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Richa Yadav
Department of Pharmacy, R.K. Pharmacy College, Surai Sathiaon, Azamgarh, Uttar Pradesh, India

Dr. Bhavana Yadav
Department of Pharmacy, R.K. Pharmacy College, Surai Sathiaon, Azamgarh, Uttar Pradesh, India

Corresponding Author:
Richa Yadav
Department of Pharmacy, R.K. Pharmacy College, Surai Sathiaon, Azamgarh, Uttar Pradesh, India

Pharmacological evalution of antiulcer activity of *Carissa carandas* leaves extract on experimental animals

Richa Yadav and Bhavana Yadav

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Abstract
In the study, *Carissa carandas* leaves extract which was prepared in order to investigate the anti-peptic ulcer activity utilising model of peptic ulcers caused by NSAID induced peptic ulcer rat model method in Wistar rats. To the extract, HPLC & preliminary phytochemical screening were used. Wistar rats were orally administered extract & investigated for gastroprotective effect on peptic ulcer & compared their effect together with the usual medication (Ranitidine 50 milligrams per kilogram p.o..) of peptic ulcer prevention. Various parameters were measured including UI, GV, FA, TA & pH. After complete the procedure animals were sacrificed with the help of cervical dislocation method & the histopathological analysis of stomach tissue was investigated. The study demonstrates the role of the leaves of the *Carissa carandas* plant play in the entire model for anti-peptic ulcer activity. The extracts appear to hold promise for the creation of phytomedicine with anti-peptic ulcer effects & the study provides the way for further investigation into the elements of the extracts that mediate peptic ulcer prevention.

Keywords: *Carissa carandas*, Peptic ulcer, Peptic ulcer caused by NSAID induced peptic ulcer rat model, Anti-peptic ulcer, ethyl acetate extract of *Carissa carandas*

Introduction

Ulcer Definition

An ulcer may be a rupture within the skin or mucous layer that comes about in discharge, deterioration & corruption of the epithelial tissue & misfortune of surface tissue. Something that spoils & corrupts like an uncovered wound.

Types of Ulcers

- Peptic Ulcer
- Venous Ulcer
- Arterial Ulcer
- Mouth Ulcer
- Genital Ulcer

Peptic Ulcer

The term "peptic ulcer" defines the breakdown of the stomach &/or duodenum's mucosal epithelium. It is among the foremost predominant illnesses that affect people currently. There have been a few estimates of the frequency, extending from 2 to 10%. Peptic ulcers can result from elevated levels of pepsin or acid & reduce mucosal resistance or from both**.**

Mucosal injuries that damage the muscularis mucosae layer & make a cavity surround by both acute & chronic irritation are known as peptic ulcers. The stomach contains peptic ulcers, which are regularly found within the region where the corpus & antrum mucosae move, along the lesser ups and downs. The duodenal bulb is where duodenal ulcers are found.

There are different variables have been found to be great for the arrangement of peptic ulcers, by the by, not each ulcer understanding has the same pathophysiological anomaly. The mucosa lining the stomach is astoundingly able of discharging acid. By implies of exudative phosphorylation, the parietal cells scattered all through the stomach fundus & mucosal organs of the body discharge hydrochloric acid (HCI). The so-called soluble tide is caused by the

discharge of one bicarbonate particle (HCO3) into the gastric venous circulation for each hydrogen particle (H) released into the gastrointestinal lumen. Carbonic acid is created from CO, by parietal cell carbonic anhydrase & bicarbonate is discharged from this acid. The control of stomach acid discharge is interceded by a number of chemical, neurological & hormonal components. There are a ew hindrances of gastrin discharge when the intra-gastric pH is decreased to 3.0, when the pH is brought down indeed more to 1.5 or lower, gastrin cannot be discharged in reaction to nearly any boost. Patients who have Gastrinomas or tumours emitting gastrin, are vulnerable to ZES (Zollinger-Ellison Disorder). Most of these tumours are found within the pancreas, in spite of the fact that they can to frame within the stomach & duodenum [1].

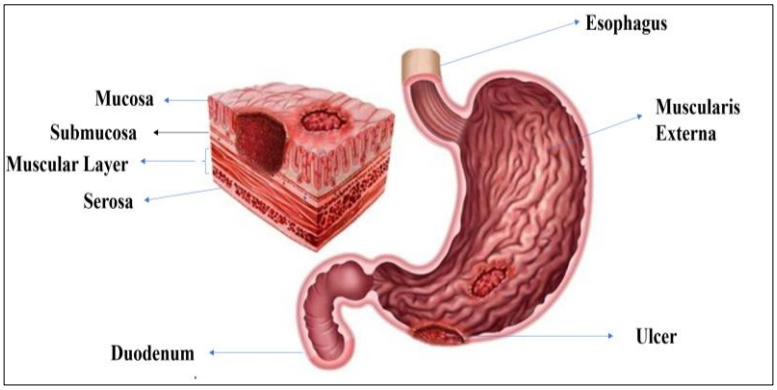

Fig 1: Schematic diagram of Peptic ulcer

Peptic ulcer Disease Pathophysiology

Pathogenesis of P.U.D is best explained by an imbalance between the mucosa's protective & damaging components.

In common, duodenal ulcer patients create more acid than individuals without the condition, especially all through the night (basal emission). Peptic ulcer patients may have ordinary or indeed diminished corrosive yield, in spite of the fact that the condition never, in case ever, happens within the total need of acid generation. Since these patients have generally lower levels of corrosive, it is likely that a compromised mucosal protection & diminished bicarbonate amalgamation contribute to the damage. Exogenous substances like NSAIDs & H. pylori associated in complex ways to form ulcers. A stomach H. pylori disease is connected to upto 50-60% of peptic ulcers [2].

Factors which is responsible for development of peptic ulcer

Common risk factors -causes for Peptic ulcer disease (PUD) and gastritis incorporate infection with *H. pylori*, and NSAIDs. Less common risk factors incorporate alcohol, smoking, cocaine, serious ailment, immune system problems, radiation treatment and Crohn disease among others.

A) *Helicobacter pylori*

Up to 90% of duodenal ulcers and 60% of stomach ulcers are caused by persistent inflammation brought on by *Helicobacter pylori*. takes over the antral mucosa. The defence mechanism is not able to eradicate the bacteria even though it appeared of antibodies. As a result, the bacteria may cause a type B gastritis that is chronically active, causing a flaw in the way that controls the generation of gastrin by that portion of the stomach, and the release of gastrin may either be reduced (in most situations), leading to hypo- or elevated or achlorhydria [3].

B) NSAIDs

NSAID use is another significant contributing factor. The mucous layer that covers the gastric mucosa, shields it from the stomach acid, whose secretion is prompted by specific prostaglandins. NSAIDs reduce the activity of cyclooxygenase-1 (COX-1), an enzymatic process required for the production of prostaglandins that provide protection. These prostaglandins serve a key role in maintaining stomach mucosal integrity [4].

C) Stress

Additionally, stress is still being investigated as a potential contributor to ulcer development, or at the very least as a consequence. A group of experts called by the Academy of Research in Behavioural Medicine found that ulcers are not only contagious illnesses, and that Indeed, psychological aspects are rather important. Function [1].

E) Smoking

Studies have shown that cigarette smoking increases the risk of developing peptic ulcers [5].

F) Caffeine

Caffeinated foods and beverages can stimulate the secretion of gastric acid in the stomach.

G) Alcohol

Ulcers are more frequently observed in individuals with liver cirrhosis; a condition often associated with chronic alcohol consumption [5].

H) Genetic factor

Hereditary impacts show up to have more significant, part in duodenal ulcers as prove by their event in family's monozygotic twins and affiliation with HLB-B5 antigen.

