ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

Ficus racemosa linn leaf extract antiulcer activity study in different solvents on experimental animals

Dr. Ankita Tiwari[1], Dr. Kartikey Tyagi[2], Dr Richa Mahant[3], Akanksha Pandey[4], Diptimayee Jena[5], Rajeev Ranjan[6], Kartikey Pandey[7], Prof. (Dr.) Kirtimaya Mishra[8]*

Assistant Professor, School of Pharmacy, Sharda University, Plot No. 32-34, Knowledge Park III, Greater Noida - 201306, Uttar Pradesh, India
Director Research HRDC & Associate Professor Dept. Of Panchakarma, Uttaranchal Ayurvedic PG Collage, Dehradun, Uttarakhand Pin: 248001
Faculty, Jiwaji University Gwalior 474001
Assistant Professor, Anjali college of pharmacy
Assistant Professor, School of Pharmacy, ARKA JAIN University, Jamshedpur, Jharkhand. 832108
Assistant Professor, Department of Chemistry, DSPM University, Ranchi-834001
Assistant Professor, Krishanarpit institute of pharmacy Prayagraj
Professor, School of Pharmacy, ARKA JAIN University, Jamshedpur, Jharkhand, 832108

Corresponding Author Details:Prof. (Dr.) Kirtimaya Mishra
kirtimishra.pharma@gmail.com

Abstract:
Peptic ulcer disease (PUD) is the most common gastrointestinal condition in the world, with significant death and morbidity rates. The many adverse effects of antiulcer drugs now available on the market include hypersensitivity, arrhythmia, impotence, gynecomastia, haematological abnormalities, and renal disease. Traditional medicine accounts for a substantial part of primary healthcare worldwide. On the crude extract of Ficus racemosa, a number of qualitative and quantitative investigations were carried out in order to determine the presence of characteristic phytochemical components. The present research looked at different solvents' potential to cure ulcers. Leaf extract from Ficus racemosa Linn. in albino rats. To measure antiulcer activity, the ethanol-induced stomach ulcer, free and total acidity, and pylorus-ligated ulcer techniques were also applied. Using the soxhlet extraction technique, the leaves of Ficus racemosa were progressively extracted with petroleum ether (60–80 C), chloroform, ethyl acetate, Petroleum ether, ethanol, methanol, and water. They were evaluated for consistency in colour, phytochemical content, phytoconstituents such glycosides, saponins, and phytosterols, and yield percentage. Early studies on the different extracts revealed the presence of flavonoids, phenols, steroids, and terpenoids all in favourable results. The results of fractionation tests showed that the methanol fraction had the highest antiulcer effectiveness and the chloroform fraction had the lowest efficacy. Due to their antiulcer effect and safety profile, the leaves of Ficus racemosa may be a viable option for treating PUD in individuals.

Key words: Peptic ulcer disease, *Ficus racemosa,* Antiulcer Activity, Leaves, Crude extract

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

INTRODUCTION

Peptic ulcer disease (PUD) is the most prevalent gastrointestinal disorder worldwide associated with high mortality and morbidity [1].It is a disease of the gastrointestinal tract (GIT), which includes both gastric and duodenal ulcers and it is characterized by an imbalance between offensive (pepsin, gastric acid, and *Helicobacter pylori*) and defensive factors like prostaglandins, bicarbonate, mucin growth factor and nitric oxide [2, 3]. The frequency of *H. pylori* infection is significant and contributes to the increase in the PUD morbidity and mortality [4].It is also a major reason for hospitalization all over the world [5]and approximately 301,400 people were died in 2013 worldwide [6, 7]. Patient undergone PUD surgery in Sub-Saharan Africa revealed that 86% had duodenal ulcer, while the remaining 14% had gastric ulcers.Perforation (355), bleeding (7%), obstruction (30%), and chronic cases (28%) were the major complications that require surgery, and the overall fatality rate was 5.7% [8]. The common etiologic factors for the PUD were *H. pylori*and by the use of Nonsteroidal anti-inflammatory drugs (NSAIDs)[9, 10]. Other risk factor included stress, tobacco use, alcohol consumption, Zollinger Ellison syndrome, and age-related decline in prostaglandin level were also reported [11]. Anti-ulcer drugs that are used currently for the management of PUD cause adverse drug reaction such as hypersensitivity, arrhythmia, impotency, gynecomastia, hematopoietic changes, and kidney diseases [10,12] and these drugs also lead significant drug- drug interactions, that could limit their potential use [13, 14]. Many medicinal plants and their secondary metabolites are known to possess anti-ulcer activity. Croton family was important source of ingredients for the therapeutic management of PUD worldwide. An active constituent Plaunotol was found and isolated from the *Croton stellatopilosus* stem, bark and /or leaf.Plaunotol induces PGE2 as well as it helps to eradicate *H. pylori* bacteria, and used as a cytoprotective antiulcer agent.Plaunotol was found to be more effective when combined with clarithromycin and a proton pump inhibitor than other combination for *H.pylori* induced PUD [15-17].

