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# Preliminary Phytochemical Screening, Antiulcer And Anti-Inflammatory Activity Of Stem Bark Extract Of Cassia Fistula (L) Using Albino Wistar Rats.

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**ABSTRACT:**

**Objectives:** This study Investigates the anti-ulcer and anti-inflammatory activity of *Cassiafistula (L)* stem bark extract in albino wistar rats.
**Methods:** Rats with pylorus ligation and ethanol were used to test for ulcers, while rats with carrageenan-induced paw edema were used to test for anti-inflammatory activity against acute and chronic phases of inflammation. A dose of *Cassia fistula (L)* (200 and 400 mg/kg p.o.) was given to rats that had been given ethanol and had their pyloruses tied. Rats that had developed pylorus ligation-induced ulcers had their gastric volume, pH, free acidity, and total acidity measured. After receiving treatment with Cassia fistula, ulcers caused by ethanol and pylorus ligation were less common.
**Results:** The antisecretory and cytoprotective properties of the extract may be the causes of the antiulcer activity. Additionally, it demonstrated a highly significant (P 0.001) decrease in inflammation caused by carrageenan induced edema.
**Conclusion:**This study indicates that *Cassia fistula (L)* bark has anti-inflammatory properties and helps prevent ulcers.

**Keywords:** Anti-ulcer activity, anti-inflammatory activity, Cassia fistula (golden shower).

## 1. Introduction

One in ten people worldwide suffer from peptic ulcer disease, a group of ulcerative disorders that affect the upper gastrointestinal tract and are brought on by exposure to acid pepsin secretions .It is now widely accepted that gastric (Zapata-Colindres et al., 2006) lesions appear when the defensive and aggressive factors are out of balance. As opposed to this, inflammation is a complex biological reaction of the body's tissues to noxious stimuli like pathogens, damaged cells, or irritants .It is a defensive reaction involving blood vessels, immune cells, and molecular mediators. Inflammation serves to remove the original source of cell injury, necrotic cells an
tissues that have been harmed by both the initial insult and the inflammatory process, and starts the healing process for damaged tissues (Maqsood et al., 2020).There is a dire need for a new natural drug to treat ulcers as well as inflammation because current anti-inflammatory medications cause ulcers. The creation of new medications from natural sources is also encouraged because, according to estimates, only 15% of the 300,000 plant species that exist in the world have had their pharmacological potential assessed. Additionally, about 25% of current medications are made from natural products (De Luca et al., 2012). The genus *Cassia fistula (L)*is a member of the Fabacae family. It is a less well-known species of Indian. The bark were traditionally used to prevent abortions as well as to treat inflammation, vesical calculi, kidney infections, and sores and ulcers with poultices Its diuretic and natriuretic,antimicrobial, antioxidant, antihyperglycemic, and hepatoprotective activities have all been demonstrated pharmacologically. The purpose of this study was to assess the antiulcer and anti-inflammatory properties of *Cassia fistula (L)* methanolic bark extract. (Jincy & Sunil, 2020)

## 2. Materials and Methods

### Drugs and Chemicals

Methanol, ethanol, petroleum ether, carrageenan, and tween 80. Ranitidine and ibuprofen werebrought from Cipla Pharmaceuticals Ltd., Mumbai, India.

### Plant Material

Botanical Survey of India Regional Centre, 10 Chatham Lines, Prayagraj, 211002 Dr. Arti Gargrecognized the specimen of *Cassia fistula(L)* Bark collected in April and May.
The Botanical Survey of India has received a specimen with the voucher number SIP/2022-23/91.

### Animals Housing and Feeding Conditions

Weighting 160–180 g, albino Wister rats were purchased from Saha Enterprises in Kolkatta, India. The animals were kept in propylene cages with rice husk bedding at 24 degree temperatures with 30–70 percent relative humidity. A 12:12 h light-dark cycle was maintained using the typical commercial pellet (M/s. Hindustan Lever Ltd., Mumbai, Maharashtra,India) and an endless supply of purified water. Following CPCSEA guidelines, the Animal Ethical Committee (15682/PO/CPCSEA) approved all experimental protocols and procedures.