Reason behind ulcer caused due to NSAID [6].

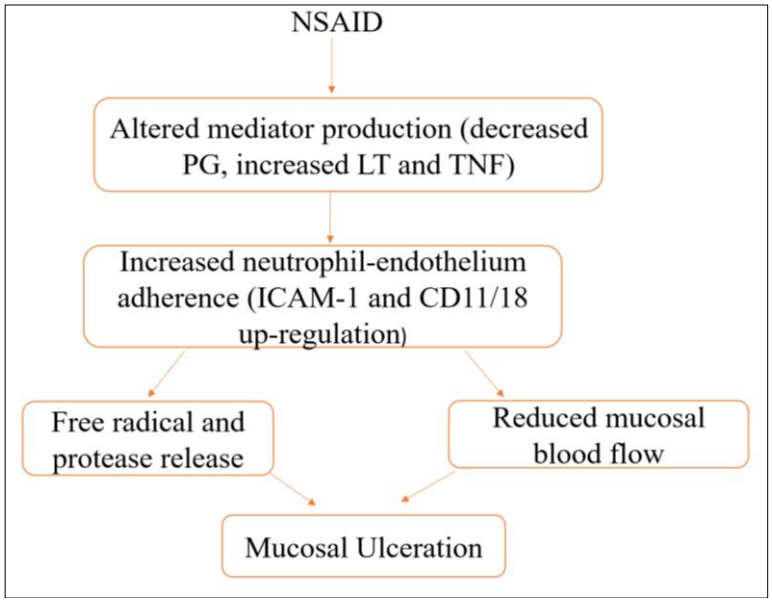

Fig 2: Reason behind ulcer caused due to NSAID

Symptoms of ulcer [7]

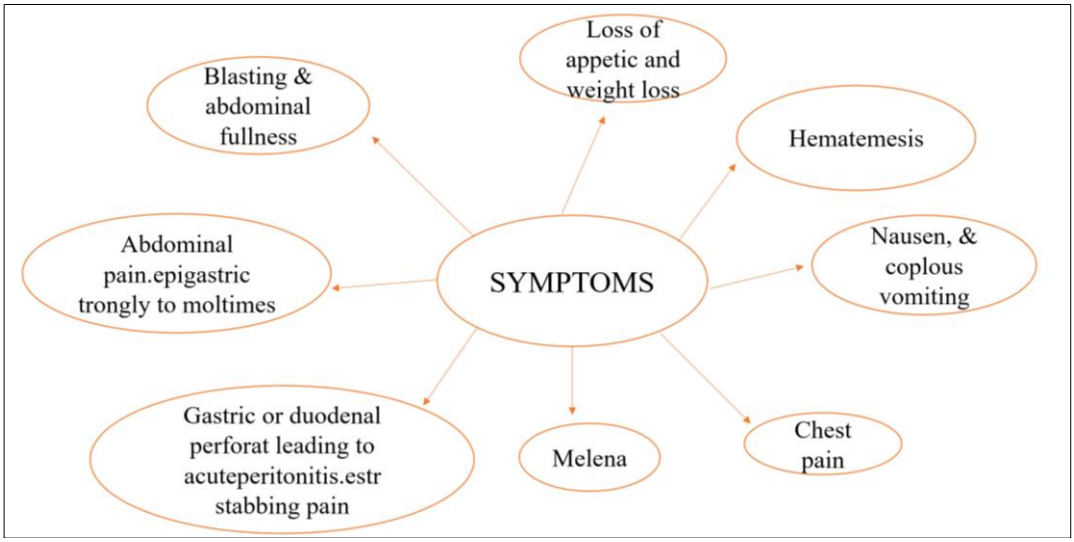

Fig 3: Symptoms of ulcer

Diagnosis

The conclusion is basically built up based on the characteristic symptoms like-

- Stool examination.
- Blood examination.
- Stomach pain is usually the first signal of a peptic ulcer.
- Endoscopy and biopsy of the upper gastrointestinal tract.
- Urea breath examination [8].

Peptic ulcer therapy

The flowing class of drugs are used reduce the production of peptic acid in order to treat peptic ulcers-

Synthetic drugs

P.P.I.

e.g.

Pantoprazole

Rabeprazole [9]

1. H_2-Receptors blockers.

e.g.

- Ranitidine
- Cimetidine
- Famotidine [10]

2. Anticholinergics.

e.g.

- Propantheline
- Pirenzepine [11]

Neutralization of peptic acid

3. Antacids.

e.g.

- Bicarbonate of sodium
- Carbonate of calcium
- Hydroxide of magnesium

B) Ulcer healing drugs.

e.g.

- Carbenoxolone sodium

C) Ulcer protectives.

e.g.

- Sucralfate

- Colloidal bismuth subcitrate

4. Anti Helico pylori drug.

e.g.

- Metronidazole
- Clarithromycine [10]

Plant Profile

- **Plant Name:** *Carissa carandas* Linn.
- **Family:** Apocynaceae
- **Synonyms**

a) *Arduina carandas* (L.) Baill.
b) *Arduina carandas* (L.) K. Schum.
c) Burm.f. *Jasminonerium carandas*
d) *Capparis carandas* (L.) Burm.f.
e) *Carissa salicina Lam*. Echites spinosus

Botanical classification

Table 1: Botanical classification

Taxonomic Rank	Name
Taxonomic Rank	Name
Kingdom	Plantae
Subkingdom	Viridaeplantae
Phylum	Tracheophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Gentianales
Family	Apocynaceae
Genus	*Carissa*

Vernacular names

Table 2: Vernacular name

State / Language	Local Names / Synonyms
Maharashtra	Karavada, Karanda, Karwant
Andhra Pradesh	Vaka, Kalivi, Kalli
Bengal	Karamacha
Gujarat	Karmarda
Karnataka	Karekayi, Garji, Kavali
Himachal Pradesh	Karondhu, Garna, Kharnu
Hindi	Karunda
Sanskrit	Karamarda, Avighna

Morphological Description

- **Plant:** Prickly plant, with forked branches.
- **Height:** Two to three metres.
- **Wood:** Exceptionally difficult.
- **Bark:** The color ranges from light brown to green.
- **Thorns:** It measures approximately 3.2 centimeters in length, featuring a brown to greenish base with a distinctly brown apex [13].
- **Leaves:** The leaves are ovoid in shape they possess a leathery texture, entire margins, and reticulate pinnate venation. Each leaf is attached by a short petiole about 3 mm long. When detached from the stem, the leaves exude a characteristic white latex.
- **Flowers:** The flowers are bisexual and complete, white in color, borne on short stalks, and emit a sweet fragrance.
- **Fruit:** The fruit is an ovoid berry, green when unripe and turning shiny black upon full ripening. It typically measures 5 to 12 mm in length and around 6 millimeters in diameter [12].

Chemical Composition

- **Fruit:** The phytochemical constituents identified include lupins, Carissol, epicatechin, quercetin, rutin, piceatannol, kaempferol, and ursolic acid.
- Ursolic acid is a triterpenoid [13].