Traditional medicine plays an important role in providing health care around the world and used by 75-80% of the people in developing countries due to its cultural acceptability, compatibility with the human body, and lack of side effects [10]. In Ayurveda system of medicine the Ayurvedic practitioners used the leaves and root of *Ficus racemosa* Linn to treat a variety of ailments, including syphilitic or other inflammatory ulcers [18-20].

However, there is currently no scientific evidence to support the above mentioned traditional claims, As a result, the current study was designed to look into the anti-ulcer activity of Ethanolic Extract of leaves *Ficus racemosa* Linn leaves in albino rats.

METHODS AND MATERIALS

Chemicals and drugs

Glacial acetic acid (Sigma -Aldrich Chemie, Steinheim, Germany), benzene (Nice Laboratory Reagent, Kerala, India), chloroform (Super TeK chemicals, Uttar Pradesh, India),ethanol (Indenta Chemicals, Mumbai, India), lead acetate trihydrate (Guangdong Chemical Reagent

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

Engineering, People's Republic of China), methanol (Nice Chemicals, Kochi, India), sucralfate (Moraceae Pharmaceuticals Pvt. Ltd, Lucknow, India). All other ingredients were used of analytical grade.

Experimental animals

For this study, healthy adult Wistar albino rats of either sex were chosen at random. The said rats were issued for study from Shri Ramnath Singh Institute of Pharmaceutical Science & Technology, Sitholi, Gwalior (M.P.).For the experiments, 160-200 g, 12 to 16 week old rats were used. The rats were kept in a plastic box cage with 12/12 h light/dark cycle at 19-25 °C in a standard environment and the rats were given free access to standard pellet feed and water. The investigation was conducted in accordance with the recommendations of the OECD and the National Research Council Guide for the care and use of Laboratory Animals [21-22]. The Department of Pharmacology's Research Review Committee also granted their approval.

Collection and authentication of plant

The leaves of *Ficus racemosa* were collected locally during the month of February from Sa Sitholi, Gwalior (M.P.). Herbarium file of plant part was prepared and authenticated by Professor, Department of Botany, Rajiv Gandhi Proudyogiki Vishwavidyalaya, Bhopal (M.P.).

Drying and size reduction of plant material

The leaves of *Ficus racemosa* were dried under shade in the laboratory. It was pulverized into a coarse powder. To preserve uniformity, the coarse powder of leaves was sieved No.18 and stored in a cool, dry place.

Extraction of Leaves.

Extraction of plants was continued by the approach of Soxhlation (Jensen, 1914). Soxhlet apparatus was used for the extraction by using ethyl alcohol as solvent. A 100 g of coarsely dried powdered leaves were Soxhlet using petroleum ether for the principle of defatting for 48 h. The obtained powder was dried under a hot air oven at 40–50°C and soxhlation was continued using ethyl alcohol at 60–80°C for 72 h. After extraction, petroleum ether was used for defatting of waxy materials. After completion of soxhlation, the extract was dried at room temperature for 5 days to obtain a dried extract. The leaves were processed by same way using different solvent like; Chloroform, Petroleum ether and methanol etc.

Phytochemical analysis of crude extract

The obtained dried crude extract of *F. racemosa* was subjected to various qualitative and quantitative tests to detect the existence of common phytochemical constituents. All the chemicals and reagents used in phytochemical testing were of analytical grade [23].

Experimental design for Leaves of *Ficus racemosa* Linn.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

Experimental design for Leaves of Ficusracemosa Linn. Albino rats of either sex weighing a range between (150-200gms) were divided into different-different groups of animal, and kept six-six animals in each group.

Group 1: Normal control six animals treated with, 1% Tween 80 treated animals.

Group 2: Disease control rats, being treated with etahnol (1 ml/200 gm, p.o.)

Group 3: One group of total six animals with standard drug, Omeprazole (20 mg/kg, p.o.) Group

4: Treated with Pet. Ether extract of F. R.-L (200 mg/kg body weight)

Group 5: Treated with Petroleum ether extracts of F. R.-L (400 mg/kg body weight)

Group 6: Animals treated with chloroform extracts of F. R.-L (200 mg/kg body weight).

Group 7: Treated with chloroform extracts of F.R.-L (400 mg/kg body weight)

Group 8: Treated with ethyl acetate of F. R.-L (200 mg/kg body weight)

Group 9: Ethyl acetate extract of F. R.-L, treated with 400 mg/kg, b.w.

Group 10: Ethanolic extract of F. R.-L, treated with 200 mg/kg, b.w.

Group 11: Treated with ethanolic extracts of F. R.-L (400 mg/kg body weight).