### Preparation of Plant Extracts

The bark of Cassia fistula (L) was machine-pulverized after being dried in the shade. The coarse powder was defatted with petroleum ether and then the methanol was extracted by cold maceration. The extract was concentrated using a rotating evaporator at low pressure.

Phytochemical screening was done on them. They had been administered to the various groups in the right amounts based on their body weights after being dissolved in 0.5 percent carboxymethyl cellulose.

**Acute Toxicity Studies-**

The 20–25 g healthy Swiss albino mice were placed randomly into one of five (n = 3) groups after being given only water for 3–4 hours. They received extracts orally along with a 0.5 percent CMC control at doses of 5, 50, 300, and 2000 mg/kg b.w. post-esophageal (p.o.). The study was

Conducted in accordance with OECD recommendations (423: acute toxic class method). The animals were monitored for signs of toxicity, morbidity, and death for the first 24 hours, with particular focus on the first 4 hours, and their behavioural, neurological, and autonomic profiles were assessed. They were also observed for the following 72 hours and for the remaining 14 days. The test dose was determined. (OECD, 2002)

**Antiulcer Studies:**

**Ethanol-induced ulcer study in rats.**

Rats were divided into five groups of six, each weighing between 200 and 250 g. Overnight-fasted rats received the following treatments: vehicle, ranitidine (30 mg/kg), and Cassia fistula
(L) (200 and 400 mg/kg). Giving a patient 1 mL of pure ethanol resulted in the development of a gastric ulcer an hour after the treatment. Rats were placed in carbon dioxide chambers an hourafter receiving ethanol. The rats' stomachs were then cut open along their natural curved line, and any ulcers were looked for.(Jincy & Sunil, 2020)A portion of the stomach was used for the histopathological analysis.

Ulcer scores were given as follows;
0.0 = normal colored stomach
0.5 = red coloration
1.0 = spot ulcers
1.5 = hemorrhagic streaks
2.0 = ulcers with area >3 but 5 mm2
3.0 = ulcers > 5 mm2
Ulcer index was calculated using the equation; UI = (UN + US +UP) £ 10—1 Where, UI = Ulcer Index
UN = Average number of ulcers per rats US = Average of severity score UP = Percentage of rats with ulcer
Percentage inhibition was calculated using the following formula.(Jincy & Sunil, 2020) Percentageprotection= Control U.I.—Test U.I X 100/ Control U.I

**Pylorus Ligation Induced Ulcers in Rats**

The Wistar rats (200 250 g) were split into four groups of six rats each, and the overnight-fasted rats were given a vehicle (group I). Ranitidine (30 mg/kg) was administered to rats in group II, while Cassia fistula (L) was administered to rats in groups III and IV at 200 and 400 mg/kg, respectively. Rats were given ether anaesthesia for an hour following treatment. A surgical incision was made in the abdomen under the sternum. The pyloric sphincter was exposed, and the blood vessels were spared by carefully tying the thread around it. After collodion was applied to the wound, the abdominal wall was sutured. Rats were sacrificed in a carbon dioxide chamberafter four hours. The abdomen was cut open and fastened to

the esophageal end of the stomach.The gastric contents were then collected in a graduated centrifuge, which was then centrifuged at 1000 rpm for 10 minutes (Rao et al., 2008). The gastric contents' volume and pH were recorded. Pipetting out 1 ml of the supernatant liquid and diluting it with 10 ml of distilled water. Using Topfer's reagent as an indicator, the solution was titrated against 0.01 N NaOH until the endpoint, at which point the solution became strange. It was determined how much NaOH was required to balance the free acidity. After adding two drops of phenolphthalein, the solution was further
Diluted until it once again took on the color of ink, at which point the amount of total acidity was determined (Guzmán-Gómez et al., 2018)
Acidity was calculated using the equation;
Acidity ¼ Volume of NaOH × Normality × 100 =0:1 N mEq=L