Fig 4: Plant of *Carissa carandas*

Materials and Methods

Collection & Authentication of the plant

Plant was collected from Jaunpur, Uttar Pradesh, India, area throughout the months of 10th January. & it was recognized and verified by Ms. Neelima Naveen a botanist at botanical Survey of India,Prayagraj by deposit of herbarium of vide number: B.S.I/C.R.C./2024&25/778 [14]

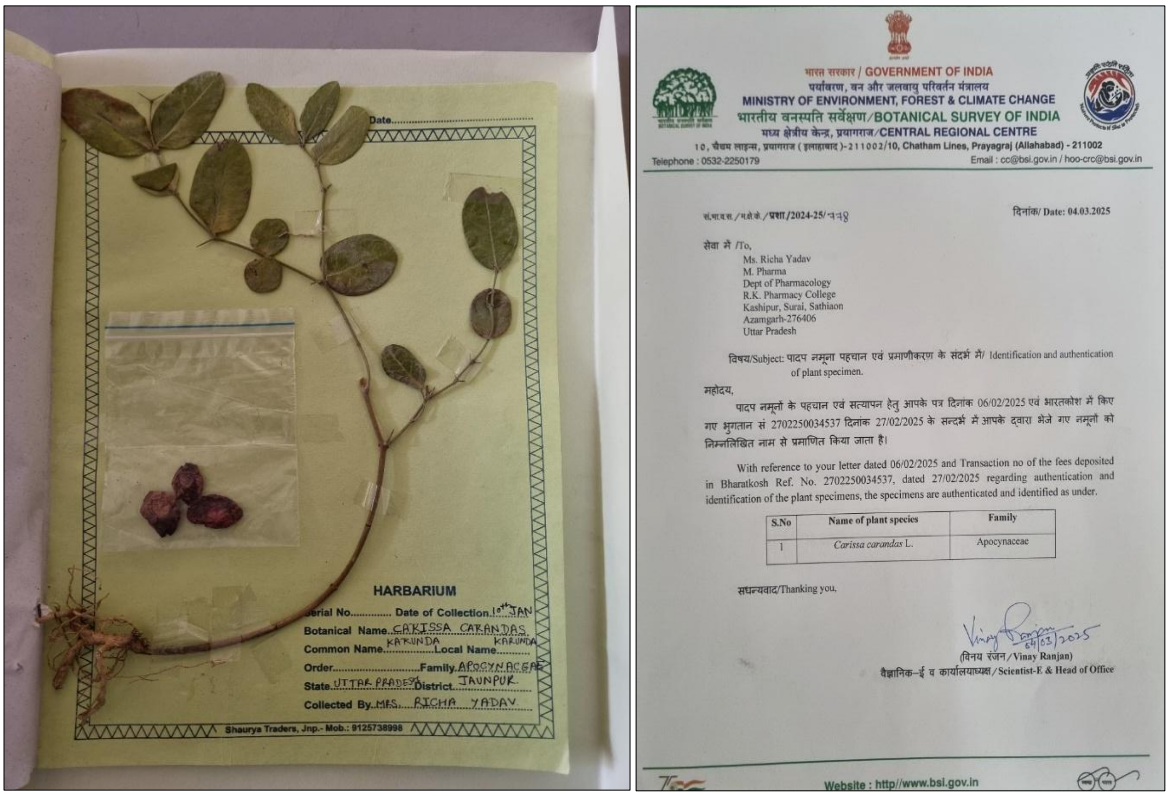

Fig 5: Collection & Authentication of the plant

Fresh *Carissa Carandas* leaves were collected from the verified plant by the B.S.I., Prayagraj. The foliage of plants was collected, properly divided & then given a thorough water wash to get rid of any dust. After being laid out in thin layers on drying trays & left in a shaded area for two weeks, the leaves of *Carissa Carandas* were allowed to dry naturally. Upon weighing the dried leaves, 1200 g of weight was showed [14]

Fig 6: Dry Carissa carandas leves

Preparation of plant extract

After being gathered, the Carissa Carandas leaves were shade-dried until they were completely dry. Grinding mechanically into a powder and then filtered through a No.twenty mesh screen. To remove fatty substance, 50 g of powdered fruit pulp was extracted using petroleum ether, then dried powder is extracted with ethyl acetate by using Soxhlet extraction method. After completing the extraction, the solvent was removed by using water both. Finally, *Carissa Carandas* leaves extract were obtained. *Carissa Carandas* leaves Extracts were stored in a sealed container and kept between 4 and 8 degrees Celsius until they were used in additional research [14]

Fig 7: Extraction of plant material by continuous Soxhlet apparatus

Fig 8: Preparation & Collection of powder

Physiochemical parameters

The tab below displays the physiochemical characteristics of the powdered Carissa carandas leaf medication [15]

Table 3: Physiochemical parameters of Carissa carandas leaves powder drug

S.N.	Parameter	Value (%) of Carissa carandas leaves	Standard Value
1.	Foreign matter	0%	Not More Than 2%
2.	Loss on drying	0.9%	Not More Than 3%
3.	Ash value	1.6%	Not More Than 5%
4.	Water extractive value	8%	Not Less Than 7%
5.	Alcohol extractive value	13%	Not Less Than 4%

Phytochemical Analysis

Carissa carandas leaf powder's physiochemical characteristics are shown in the tab below [16]

Table 4: Physiochemical parameters of Carissa carandas leaves powder drug.

S.N.	Phytochemical Test	Result
1.	**Tests for carbohydrates**	
	Molisch's test	+
	Benedict's test	+
2.	**Test for Proteins**	
	Millon's test:	+
	Biuret test:	+
3.	**Test for Flavonoids**	
	Sulphuric acid test	+
	Shinoda test	+
4.	**Test for Tannins& phenolic compound**	

	Lead acetate solution	+
	5% FeCl3 solution	-
5.	**Test for Alkaloids**	
	Tannic acid test	+
	Hager's test	+
	Dragendorff's test	+
	Wagner's test	+
6.	**Test for Glycosides**	
	Legal's test	+
	Keller-Killiani test	+
7.	**Test for saponins**	
	Foam test	+
8.	**Test For Amino Acids**	
	Ninhydrin test	-
9.	**Test fot Triterpenoids**	
	Salkowski's test	+

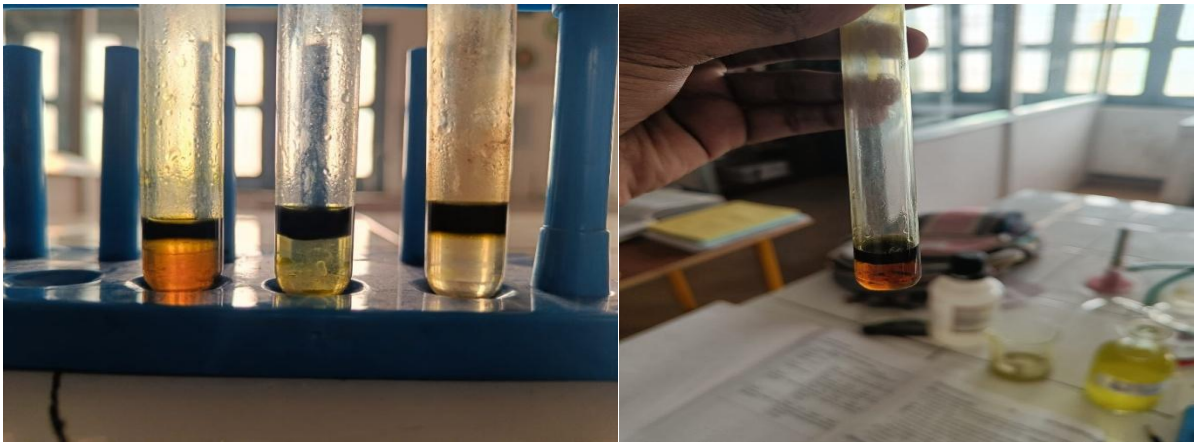

Fig 9: Phytochemical analysis

High Performance Liquid Chromatography (HPLC)
Chromatographic method

- **Column:** C18, (250 X 4.6mm), 5 Micron
- **Flow:** 0.6 ML/MIN
- **Wavelength:** 210nm
- **Injection Volume:** 20µl
- **Mobile Phase:** Methanol: CAN 3 : 70
- **Column Temp:** Ambient

Procedure

Standard preparation: Weigh accurately 5.0mg of Standard in 100ml volumetric flask and add 10ml methanol shake sonicate and then cool and make up volume 100ml of methanol.