Group 12: Treated with methanolic extracts of F. R.-L (200 mg/kg body weight).

Group 13: Treated with methanolic extracts of F. R.-L (400 mg/kg body weight)

Group 14: Aqu. Extract of F.R.-L, treated with 200 mg/kg, b.w.

Group 15: Aqueous extract of FR-L, treated with 400 mg/kg b.w.

Evaluation of Antiulcer Activity of leaves of *Ficus racemosa*.

a. Ethanol Induced Gastric Ulcer

Gastric ulcer was induced by administration of 96% ethanol (5 mL/kg, po). One hour after ethanol instillation, the animals were anesthetized with intraperitoneal administration of ketamine (50 mg/kg) and xylazine (10 mg/kg). The stomachs were dissected and opened along greater curvature for evaluating the number and the length of gastric lesions. A portion of the stomach was dissected and was subsequently homogenized in cold potassium phosphate buffer (0.05 M, pH 7.4). The homogenate was centrifuged at 5000 rpm for 10 min. The supernatant was stored at −80 °C until measurement of malondialdehyde and nitric oxide [24]. Ulcer index and % ulcer protection were calculated.

b. Determination of free acidity and total acidity

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

One milliliter of gastric juice was pipetted into a 100 ml conical flask, two or three drops of Topfer's reagent were added and this was titrated with 0.01 N sodium hydroxide until all traces of red color disappeared and the color of the solution became yellowish-orange. The volume of alkali added was noted. This volume corresponds to free acidity. Two or three drops of phenolphthalein solution were added and titration was continued until a definite red tinge appeared. The total volume of alkali added was noted [25]. The volume corresponds to total acidity. Acidity was calculated by using the standard formula.

c. Pylorus ligated Ulcer

In this the albino rats were kept fasted in individual cages for 24 hour extract, reference drug and control vehicle was administered 1 hour prior to pyloric ligation. Then the pre-treated animals were anaesthetised by anaesthetic ether;A small midline incision below the xiphoid process was used to open the abdomen. The stomach's pyloric portion was ligated without causing any damage to its blood vessels. The stomach was taken out gently and the abdominal wall was sealed with interrupted sutures. The animals were deprived of water during the postoperative period. Four hours after ligation, the stomach was dissected out and contents were collected into clean tubes.The volume, pH and total acid content of gastric juice were measured.The contents were centrifuged, filtered and subjected to titration for estimation of total acidity. From the supernatant, aliquots (1 ml each) were taken for the determination of pH, total or free acidity and pepsin activity. Each stomach was examined for lesions in the fore stomach portion and indexed according to severity. The numbers of ulcers were counted and scoring of ulcer was made as follows: Normal colored stomach (0), Red coloration (0.5), Spot ulcer (1), Haemorrhagic streak (1.5), Deep ulcers (2) and Perforation (3). Mean ulcer score for each animal was expressed as ulcer index [27]. Ulcer index (UI) was measured by using following formula: $UI = UN + US + UP \times 10{-}1$ Where, UI (Ulcer Index); UN (Average number of ulcers per animal); US (Average number of severity score); UP (Percentage of animals with ulcers). The percentage inhibition of ulceration was calculated and compared with control [26-27, 29-42].