**Anti-Inflammatory Studies**

**Carrageenan Induced Paw Edema**
Six Wistar rats were divided into four groups of four. Group I rats were given a vehicle; Group II rats were given ibuprofen (10 mg/kg), and Group III and IV rats were given *Cassia fistula (L)* doses of 200 and 400 mg/kg, respectively. Paw edoema was induced 30 minutes after treatment by injecting 0.1 ml of 1 percent carrageenan into the subplantar region of the right hind paw. The rat paw volume up to the ankle joint was measured using a digital plethysmometer at 0 hr, 1 hr, 2 hr, 3 hr, 4 hr, and 6 hr after carrageenan injection. (Babu et al., 2009) An increase in paw edoema volume was defined as the difference between 0 hr and 1 hr, 2 hr, 3 hr, 4 hr, or 6 hr. The difference in paw volume inhibition between the treated and control groups was calculated as follows:

Percent inhibition ¼ ½V —V =V] × 100

Where $V_C$ and $V_t$ represent the mean increase in paw volume in control and treated groups respectively.

**Statistical Analysis**
The results were presented as mean SEM. All data obtained were statistically analysed using a one-way ANOVA followed by Dunnett's post-hoc multiple comparison test. Graph Pad Prism software was used to create graphs from all of the results (v.5). p values less than 0.05 were considered statistically significant.

## 3. Results

**Extraction-**
Table 1: The extraction value of Cassia fistula (L) bark powder by hot extraction method.

| S.N. | Nature of extract | Values (% w/w) by hot extraction |
|---|---|---|
| 01 | Petroleum ether | 2.70 |
| 02 | Chloroform | 2.69 |
| 03 | Ethanol | 6.20 |
| 04 | Ethyl acetate | 10.65 |
| 05 | Aqueous | 9.89 |

**Phytochemical Screening**
Phytochemical screening of the extract showed the presence of sterols, terpenoids, flavones, tannins and glycosides.

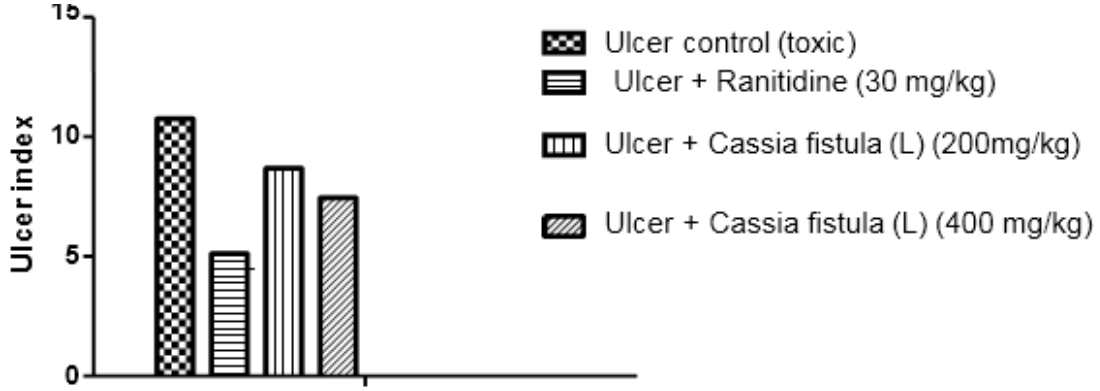
**Effect of Cassia Fistula (L) on Ethanol-Induced Ulceration in Rats**

In ethanol-induced ulcerations, the positive control group (ranitidine) had a (5.12 ± 0.53) ulcer index, whereas the ulcer control group had a (10.75±0.44). *Cassia fistula (L)*(200 and 400 mg/kg) reduced the ulcer index by (8.68±0.73) and (7.45±0.86), respectively, with P 0.05 and P 0.01, respectively. The ulcer index was reduced after pre-treatment with the extract. *Cassia fistula (L)* (200 and 400 mg/kg) provided 22.73 percent and 40.23 percent gastroprotection,respectively, while ranitidine provided 70.19 percent protection (Table 1 and Fig. 1).

Table1. Effect of Cassia fistula (L)) on ethanol-induced ulceration in rats.