Test preparation

Weigh accurately 500 mg of the extract in 100ml volumetric flask and add 10ml methanol, shake, and sonicate, then and cool and make up volume 100ml with methanol.

Calculation

$$\%\,w/w = \left(\frac{\text{Test area}}{\text{Std area}}\right) \times \left(\frac{\text{Std wt}}{\text{Test wt}}\right) \times \text{Potency} \times 100$$

Pharmacological evaluation

Animals

Wistar rats of roughly the same age and weighing 120-200 g were purchased from a licensed breeder. The animals were acclimated to the lab environment, which was kept at 25 ± 2 °C and 43-57% relative humidity. There was a 12-hour cycle of light and dark.Rats were provided with a standard pellet diet and water ad libitum, except for a 24-hour fasting period prior to the commencement of the experiment, during which only water was allowed. According to the most recent recommendations for assessing experimental pain in conscious animals, all tests were carried out in the morning. The Institutional Animal Ethics Committee (IAEC) gave its approval to the study protocol., approval number: IAEC/RK/25/08.

Evaluation of toxicological study of *Carissa Carandas* leaves

Acute Toxicity Study

Acute toxicity testing is done on experimental animals to determine the LD50 value. In accordance with OECD guidelines 423, the LD50 was determined in experimental animals.

It is an international organization whose goal is to reduce both the pain and the quantity of animals used in acute toxicity test.

Determination of Acute Oral Toxicity

The OECD guideline 423 were followed in determining the lethal median dose (LD50) in rats. Oral gavage was used to administer a single dosage of the extracts (five mg per kilogram, fifty mg per kilogram, three hundred mg/kg, two thousand mg per kilogram, and five thousand mg/kg) to different groups of rats.

Water & food were freely available to the animals, but they were all given food for two hours before and four hours after dosage. During the first twelve hours, the creatures were observed every hour for the first 4 hours, and any unfavourable outcomes. Afterwards, during the study period (14 Days), they were observed twice a day for any unusual changes [17]

Antiulcer activity study

NSAID induced peptic ulcer rat model

A study involving five groups of rats and each groups contain six animals [18]

Table 5: Experimental design

S. No	Group of animals	Treatment
1.	Group I (Negative Control)	Distilled water was given to the animals.
2.	Group II (Positive Control)	Peptic Ulcer induced in animals by using Indomethacin with dose 30mg/kg body weight (p.o.)
3.	Group III (Standard Treated)	Peptic ulcer induced animals by using Indomethacin with dose 30mg/kg body weight (p.o.) provided prior treatment by Ranitidine 50mg/kg body weight for 21 days.
4.	Group IV (*Carissa carandas* leaves treated with 250mg/kg body weight)	Peptic ulcer induced animals by using Indomethacin with dose 30mg/kg body weight (p.o.) prior treatment with test drug (low dose) for 21 days.
5.	Group V (*Carissa carandas* leaves treated with 500mg/kg body weight)	Peptic ulcer induced animals by using Indomethacin with dose 30mg/kg body weight (p.o.) prior treatment with test drug (high dose) for 21 days.

Thirty albinos five randomly selected groups of six wistar rats each were created. All that was given to Group 1 (the typical control) was distilled water. Only indomethacin was given to Group 2 (ulcerated control). Before indomethacin was administered, Group 3 got a pretreatment of ranitidine at a dose of 50 mg per kilogram body weight. A moderate dose (250 mg per kilogramb.w.) of Carissa carandas fruit pulp extract was administered to Group 4, and a high dose (500 mg per kilogram b.w.) was administered to Group 5. Before indomethacin induction, the plant extracts and the usual medication (ranitidine) were both given orally once day by gavage for 21 days in a row. Animals had unrestricted access to common food and water during the trial. PEG400 was used as the solvent to manufacture indomethacin; any remaining residues were filtered out of the solution before it was suitably diluted. To make the dosages of Carissa carandas fruit pulp extract, the material suspended in a 0.5% carboxymethylcellulose (CMC) aqueous solution was sonicated.

Fig 10: Experimental procedure

Stomach isolation and gastric juice collection:

The animals were mercifully killed by cervical dislocation on the twenty-third day, four hours after the ulcer was induced. The stomach was gently removed when the abdominal cavity was opened. The stomach contents were subsequently extracted by cutting along the larger curvature, and they were gathered in a centrifuge tube. After adding five milliliters of pure water, the mixture was centrifuged for ten minutes at 14,000 rpm. One milliliter of the supernatant was mixed with one to three drops of methyl orange indicator after centrifugation, and the mixture was titrated with 0.01 N NaOH until a yellowish-orange endpoint was achieved. The amount of free acidity matched the amount of NaOH utilized. One milliliter of the same supernatant was then mixed with phenolphthalein indicator, and the titration was carried out until a persistent pink hue developed. The total acidity was indicated by the volume of NaOH used in this phase [18]

Fig. 11: Stomach isolation and gastric juice collection

Determination of abdominal secretion parameters:
By using Toepfer's reagent as an indicator and titrating with 0.0025 N NaOH, the gastric acid yield (volume) inside the supernatant (2 ml) was determined. A pH meter was used to measure the pH of the gastric juice, which was then utilized to measure the concentration of mucin and specific pepsin activity [18]

Table 6: Ulcer scores and descriptive remark

Score	Remark
0	Almost normal mucosa
1	Vascular blockages
2	1 or 2 injuries
3	Severe injuries
4	Very extreme injuries
5	Mucosa with many wounds

Evaluation of ulceration
Using a common scoring system, the degree of ulceration in animals treated with indomethacin was evaluated. In short, the stomachs that had been removed and cleaned were placed on corkboards, and any ulcers were examined using a dissecting microscope that had a square-grid lens. As indicated in Table 3.2, a scoring system ranging from 0 to 5 was utilized to assess the degree of vascular congestion and mucosal lesions or haemorrhagic erosions.

Histopathological study
The cervical dislocation method was used to sacrifice the animal. The animal's stomach was exposed after they were dissected, and for histopathological examination, they were subsequently perfused with cold saline phosphate buffer with a pH of 7.4. The stomach was removed and put into individual containers with 20% v/v formalin. The histopathological estimation, induction was carried out under controlled conditions at 37 °C. The histopathology work was done in Jaunpur at Shree Pathology & Diagnostic Centre.

Statical Analysis
The GraphPad/Prism.exe window software was utilized to conduct the analysis of the statical data using Sidak's one-way Anova multiple compression test method.

Results and Discussion
(HPLC) analysis

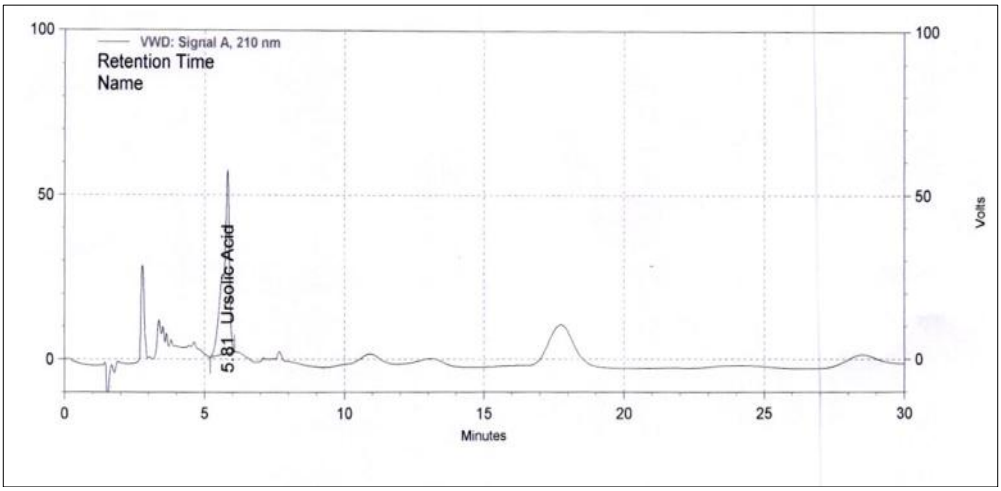

Fig 12: Retention time and Absorbance Ursolic acid (Standard)