RESULTS

Determination of physicochemical parameters

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

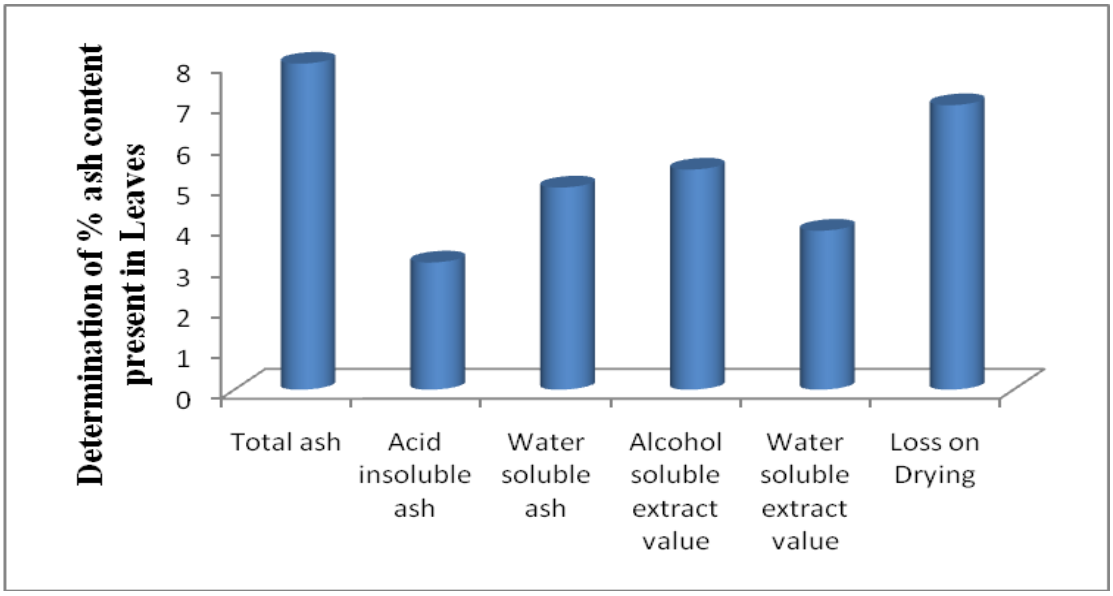

Figure 1: Physico-chemical parameters of *Ficus racemosa*

Determination of Moisture content

Moisture content determination is imp. not only to know excess water, but also inthe conjunction with suitable temperature , moisture will lead to activation of enzymes, and provide comfortable environment to proliferate living organisms. The selected plant material studies, exhibit that, the difference of two consecutive weighing after drying for 30 minutes and cooling for also 30 minutes in a desiccators-0.09 & 0.23 gm for leaves and bark of *Ficus racemosa.*

Determination of Swelling Index

The Experimental results on selected plant material exhibited – volume occupiedby 1 gm of plant material= 1.62, 1.45 ml for leaves.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

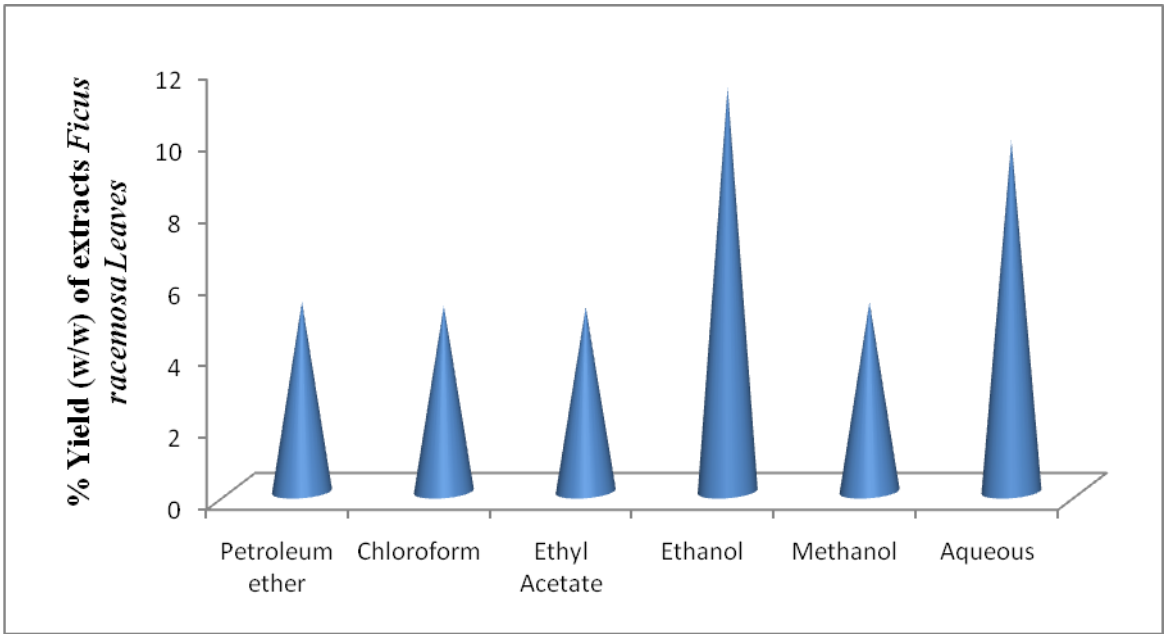

Figure 2: % Yield (w/w) of extracts *Ficus racemosa* Leaves

Phytochemical analysis of crude leaves extract

Phytochemical screening of different extract exhibited the presence of different phytochemical.

Table 3: Preliminary Phytochemical test for different extract of *Ficus* racemosa

S. No.	Test	Pet. ether	Chloroform	Ethyl acetate	Ethanol	Methanol	Aqueous
1.	Carbohydrate Molish test Felling test	- -	- -	- -	- -	+ +	+ +
2.	Glycosides Bronteger test	-	-	+	-	+	+
3.	Phytosterol Triterpinoids Salkowaski test	+ -	+	-	+	+	-
4.	Protein + Amino acid Biuret test Ninhydrin test	- -	- -	- -	- -	- -	- -

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

5.	Phenolic test Ferrictest Lead Acetate test	- -	+ +	+ +	+ +	+ +	- -
6.	Flavonoids Alkaline test	-	-	+	+	+	+
7.	Saponin Foam test	-	-	-	-	+	+
8	MucilageIodine test Ethanol test	- -	- -	- -	- -	- -	 + +
9.	Alkaloid Mayer test Hager test	- -	+ +	+ +	- -	+ +	- -

Note: (+) *ve* indicates positive result, whereas (–) *ve* indicates negative result

Evaluation of Antiulcer activity

a. Antiulcer activity of Leaves of *Ficus racemosa* Linn. Ethanol Induced Ulcer.