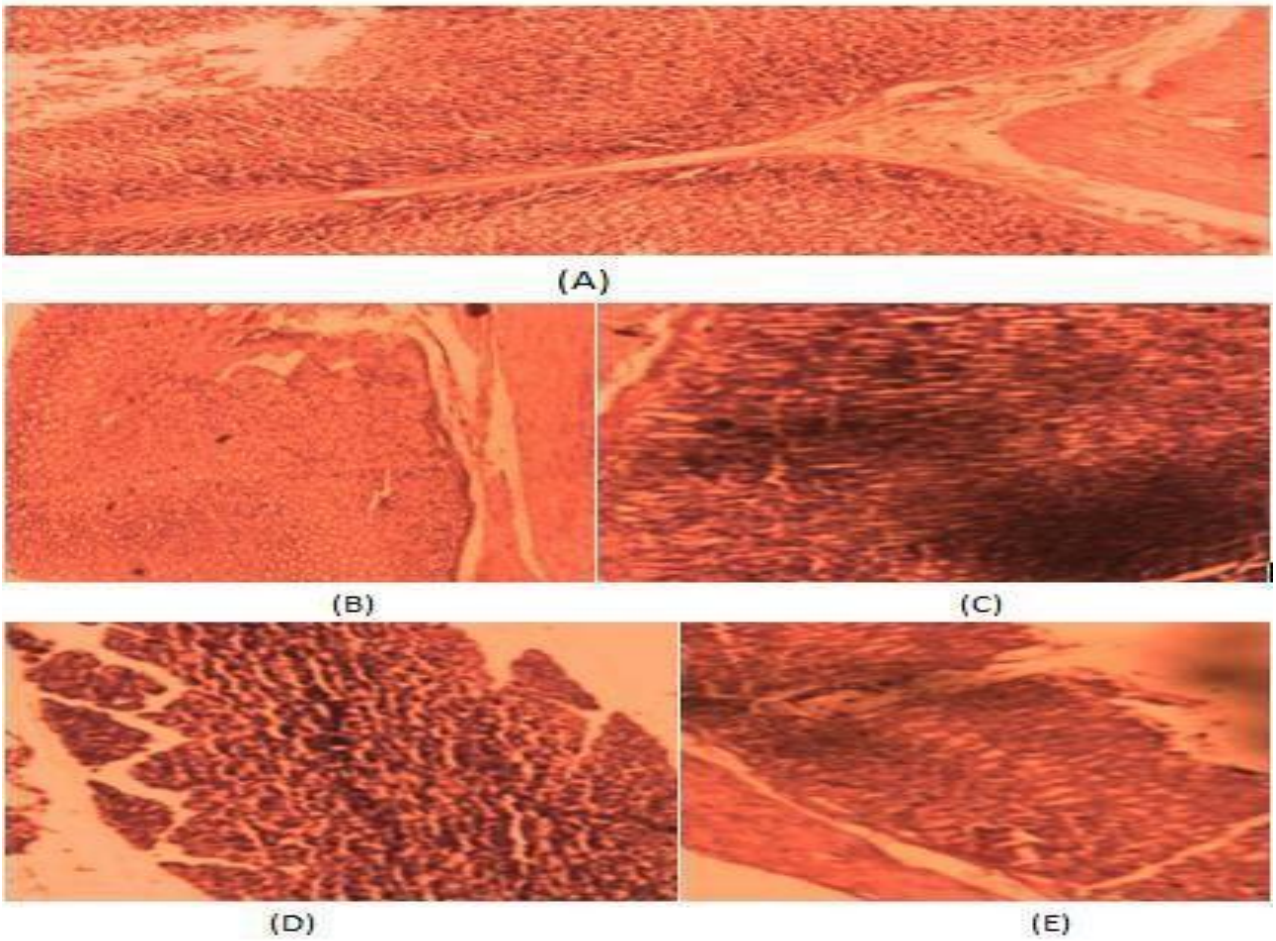
| Groups | Ulcer index | Percentage inhibition |
|---|---|---|
| Normal | --- | --- |
| Ulcer control(toxic) | 10.75±0.44 | - |
| Ulcer + Ranitidine (30 mg/kg | 5.12 ± 0.53 | 70.19% |
| Ulcer + Cassia fistula(L)(200 mg/kg) | 8.68±0.73 | 22.73% |
| Ulcer + Cassia fistula(L))(400 mg/kg) | 7.45±0.86 | 40.23% |

Effect of Cassia fistula (L) on ethanol-induced ulceration in rats.