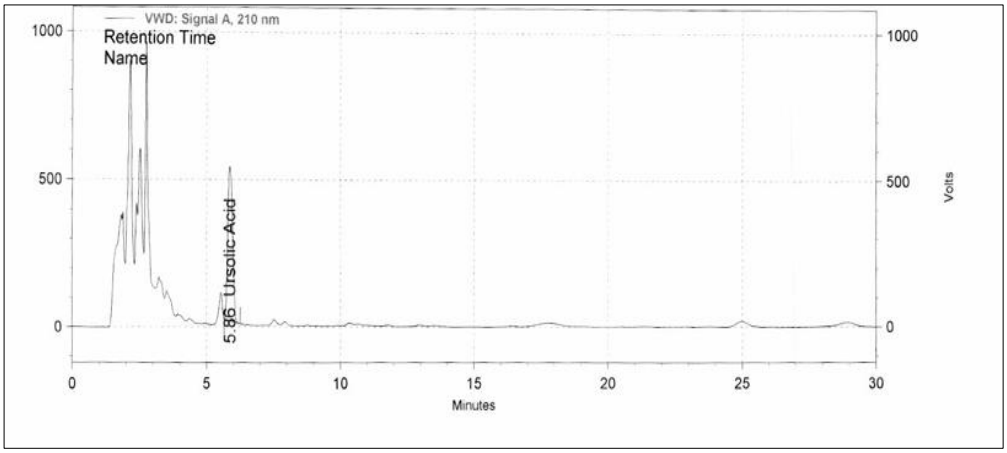

Fig 13: Retention time and Absorbance Ursolic acid (Sample)

Table 7: (HPLC) Analysis

S.No.	Ursolic acid	Retention time	Absorbance
1.	Ursolic acid (Standard)	5.81	210nm
2.	Ursolic acid (Sample)	5.86	210nm

Quantity of Ursolic acid in sample by HPLC Chromatogram was found to be 14.78%W/W.

Acute Toxicity Studies

Fixed doses of 5, 50, 300, 2000 & 5000 mg/kg p.o. were to be administered orally with the aid of oral gavage, according to OECD 423 standards. The results of acute toxicity studies mention in Tab.

Table 8: Acute toxicity studies

No. of Animals	Dose	No. of death of Animals
3	5 mg/kg	0
3	50 mg/kg	0
3	300 mg/kg	0
3	2000 mg/kg	0
3	5000 mg/kg	0

An oral dosage of 2000 mg/kg of the ethyl acetate extract from Carissa carandas leaves was proven to be safe for use in animals. One tenth of the maximum tolerable dose, or 250 and 500 mg/kg body weight, were chosen for the trial as a result of these results.

Anti-peptic ulcer activity

It has been demonstrated that taking different plant extracts orally considerably lowers the ulcer index. Specifically, ulcer severity was significantly reduced after treatment using raw ethyl acetate extract of Carissa carandas leaf at doses of 250 milligrams per kilogram and 500 mg per kilogram of body weight. Because gastric lesions restrict stomach blood flow, they are frequently linked to bleeding and necrotic tissue destruction. The therapeutic efficacy of the reference medication, ranitidine (50 mg/kg b.w.), was demonstrated by a statistically significant decrease in ulcer index across groups for therapy ($P < 0.0001$).

Table 9: Effects of ethyl acetate extract of Carissa carandas leaves in NSAID induced peptic ulcer in rats.

Group of animals	Ulcer Index (UI)	Gastric Volume (GV) (ml\100g)	Free Acid (FA) (mEq\100g)	Total Acid (TA) (mEq\100g)	pH
Group I (Negative Control)	1.38±0.42	1.1±0.44	2.13±0.65	10.1± 0.49	3.3±0.46
Group II (Positive Control)	5.56±0.46^{a****}	3.1±0.68^{a****}	8.17 ±0.41^{a****}	15.13± 0.46^{a****}	1.18±0.51^{a****}
Group III (Standard Treated)	1.70 ±0.69^{b****}	1.4±0.56^{b****}	5.90± 0.58^{b****}	9.16± 0.49^{b****}	3.05±0.45^{b****}
Group IV (Test drug Treated with 250mg/kg)	3.48±0.46^{b****}	2.38±0.72^{b}	7.04 ±0.54^{b**}	13.16± 0.53^{b****}	2.7±0.74^{b****}
Group V (Test drug Treated with 500mg/kg)	2.66±0.41^{b****}	2.13±0.65^{b*}	6.50± 0.50^{b****}	12.13 ±0.44^{b****}	2.9±0.67^{b****}

Values are expressed as mean ± standard deviation (SD) for each group of six animals. For statistical comparisons, Tukey's multiple comparability test was employed. There were comparisons among the negative control group and the positive control group, as well as between the drug-treated groups and the positive control group. The significant levels were denoted by the following: p<0.0001(a**) and p<0.0001b****), respectively.**

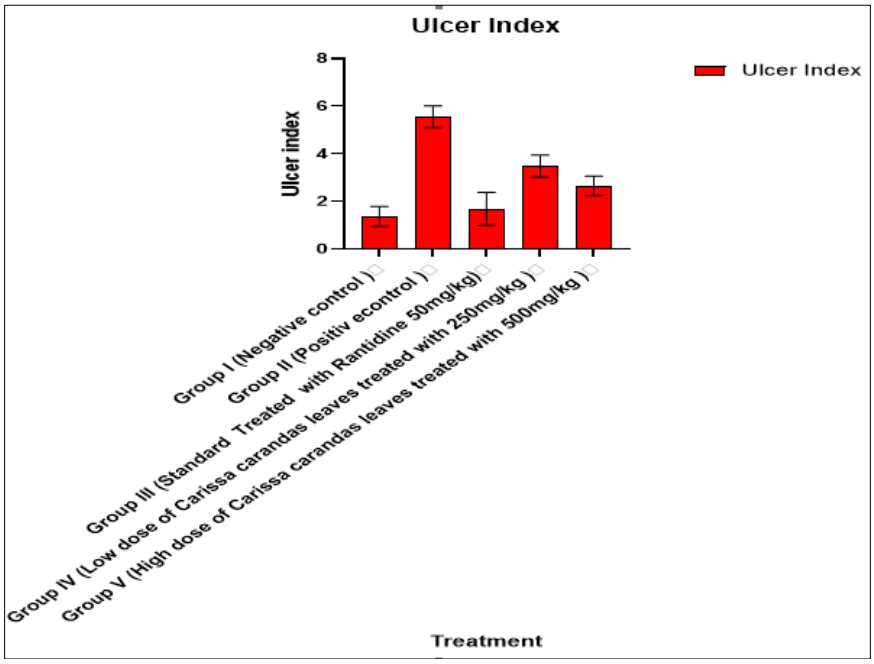

Fig 14: Graphical representation of Ulcer Index (UI) of different treatment groups