The gastric mucosa of ethanol (1ml/200 gm b.w.) administration induced ulceration in rats of the control group characterized by hemorrhagic gastric lesions. The methanolic extract of leaves caused a reduction in the severity of these lesions inducedby ethanol which was evident by a moderately significant ($p<0.01$) reduction in the ulcer index and an increased in the percentage protection of ulcers when compared with the control group. Rats treated by omeprazole that is a drug of choice as standerd, caused a reduction in the severity of these lesions induced by ethanol which was evident by a significant ($p<0.001$) reduction in the ulcer index and an increase in the percentage protection of ulcers when compared with the control group.

Table 4: Antiulcer activity of Leaves of *Ficus racemosa* Linn.

S. No.	Treatments	Mean Ulcer Index±SEM	% Protection
1	Normal Control	0±0	0
2	Disease Control (Ethanol Treated)	4.5±0.341	0%
3	Omeprazole Treated (20 mg/kg)	0.58±0.08***	87.11%
4	F. R.-L(P.E)-200 mg/kg	3.25± 0.33*	27.77%

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

5	F. R.-L(P.E)--400 mg/kg	3.16±0.21*	29.77%
6	F. R.-L(Chl)--200 mg/kg)	3.51±0.22*	22%
7	F. R.-L(Chl)--400 mg/kg	3.18±0.07*	29.33%
8	F. R.-L(EA)--200 mg/kg	3.15± 0.31*	30%
9	F. R.-L(EA)--400 mg/kg	2.16±0.23*	52%
10	F. R.-L(Eth)--200 mg/kg	3.57±0.21*	20.66%
11	F. R.-L(Eth)---400 mg/kg	3.11±0.01*	30.88%
12	F. R.-L(Meth)---200 mg/kg)	2.15± 0.23**	52.22%
13	F. R.-L(Meth)--400 mg/kg	2.09±0.31**	53.55%
14	F. R.-L(Aqu)-200 mg/kg	3.22±0.42*	28.44%
15	F. R.-L(Aqu)---400 mg/kg	3.10±0.02*	31.12%

Mean ± SEM in each group (n=6).*P <0.05, **P<0.01 as compared with the control(ANOVA test)

F.R = *Ficus racemosa* (F.R), leaves (L), Paetroleum ether (P.E), Chloroform(chl), Ethyl acetate (EA), Ethanol (Eth). Methanol (Meth) and Aqueous (Aqu).

b. Determination of free acidity and total acidity

Gastric juice examinations, means an amount of hydrochloric acid that is total acids or free acids- organic and inorganic, which it consists, are find out. Gastric juice estimation in our study/research, indicated that there was a significant ($p<0.01$) decreased in the free acidity (released total acid amounts) and total acidity of the gastric juice in experimental animals, treated with 200 mg/kg and 400mg/kg of methanolic extract of barks of *Ficus racemosa* and was compared to that of, a standard drug with standar Omeprazole (20 mg/kg)d dose-treated group ($p<0.001$).

Table 6.9: Effect on free acidity and total acidity

S. No.	Treatments	Gastric Volume (ml/100g)	pH	Free Acidity (mEq/l/100g)	Acidity Total [mEq/l/100g]
1	Normal Control	1.01±0.089	2.3 ±0.261	20.93±0.368	57.22±0.128
2	Disease Control	4.66±0.11	1.4 ±0.092	75.68±2.257	154.48±3.244
3	Omeprazole (20mg/kg)	2.18±0.079**	4.3 ±0.241**	25.15±0.321**	64.21±0.126**
4	F. R.-L (Meth)- 200 mg/kg)	3.08±0.070	2.13±0.017**	56.48±0.496**	104.25±0.862**

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

5	F. R.-L (Meth)- --400 mg/kg)	2.65±0.28**	3.66±0.038**	44.1±0.174**	82.13±0.357**

Values are shown as mean ± SEM in each group (n=6). **P<0.01, *P <0.05, compared with the control (ANOVA test)

c. Antiulcer activity of leaves of *Ficus racemosa* Linn. Pylorus Ligation Induced Ulcer

The results indicated that methanolic extract at dose levels of 200 mg/kg and 400 mg/kg significantly decreased the ulcer index (p<0.001) which was also evidenced by significant increase in percentage ulcer protection at both the dose levels.The percentage protection of ulcers in the treated groups at 200 and 400 mg/kg of ethanol extract of leaves was found to be 57.97% and 67.70% respectively. Omeprazole at 20 mg/kg showed a protection index of 88.51%.

