14] In the excitable model of pylorus ligature, activation of the postganglionic reflux by activation of pressure receptors in the gastric mucosa is suggested to enhance gastric acid secretion. The current findings clearly show a dose-dependent reduction in stomach acid secretion.[20]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most frequently given pharmacological classes in the world. The most typical cause of stomach ulcers is nonsteroidal anti-inflammatory drugs (NSAIDs).[21] For example, indomethacin is a widely used and therapeutically appropriate experimental model for developing stomach ulcers. Indomethacin causes gastric ulcers by suppressing the formation of prostaglandins, generating ROS, commencing lipid peroxidation, causing stomach cell apoptosis and necrosis, and lowering bicarbonate levels.[22] For example, indomethacin is a widely used and therapeutically appropriate experimental model for the development of stomach ulcers. Indomethacin causes gastric ulcers by suppressing the synthesis of prostaglandins, generating ROS, commencing lipid peroxidation, causing stomach cell apoptosis and necrosis, and lowering the bicarbonate level.[23] The chelation of metal ions like copper and iron, the scavenging of free radicals, and inhibition of free radical-generating enzymes are only a few of the processes through which flavonoids' antioxidative activities come about.[24]

Conclusion

The findings support the assertion that EESIL has antioxidant action. No mortality was observed with oral administration of *S. indicum*, even at the maximum dose (2000 mg/kg). EESIL was found to significantly inhibit gastric volume, acidity, pepsin activity, ulcer score, UI, pepsin content, and total protein content and exhibit gastric pH, % inhibition of ulcers, and mean mucin in the pyloric ligation model. In ethanol-induced ulcers, EESIL was reported to dramatically improve gastric pH, prevent ulcer growth, and reduce UI, ulcer score, and gastric content. In indomethacin-induced ulcers, EESIL was found to significantly increase gastric pH and% inhibition of ulcers while decreasing gastric content, score, and index. The fallout of the study indicated that the EESIL had improved antiulcer potential due to the decrease in offenive factors and increase in defensive factors.

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Conflicts of interest
There are no conflicts of interest.

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