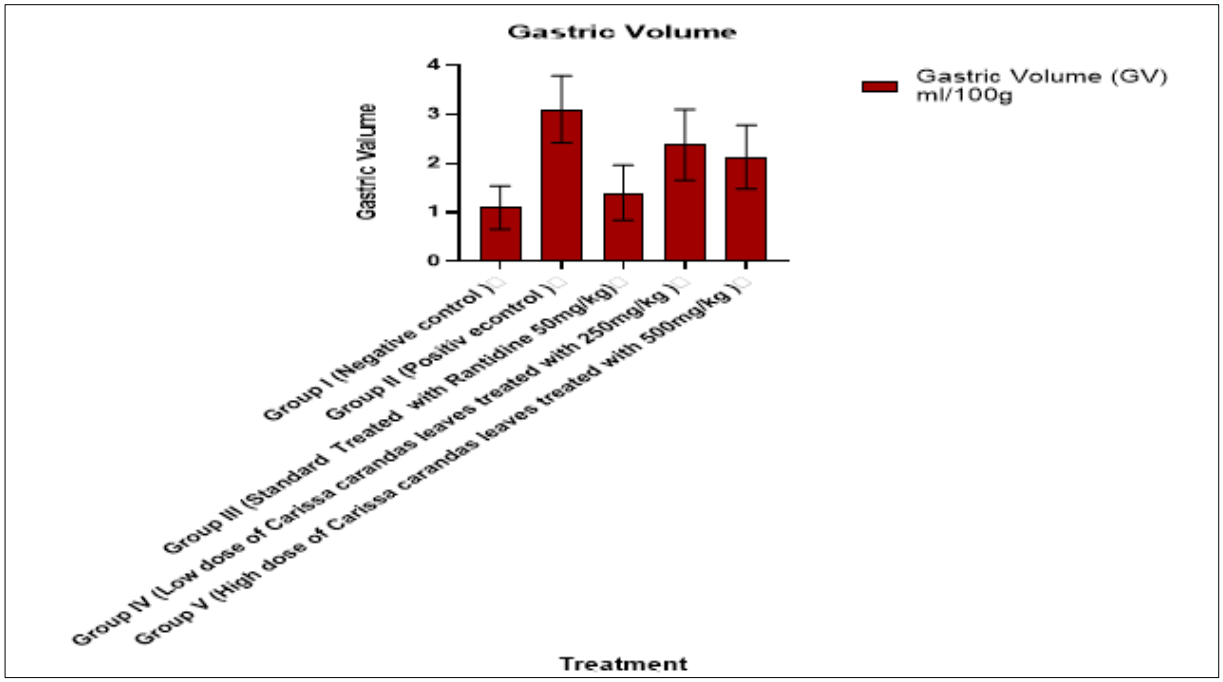

Fig 15: Graphical representation of Gastric Volume (GV) of different treatment groups

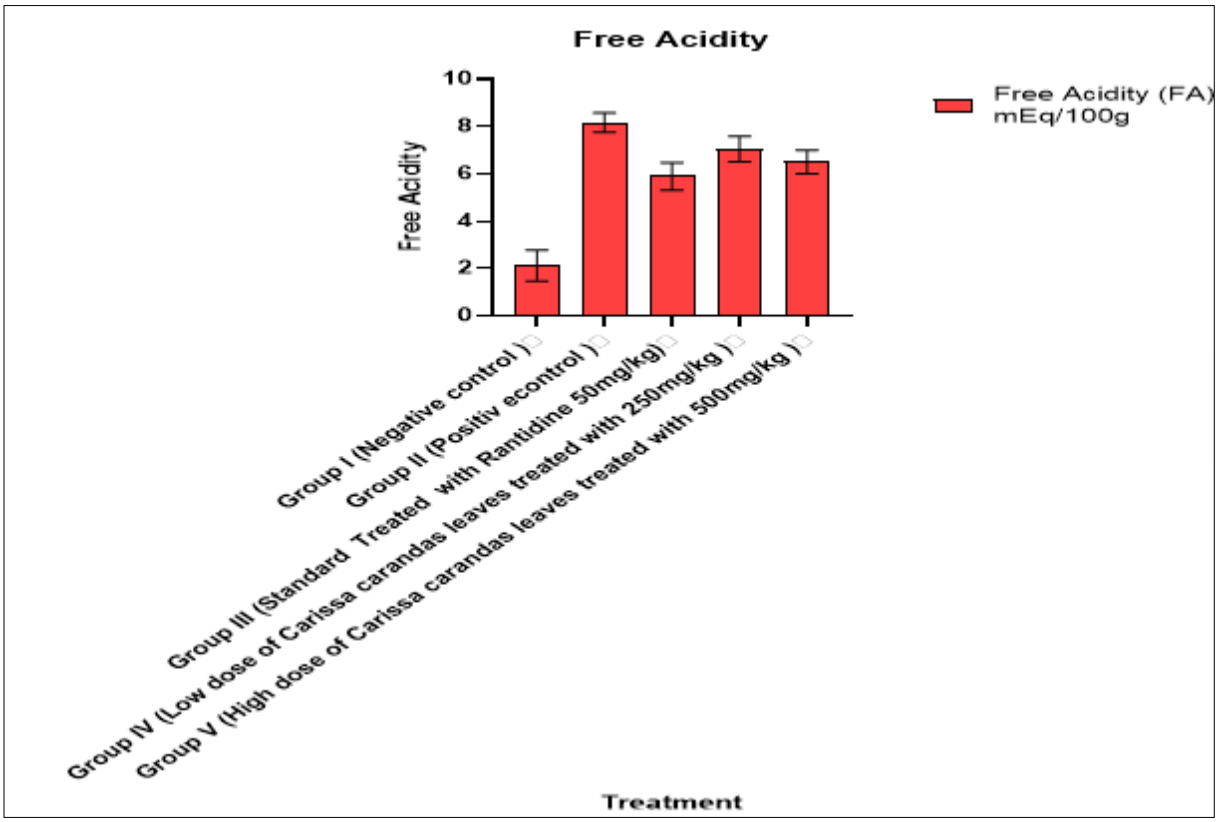

Fig 16: Graphical representation of Free Acidity (FA) of different treatment groups