Table 6.7: Antiulcer activity of leaves of *Ficus racemosa* Linn.

S. No.	Treatments	Mean Ulcer Index ± SEM	% Protection
1	Normal Control	0±0	0
2	Disease Control (Ethanol Treated)	7.4±0.50***	0%
3	Omeprazole Treated (20 mg/kg)	0.85±0.21***	88.51%
4	F. R.-L(P.E)-200 mg/kg	6.15± 0.33*	16.89%
5	F. R.-L(P.E)--400 mg/kg	6.09±0.21*	17.70%
6	F. R.-L(Chl)--200 mg/kg)	6.42±0.32*	13.24%
7	F. R.-L(Chl)--400 mg/kg	6.22±0.17*	15.94%
8	F. R.-L(EA)--200 mg/kg	5.13± 0.32*	30.76%
9	F. R.-L(EA)--400 mg/kg	5.18±0.13*	30%
10	F. R.-L(Eth)--200 mg/kg	5.19±0.11*	29.86%
11	F. R.-L(Eth)---400 mg/kg	4.45±0.11*	39.86%
12	F. R.-L(Meth)---200 mg/kg)	3.11± 0.33*	57.97%
13	F. R.-L(Meth)--400 mg/kg	2.39±0.31*	67.70%
14	F. R.-L(Aqu)-200 mg/kg	5.32±0.32*	28.10%
15	F. R.-L(Aqu)---400 mg/kg	5.30±0.25*	28.37%

Mean ± SEM in each group (n=6).**P<0.01, *P <0.05compared with the control(ANOVA test)

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

DISCUSSION

The current work includes testing the leaves of *Ficus racemosa* for anti-ulcer efficacy using phytochemical and pharmaceutical methods. The research project includes a thorough and organised phytochemical analysis as well as an examination of different plant leaf extracts. Three different experiments were conducted for this dissertation. The first section consists of physicochemical and phytochemical analysis as well as a preliminary assessment of plant leaves' ability to treat ulcers caused by ethanol in a pylorus ligation model.

The plant is being verified and assessed for several physicochemical characteristics, such as ash levels, moisture content, and extractive values, among others. Inside the proximate analysis, it was discovered that the acid insoluble ash value was less than the total ash value and the water soluble ash value was much less than the total ash value. The extractive value of alcohol was much higher than the extractive value of water. The leaves of *Ficus racemosa* were successively extracted using the soxhlet extraction method with petroleum ether (60-80 C), chloroform, ethyl acetate, Petroleum ether, ethanol, methanol, and water. Their colour consistency, phytochemical assessment, phytoconstituents like glycosides, saponins, and phytosterols were assessed, as well as the percent yield. Flavonoids, phenols, steroids, and terpenoids all tested positively in early tests on the various extracts. Another researcher looked into the fact that in an acute toxicity assay, no hazardous effects appeared at 2000 mg/kg body weight following a single administration of several extracts [28, 43]. Hence, the 1/5th and 1/10th portions of 2000 mg/kg were chosen for additional research.

According to fractionation experiments, the methanol fraction had the strongest antiulcer efficacy, while the chloroform fraction was determined to be the least effective. The leaves of *Ficus racemosa* might be a promising choice for the treatment of PUD in people due to their antiulcer action and safety profile.

STATISTICAL ANALYSIS

Information was presented as mean ± S.E.M. One-way analysis of variance (ANOVA) was used to compare the means of several groups, followed by Tukey's post hoc analysis. The cutoff point for significance was set at $P \leq 0.05$. All statistical analyses were performed using the Graph Pad Prism software package, version 5 (Graph Pad Software, Inc., San Diego, CA, USA).

CONCLUSIONS

In conclusion, the current investigation supported the conventional claim of the experimental plant by demonstrating that the leaves extract of *Ficus racemosa* in various solvents had strong antiulcer action. According to fractionation experiments, the methanol fraction had the strongest antiulcer efficacy, while the chloroform fraction was determined to be the least effective. The leaves of *Ficus racemosa* might be a promising choice for the treatment of PUD in people due to their antiulcer action and safety profile.

CONFLICTS OF INTEREST

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

The authors declare that they have no conflicts of interest.