**Histopathology of Rat's Stomach**

The gastric mucosa of ethanol-treated ulcer control rats (Fig. 1a) showed erosion of the superficial epithelium and infiltration of mononuclear cells. Hemorrhage in the lamina propria, degenerative changes in the gastric glands, blood vessel congestion, and gastric lesions are all possible. Groups of rats treated with ranitidine (Fig. 1b) and *Cassia fistula (L)* (200 and 400 mg/kg) (Fig. 1c and d) significantly reduced these changes in gastric mucosa and protected against alcohol-induced gastric lesions.




**Histopathology of stomach: (A)** Normal Ulcer **(B)** Ranitidine (30 mg/kg) section of stomach shows normal mucosal glands lined by columnar cells. A few inflammatory cells are seen in the mucosa and submucosa. **(C)** controls shows ulceration of mucosa in some places. The ulcerated area shows necrosis. Inflammatory cells were seen in mucosa and submucosa. **(D)** Cassia fistula (L)) 200 mg/kg shows mild inflammatory cells in mucosa and submucosa. **(E)** Cassia fistula (L)) 400 mg/kg shows diffuse inflammatory cell infiltration in mucosa and submucosa.

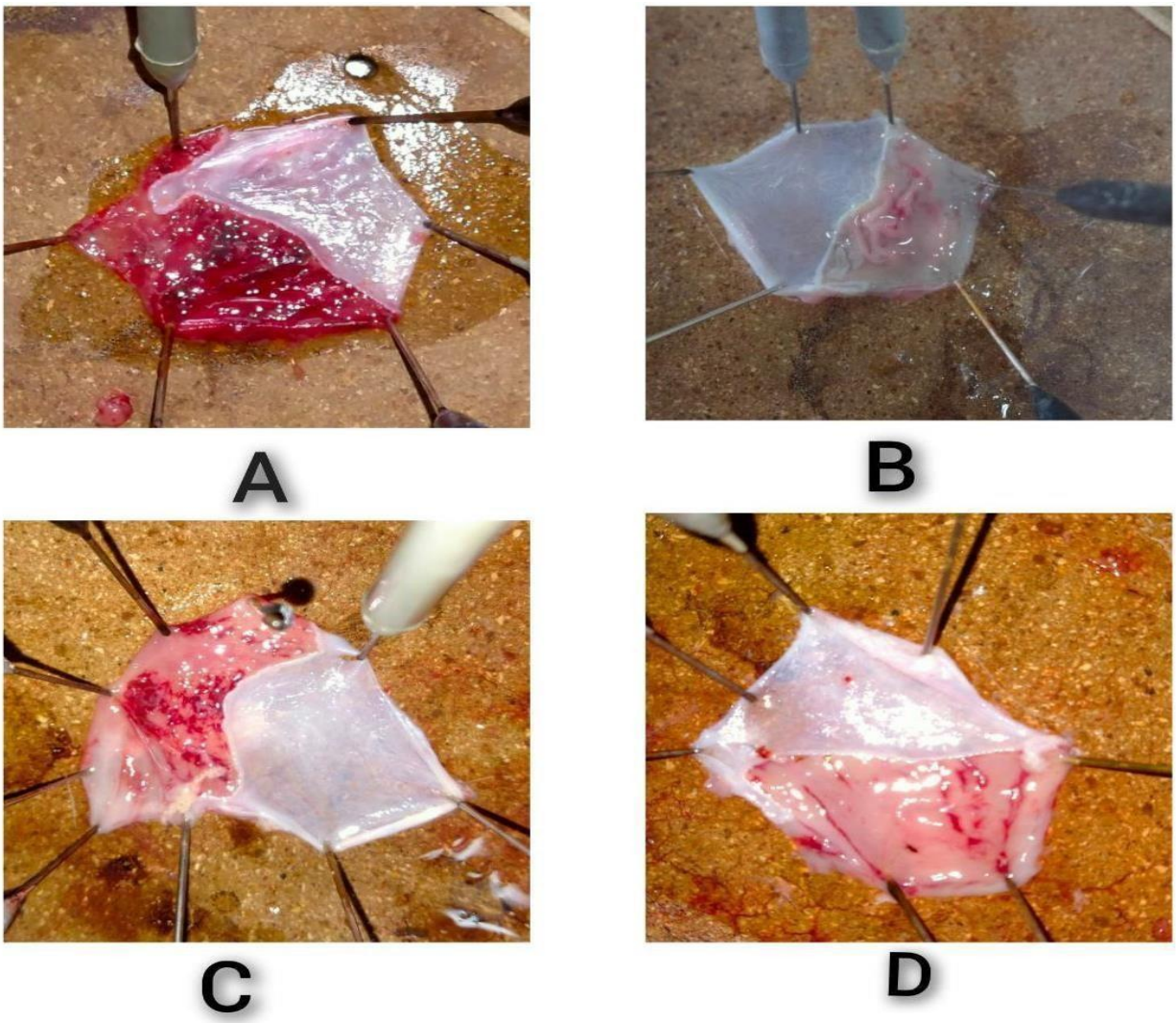


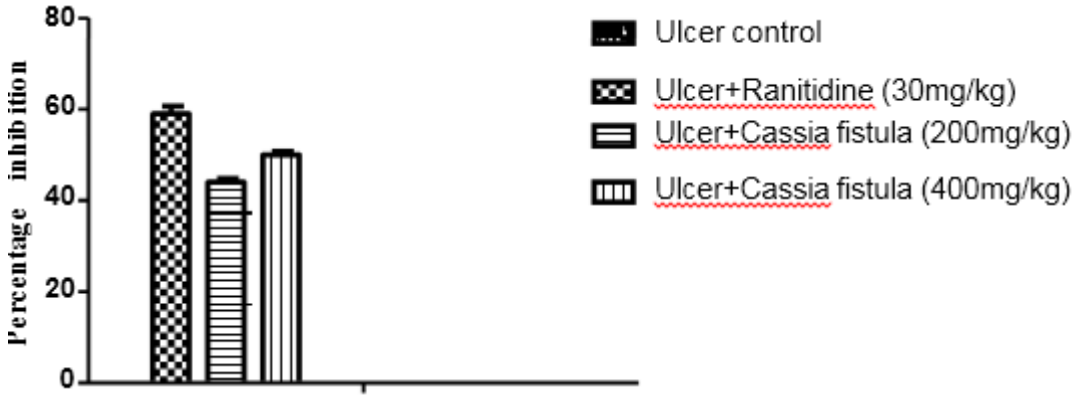

Fig. 1. Stomach with hemorrhagic streaks of ulcer control (A), Ranitidine 30 mg/kg treated (B)Cassia fistula (L) 200 mg/kg treated (C) and Cassia fistula (L) 400 mg/kg (D) treated rats.

**Effect of *Cassia Fistula (L)* on Pylorus Ligation InducedUlceration in Rats**

As shown in Table 2, pretreatment with *Cassia fistula (L)* significantly (P 0.01, P 0.001) increased pH and decreased gastric volume in pylorus ligation induced ulcers at doses of 200 and 400 mg/kg compared to the control group. The antisecretory property of elasticus (200 and 400 mg/kg) in the pylorus ligation model was demonstrated by a significant reduction in free acidity (P 0.001) and total acidity (P 0.01, P 0.001). The positive control (ranitidine) group scored (10.080.54) in pylorus ligation induced gastric ulceration, whereas the negative control group scored (25.68 0.88). When compared to the ulcer control, the ulcer index in pylorus ligation induced rats treated with 400 mg/kg of *Cassia fistula(L)*and ranitidine 10 mg/kg was extremely significantly (P 0.001) reduced, whereas the ulcer index in 200 mg/kg of *Cassia fistula(L)*was moderately significant (P 0.01). The extract (200 and 400 mg/kg) demonstrated 44.2 percent and
50 percent gastroprotection, respectively, whereas the positive control (ranitidine) demonstrated a
59.7 percent reduction in ulcer index when compared to the ulcer control.