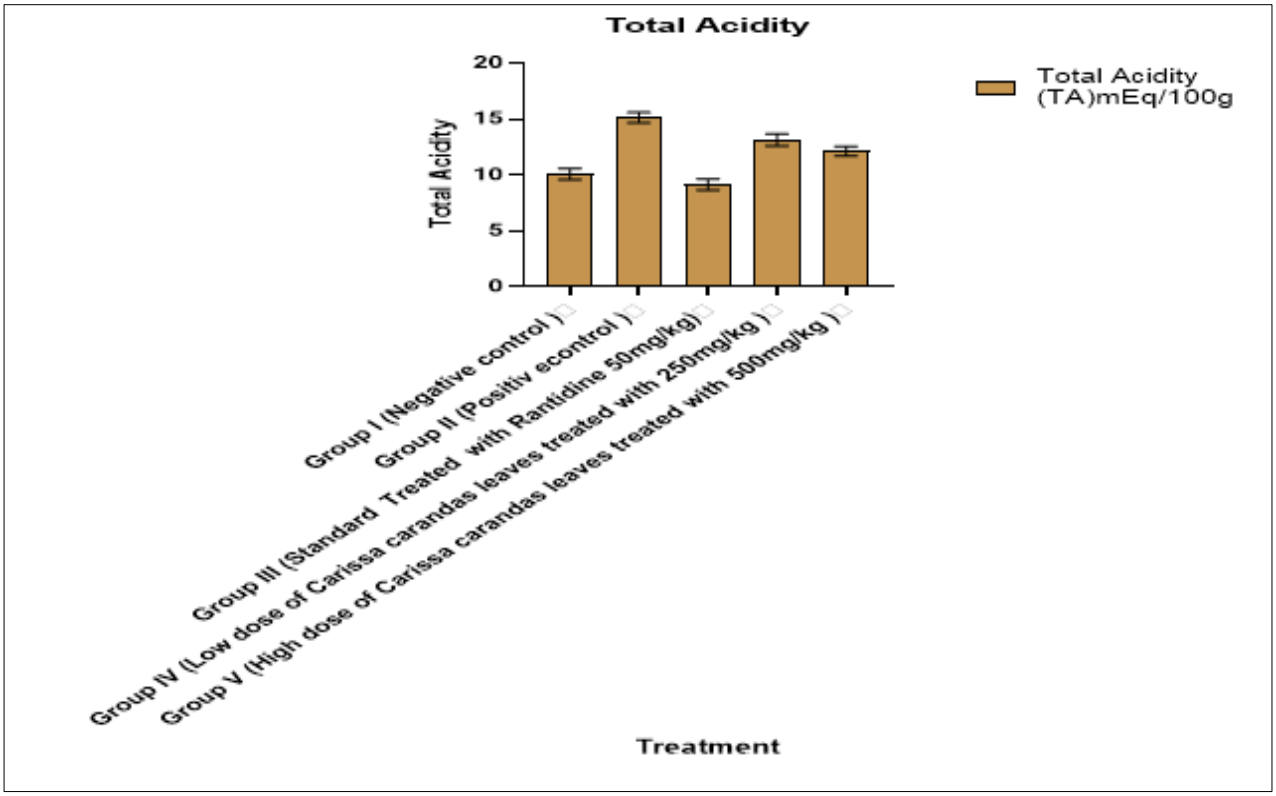

Fig 17: Graphical representation of Total Acidity (TA) of different treatment groups

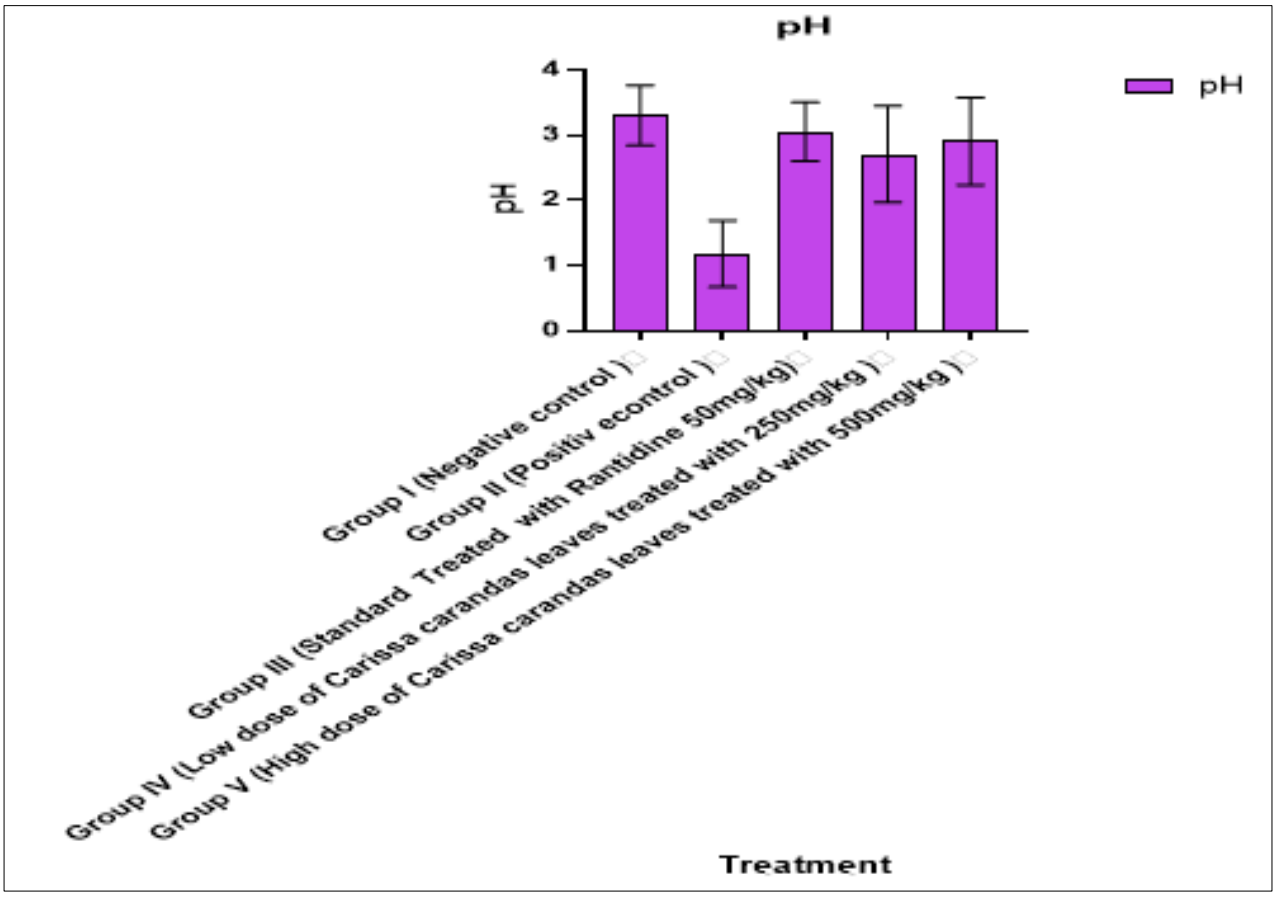

Fig 18: Graphical representation of pH (of different treatment groups

Study of histopathological examination

The stomach histology of normal controls groups Fig. A. exhibits very less numbers of ulcers, since small gastric lesion was found. This was confirmed by looking at a dissected portion of the stomach's larger curvature, where the cell arrangement was consistent throughout (Fig. B). Due to ulcers, rats in positive control groups had severely deformed cells (Fig. C). The groups who got the Ranitidine, also fifty milligrams per kilogram of body weight p.o. showed incredibly well-organized cell topologies (Fig. D). Compared to positive control groups, rats administered the test medication (250 mg per kilogram p.o. of Carissa carandas leaf) had less ulceration (Fig. E). Positive control groups saw much less ulceration than those receiving the test medication (500 mg per kilogram p.o. of Carissa carandas leaf).