REFERENCES

1. V. T. Daniel, J. T. Wiseman, J. Flahive, and H. P. Santry, "Predictors of mortality in the elderly after open repair for perforated peptic ulcer disease," *Journal of Surgical Research*, vol. 215, pp. 108–113, 2017.
2. A. A. Ayantunde, "Current opinions in bleeding peptic ulcer disease," *Journal of Gastrointestinal & Digestive System*, vol. 4, p. 172, 2014.
3. N. Byrge, R. G. Barton, T. M. Enniss, and R. Nirula, "Laparoscopic versus open repair of perforated gastroduodenal ulcer: a National surgical quality improvement program analysis," *The American Journal of Surgery*, vol. 206, no. 6, pp. 957–963a, 2013.
4. K. Sugano, J. Tack, E. J. Kuipers et al., "Kyoto global consensus report on Helicobacter pylorigastritis," *Gut*, vol. 64, no. 9, pp. 1353–1367, 2015.
5. K. Søreide, K. Thorsen, and J. A. Søreide, "Strategies to improve the outcome of emergency surgery for perforated peptic ulcer," *British Journal of Surgery*, vol. 101, no. 1, pp. e51–e64, 2014.
6. I. Abubakar, T. Tillmann, and A. Banerjee, "Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global burden of disease study 2013," *Lancet*, vol. 385, no. 9963, pp. 117–171, 2015.
7. C. Harsha, K. Banik, D. Bordoloi, and A. B. Kunnumakkara, "Antiulcer properties of fruits and vegetables: a mechanism based perspective," *Food and Chemical Toxicology*, vol. 108, pp. 104–119, 2017.
8. J. Rickard, "Surgery for peptic ulcer disease in sub-Saharan Africa: systematic review of published data," *Journal of Gastrointestinal Surgery*, vol. 20, no. 4, pp. 840–850, 2016.
9. B. Teka, S. Gebre-Selassie, and T. Abebe, "Sero - prevalence of *Helicobacter Pylori* in HIV positive patients and HIV negative controls in St. Paul's general specialized hospital, Addis Ababa, Ethiopia," *Science Journal of Public Health*, vol. 4, no. 5, pp. 387–393, 2016.
10. M. Kumar, M. Niyas, T. Mani, O. Rahiman, and S. Kumar, "A review on medicinal plants for peptic ulcer," *Pharmaceutical Letters*, vol. 3, no. 3, pp. 414–420, 2011.
11. D. J. Stewart and R. Ackroyd, "Peptic ulcers and their complications," *Surgery*, vol. 29, no. 11, pp. 568–574, 2011.
12. S. M. Toth-Manikowski and M. E. Grams, "Proton pump inhibitors and kidney disease-GI upset for the nephrologist?" *Kidney International Reports*, vol. 2, no. 3, pp. 297–301, 2017.
13. M. Ingelman-Sundberg, "Pharmacogenetics of cytochrome P450 and its applications in drug therapy: the past, present and future," *Trends in Pharmacological Sciences*, vol. 25, no. 4, pp. 193–200, 2004.
14. L. S. Welage and R. R. Berardi, "Evaluation of omeprazole, lansoprazole, pantoprazole, and rabeprazole in the treatment of acid-related diseases," *Journal of the American Pharmaceutical Association*, vol. 40, no. 1, pp. 52–62, 2000.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

15. Y. M. Kang, R. Komakech, C. S. Karigar, and A. Saqib, "Traditional Indian medicine (TIM) and traditional Korean medicine (TKM): aconstitutional-based concept and comparison," *Integrative Medicine Research*, vol. 6, no. 2, pp. 105–113, 2017.
16. S. Getaneh and Z. Girma, "An ethnobotanical study of medicinal plants in Debre Libanos Wereda, Central Ethiopia," *African Journal of Plant Science*, vol. 8, no. 7, pp. 366–379, 2014.
17. T. Koga, H. Inoue, C. Ishii, Y. Okazaki, H. Domon, and Y. Utsui, "Effect of plaunotol in combination with clarithromycin or amoxicillin on Helicobacter pyloriin vitro and in vivo," *Journal of Antimicrobial Chemotherapy*, vol. 50, no. 1, pp. 133–136, 2002.
18. Ahmed F, Urooj A. Traditional uses, medicinal properties, and phytopharmacology of Ficus racemosa: a review. *Pharm Biol*. 2010;48(6):672-681. doi:10.3109/13880200903241861
19. Dharmadeva S, Galgamuwa LS, Prasadinie C, Kumarasinghe N. *In vitro* anti-inflammatory activity of *Ficus racemosa* L. bark using albumin denaturation method. *Ayu*. 2018;39(4):239-242. doi:10.4103/ayu.AYU_27_18
20. Gul-e-Rana, Karim S, Khurhsid R, et al. Hypoglycemic activity of Ficus racemosa bark in combination with oral hypoglycemic drug in diabetic human. *Acta Pol Pharm*. 2013;70(6):1045-1049.
21. National Research Council . *Guide for the Care and Use of Laboratory Animals.* 8th ed. Washington, DC: The National Academies Press; 1996.
22. Organization for Economic Cooperation and Development . *OECD Guidelines for the Testing of Chemicals Acute Oral Toxicity -Up-And-Down-Procedure UDP.* France: OECD Publishing; 2008. p. 425.
23. Jha DK, Panda L, Lavanya P, Ramaiah S, Anbarasu A. Detection and confirmation of alkaloids in leaves of Justicia adhatoda and bioinformatics approach to elicit its anti-tuberculosis activity. Appl Biochem Biotechnol 2012;168:980-90. doi: 10.1007/s12010-012- 9834-1, PMID 22899014.
24. Morsy M.A., Fouad A.A. Mechanisms of Gastroprotective Effect of Eugenol in Indomethacin-Induced Ulcer in Rats. *Phytother. Res.* 2008;22:1361–1366. doi: 10.1002/ptr.2502.
25. , and melatonin against ethanol-induced gastric damage in rats. *Indian J Pharmacol.* 2004; Sener G, Paskaloglu K, Ayanoglu-dülger G. Protective effect of increasing doses of famotidine, omeprazole, lansoprazole 36:171–4.
26. Khushtar M, Kumar V, Javed K, Bhandari U. Protective Effect of Ginger oil on Aspirin and Pylorus Ligation-Induced Gastric Ulcer model in Rats. Indian J Pharm Sci. 2009 Sep;71(5):554-8. doi: 10.4103/0250-474X.58195. PMID: 20502577; PMCID: PMC2866350.
27. Nie SN, Qian XM, Wu XH, Yang SY, Tang WJ, Xu BH, Role of TFF in healing of stress induced gastric lesions *World J Gastroenterol* 2003 9:1772-76.
28. Ahmed F, Urooj A. Cardioprotective activity of standardized extract of Ficus racemosa stem bark against doxorubicin-induced toxicity. *Pharm Biol*. 2012;50(4):468-473. doi:10.3109/13880209.2011.613848