Table2. Effect of Cassia fistula (L) on pylorus ligation induced ulceration in rats.

| **Groups** | **Gastri cpH** | **Gastricvolu m e(ml/100g)** | **Free acidity(me q/ltr)** | **Total acidity(meq/l tr)** | **Ulceri nde x** | **Percentagei nhibition** |
|---|---|---|---|---|---|---|
| Ulcer control | 1.2±0. 11 | 7.06±0.55 | 30±0.50 | 52.75±0.5 | 25.10±0.88 | — |
| Ulcer+Raniti din e(30mg/kg) | 5.5±0. 04 | 2.5±0.4 | 10.2±0.38 | 29.1 4±0.4 | 9.08±0.54 | 59.7% |
| Ulcer+*Cassi a fistula (L)*(200 mg/kg) | 3.5±0. 07 | 5.5±0.04 | 16.6±0.72 | 41.75±0.48 | 13.08±0.66 | 44.2% |
| Ulcer+*Cassi a fistula (L)*(400 mg/kg) | 4.1±0. 04 | 4.4±0.04 | 14.3±0.55 | 35.17±0.41 | 11.1±0.40 | 50% |




**Effect of Cassia fistula (L) on pylorus ligation induced ulceration in rats**

**Effect of *Cassia Fistula (L)* On Carrageenan Induced Paw Edema**

Table 3 displays the paw volume and the percentage of inhibition for the control, ibuprofen, and Cassia fistula (L) (200 and 400 mg/kg). In control rats (group I), the sub-plantar injection of carrageenan resulted in a time-dependent increase in paw volume. The sixth hour after carrageenan administration was when the greatest increase was seen. When compared to inflammatory control, pre-treatment with Ibuprofen (10 mg/kg) and Cassia fistula (L) (200 and 400 mg/kg) to groups II, III, and IV before 1 h of carrageenan administration significantly (P 0.001) decreased the paw volume at 1 hr, 2 hr, 3 hr, 4 hr, and 6 hr after carrageenan injection.

Table3-Effect of Cassia fistula (L) on carrageen-induced pawedema volume.

| **Groups** | **Paw volume(ml)** | | | | |
|---|---|---|---|---|---|
| | **1h** | **2h** | **3h** | **4h** | **6h** |
| Inflammatorycontrol | 0.55±0.031 | 0.55±,0.032 | 0.74±0.027 | 0.85±0.52 | 0.88±0.025 |
| Inflammatory+Ibuprofen(10mg/kg) | 0.18±0.005 | 0.15±0.005 | 0.13±0.005 | 0.078±0.006 | 0.07 ±0.003 |
| Inflammatory+*Cassia fistula(L)*(200mg/kg) | 0.30±0.005 | 0.21±0.003 | 0.18±0.003 | 0.18±0.004 | 0.16±0.004 |
| Inflammatory+*Cassia fistula(L)*(400mg/kg) | 0.20±0.0072 | 0.18±0.007 | 0.12±0.007 | 0.13±0.004 | 0.10±0.007 |

## 4. Discussion

Due to dietary changes and stress, gastrointestinal conditions like gastric ulcers and hyperacidity are now the most prevalent. However, very little is still known about the mechanism. Although there are many medications available for the treatment of gastric ulcers (such as antihistamines and acids), the majority of these medications cause a number of side effects, including arrhythmias, impotence, gynecomastia, and hematopoietic changes.(Rao et al., 2008) Due to dietary changes and stress, gastrointestinal conditions like gastric ulcers and hyperacidity are nowthe most prevalent. However, very little is still known about the mechanism. Although there are many medications available for the treatment of gastric ulcers (such as antihistamines and acids), the majority of these medications cause a number of side effects, including arrhythmias, impotence, gynecomastia, and hematopoietic changes.

Using ethanol and pylorus ligation-induced gastric ulcer models, we evaluated the antiulcer activity of a methanolic bark extract of Cassia fistula (L). With the aid of macroscopically and microscopically visible lesions, absolute ethanol-induced gastric lesions in rats provide a more practical and quick method of evaluating herbal extracts for antiulcer and cytoprotective activities (plant). Alcohol causes a disruption in the integrity of the gastric mucosal barrier through cell exfoliation, increasing mucosal permeability and, in some cases, inducing bleeding. The mechanism of ethanol-induced ulcers is complicated and poorly understood. (Guzmán-Gómez et al., 2018). According to our findings, Cassia fistula (L) can reverse the histopathological changes in the stomach and lower the ulcer index. There have been reports of four significant compounds in Cassia fistula, including lupeol, sitosterol, friedelin, quercetin, tannins, and ellagic acid (L). Through the inhibition of TNF-a, apoptosis, and stimulation of K+ ATP channel opening via significant PGE2 production by COX-1 facilitated pathway with a reduction in vascular permeability and pro-inflammatory cytokines, Friedelin confirmed antiulcer activity in that instance. (Jincy & Sunil, 2020).