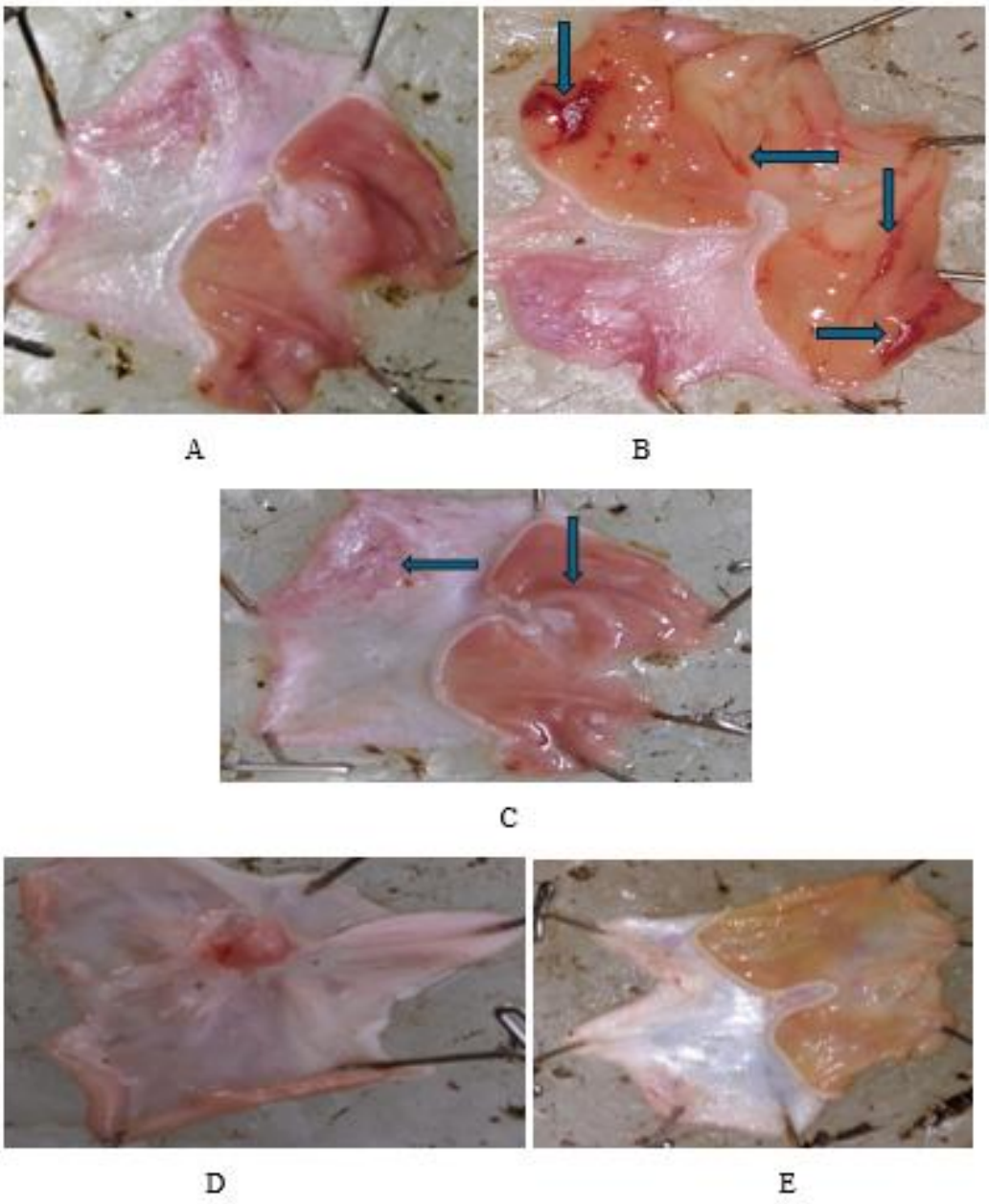

Fig. 19: The stomach of the NSAID induced rat was dissected & the rumen of the stomach where the ulcers were predominantly found & seen the preventive effect of drugs.

* ⟹ Arrow indicated the ulcerated area

A)Negative control, B) Positive control, C) Standard treated with Ranitidine 50 mg/kg b.w. p.o., D) Test drug Treated with 250mg/kg b.w. p.o., E) Test drug Treated with 500 mg/kg b.w. p.o.,

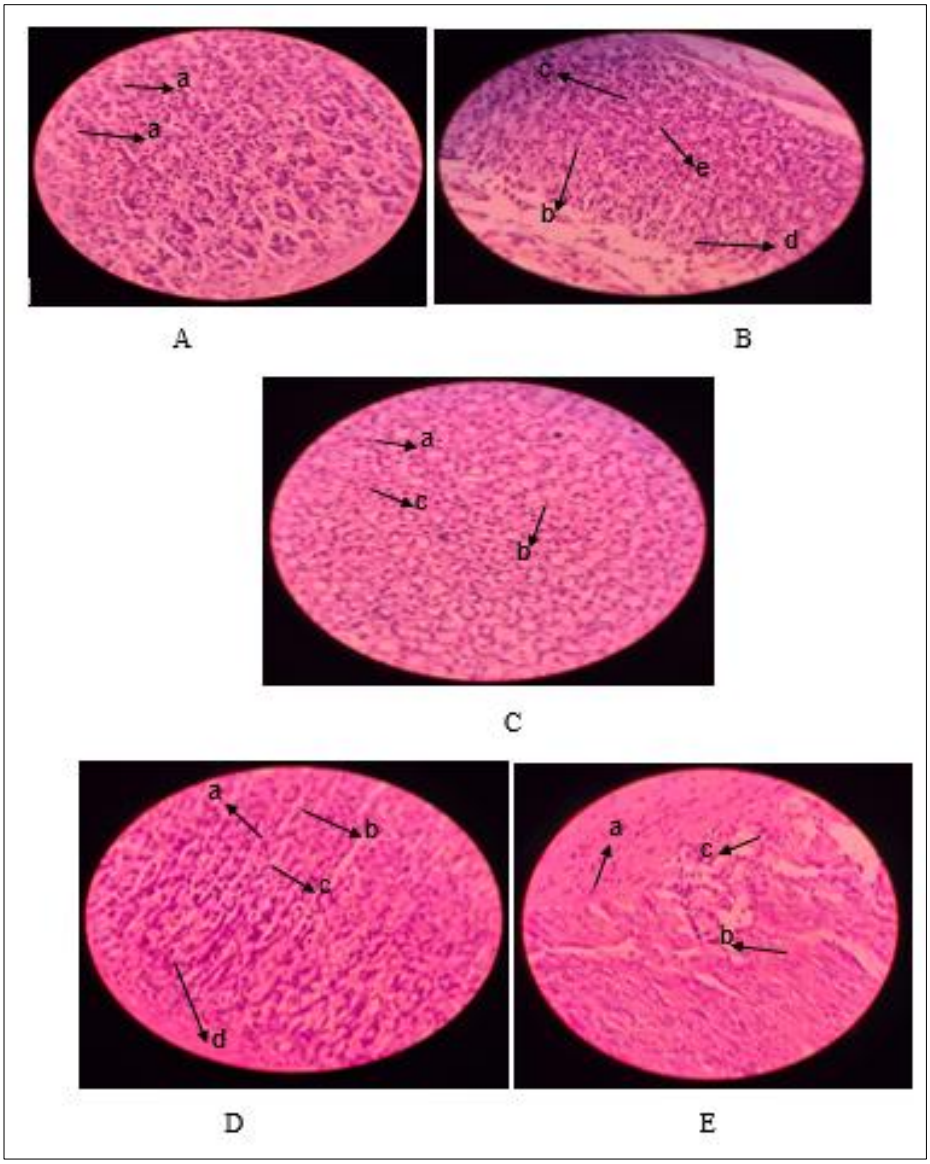

Fig 20: Histopathological section of the stomach of rat

A) Negative control, (B) Positive control, (C) Standard treated with Ranitidine 50 mg/kg b.w. p.o., (D) Test drug Treated with 250mg/kg b.w. p.o., (E) Test drug Treated with 500 mg/kg b.w. p.o.,

a) Necrotic zone, b) intact mucosa, c) Granulation tissue zone, d) Ulcerated mucosa,e) Superficial exdative zone

Conclusion

In a rat model of stomach ulcers caused by NSAIDs Carissa carandas leaf ethyl acetate extraction shown potent anti-peptic ulcer properties. Oral administration of the extract at 250 mg per kilogram and 500 mg per kilogram of body weight resulted in significant gastroprotective impacts, demonstrating its analgesic and anti-inflammatory efficacy across a variety of evaluated measures. As a pharmacologic perspective, these findings validate the conventional application of Carica carandas leaves for the treatment of inflammatory conditions such peptic ulcers.

In addition, treatment with ranitidine (50 milligrams per kilogram p.o.) and both doses of the Carissa carandas extract significantly reduced peptic acid secretion, indicating a protective mechanism.

Histopathological analysis of gastric tissues confirmed ulceration and mucosal lesions, with reduced ulcer index values observed in the treatment groups, further supporting the extracts' protective role. These encouraging results underscore the potential of this plant extract in the development of phytomedicines for ulcer treatment.

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Conflicts of Interest: Nil

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