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

29. Pal N, Mandal S, Shiva K, Kumar B. Pharmacognostical, Phytochemical and Pharmacological Evaluation of Mallotus philippensis. Journal of Drug Delivery and Therapeutics. 2022 Sep 20;12(5):175-81.
30. Singh A, Mandal S. Ajwain (Trachyspermum ammi Linn): A review on Tremendous Herbal Plant with Various Pharmacological Activity. International Journal of Recent Advances in Multidisciplinary Topics. 2021 Jun 9;2(6):36-8.
31. Mandal S, Jaiswal V, Sagar MK, Kumar S. Formulation and evaluation of carica papaya nanoemulsion for treatment of dengue and thrombocytopenia. Plant Arch. 2021;21:1345-54.
32. Mandal S, Shiva K, Kumar KP, Goel S, Patel RK, Sharma S, Chaudhary R, Bhati A, Pal N, Dixit AK. Ocular drug delivery system (ODDS): Exploration the challenges and approaches to improve ODDS. Journal of Pharmaceutical and Biological Sciences. 2021 Jul 1;9(2):88-94.
33. Shiva K, Mandal S, Kumar S. Formulation and evaluation of topical antifungal gel of fluconazole using aloe vera gel. Int J Sci Res Develop. 2021;1:187-93.
34. Ali S, Farooqui NA, Ahmad S, Salman M, Mandal S. Catharanthus roseus (sadabahar): a brief study on medicinal plant having different pharmacological activities. Plant Archives. 2021;21(2):556-9.
35. Mandal S, Jaiswal DV, Shiva K. A review on marketed Carica papaya leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback. International Journal of Pharmaceutical Research. 2020 Jul;12(3).
36. Mandal S, Vishvakarma P, Verma M, Alam MS, Agrawal A, Mishra A. Solanum Nigrum Linn: An Analysis Of The Medicinal Properties Of The Plant. Journal of Pharmaceutical Negative Results. 2023 Jan 1:1595-600.
37. Vishvakarma P, Mandal S, Pandey J, Bhatt AK, Banerjee VB, Gupta JK. An Analysis Of The Most Recent Trends In Flavoring Herbal Medicines In Today's Market. Journal of Pharmaceutical Negative Results. 2022 Dec 31:9189-98.
38. Mandal S, Vishvakarma P, Mandal S. Future Aspects And Applications Of Nanoemulgel Formulation For Topical Lipophilic Drug Delivery. European Journal of Molecular & Clinical Medicine.;10(01):2023.
39. Chawla A, Mandal S, Vishvakarma P, Nile NP, Lokhande VN, Kakad VK, Chawla A. Ultra-Performance Liquid Chromatography (Uplc).
40. Mandal S, Raju D, Namdeo P, Patel A, Bhatt AK, Gupta JK, Haneef M, Vishvakarma P, Sharma UK. Development, characterization, and evaluation of rosa alba l extract-loaded phytosomes.
41. Mandal S, Goel S, Saxena M, Gupta P, Kumari J, Kumar P, Kumar M, Kumar R, Shiva K. Screening of catharanthus roseus stem extract for anti-ulcer potential in wistar rat.
42. Shiva K, Kaushik A, Irshad M, Sharma G, Mandal S. Evaluation and preparation: herbal gel containing thuja occidentalis and curcuma longa extracts.