In addition, rat pylorus ligation-induced ulcers were used to assess Cassia fistula (Lantisecretory)'s activity. A straightforward, repeatable, and highly predictable model for testingpotential antiulcer medications is the pylorus ligation-induced ulcer. (Zapata-Colindres et al., 2006). Stress induced increase in gastric acid secretion is believed to be the cause of ulcers in pylorus ligated models (Babu et al., 2009). The unprotected lumen of the stomach is exposed to the gastric acid as a result of excessive gastric acid secretion, which also causes accumulation.

Which further causes autodigestion of the gastric mucosa, decreased mucosal blood flow, and a breakdown of the mucosal barrier (Vats and Gupta, 2017)? As a result, ulcers brought on by this method can be prevented by using medications that reduce gastric acid secretion and/or increase mucus secretion. (Maqsood et al., 2020). This result confirms the antisecretory nature of the extract. Pre-treatment with Cassia fistula (L) showed a significant rise in pH and a decrease in
Gastric volume, ulcer index, free acidity, and total acidity. According to reports, the main chemical in Cassia fistula (L), ellagic acid, significantly reduces acid secretion by inhibiting H+ and K+-ATPase activity. It was discovered that the chemical friedelin could stimulate the production of prostaglandin, which protects the stomach from irritation and injuries by encouraging the secretion of protective substances like mucus and bicarbonates. Histidine decarboxyl-ase is known to be inhibited by flavonoids like quercetin and lupeol. (Madhulatha et al., 2013) reducing the production of histamine in the gastric mucosa, which in turn reduces the production of pepsinogen and hydrochloric acid, which are both secreted when histamine is present. Thus, the prophylactic effect of the Cassia fistula (L) against gastric ulceration in rats is due to the stimulation of prostaglandin synthesis, antioxidant, antisecretory, and anti-histaminic activities. Acute anti-inflammatory activity of Cassia fistula (L) was assessed after antiulcer activity using rat paw edoema caused by carrageenan, a sulphated polysaccharide derived from red green algae (Rhodophyceae). (Babu et al., 2009). The hallmark of inflammation is an increase in vascular permeability, and cellular infiltration causes edema as a result of fluid extravasation and leukocyte accumulation at the inflammatory site. Our findings showed that administration of Cassia fistula (L) inhibited paw volume beginning at the first hour and all phases of inflammation, which is likely because it inhibited various inflammation-related events and chemical mediators. When compared to the inflammatory control, the Cassia fistula (L) and Ibuprofen showed a highly significant reduction in paw volume. Additionally, in the sixth hour, it demonstrated a high level of percentage protection. One-octadecen, neophytadeine, hexadecenoic acid ethyl ester, octadecanoic acid ethyl ester, stigmasterol, g-stigmas-terol, b-stigmasterol-3-ol, pentacosane, and -sitost-4-en-3-one were among the substances found in the bark extract. Friedelin, epifriedelionol, b-amyrin, b-sitosterol, ethyl gallate, gallic acid, and b-sitosterol 3-b-D Glucopyranoside was also detected in the column chromatography of the ethyl acetate extracts. (Maqsood et al., 2020). Therefore, Cassia fistula (Loverall)'s activity of sterols, terpenoids, flavones, tannins, and glycosides is what gives the extract its antiulcer and anti-inflammatory properties. These substances are what give Cassia fistula (L) its antiulcer and anti-inflammatory properties. It was drawn from the positive outcomes of these compounds, which were isolated from numerous other plants and tested on various models.

## 5. Conclusion

Cassia fistula (L) demonstrated antiulcer activity in rats against ethanol and pylorus ligation-induced ulcers, as well as anti-inflammatory activity in rats against carrageenan-induced paw edoema. As a result, Cassia fistula (L) may be beneficial in the treatment of ulcers, inflammation, and pain. Furthermore, the precise mechanism (s) and site (s) of these activities,as well as the isolation of active constituents of Cassia fistula (L), remain unknown.

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