 International Standard Serial Number (ISSN): 2319-8141

International Journal of Universal Pharmacy and Bio Sciences 9(4): July-August 2020

INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES

IMPACT FACTOR 4.018***

ICV 6.16***

Pharmaceutical Sciences **Research Article……!!!**

EVALUATION OF ANTIULCER ACTIVITY OF HYDROALCOHOLIC LEAF EXTRACT OF *Pisonia grandis* R.Br USING INDOMETHACIN AND PYLORUS LIGATION INDUCED GASTRIC ULCER IN RATS

Dr.P.AMUDHA[1*], P.SUBATHIRADEVI[2], M.PERIYANAYAGI[3]

[1*] Professor, Department of Pharmacology, C.L Baid Metha College of Pharmacy, Rajiv Gandhi Salai, Old Mahabalipuram Road, Jyothinagar, Thoraipakkam, Chennai – 600 097, Tamil Nadu, India.

[2] Department of Pharmacology, C.L Baid Metha College of Pharmacy, Rajiv Gandhi Salai, Old Mahabalipuram Road, Jyothinagar, Thoraipakkam, Chennai – 600 097, Tamil Nadu, India.

[3] Department of Pharmacology, C.L Baid Metha College of Pharmacy, Rajiv Gandhi Salai, Old Mahabalipuram Road, Jyothinagar, Thoraipakkam, Chennai – 600 097, Tamil Nadu, India.

KEYWORDS:

Peptic ulcer, Hydroalcoholic extract, Leaf of Pisonia grandis R.Br, Omeprazole

FOR CORRESPONDENCE:
Dr.P.Amudha *
ADDRESS:
Professor, Department of Pharmacology, C.L Baid Metha College of Pharmacy, Rajiv Gandhi Salai, Old Mahabalipuram Road, Jyothinagar, Thoraipakkam, Chennai 600 097, Tamil Nadu, India.

ABSTRACT

Peptic ulcer is a disorder of the upper gastrointestinal tract that is caused by gastric acid. There are various chemical agents available for the treatment of peptic ulcers, but claim serious side effects. Herbal drugs are preferred over chemical agents due to their relatively less toxicity, better acceptability and better compatibility with human body. Lesser adverse effects, economical, effective and easy availability. The present research has been carried out to investigate antiulcer activity of Hydroalcoholic leaf extract of Pisonia grandis R.Br (HEPG) using Indomethacin induced gastric ulcer and Pylorus ligation induced gastric ulcer in wistar rats. Ulcer score, ulcer index and number of ulcers were determined for indomethacin and pylorus ligation induced gastric ulcers. Antiulcer effect of Pisonia grandis R.Br (HEPG) was compared with standard drug omepprazole (20mg/kg). These observations helped us to conclude that Hydroalcoholic leaf extract of Pisonia grandis R.Br had significant antiulcer properties.

INTRODUCTION:

Peptic ulcer occurs in the gastrointestinal tract (GIT) which is exposed to gastric acid and pepsin, i.e. stomach and duodenum, esophagus. The pathophysiology of these disorders has focused on an imbalance between aggressive (acid, pepsin, bile and *H. Pylori*) and defensive or protective force (gastric mucosa and bicarbonate secretion, prostaglandins, nitric oxide, innate resistance of the mucosal cells) factors in the stomach [1]. Peptic ulcer disease (PUD), also known as a peptic ulcer or gastric ulcer, is a break in the lining of the stomach, first part of the lower oesophagus. Though they can occur at any level of the alimentary tract that is exposed to hydrochloric acid and pepsin, they occur most commonly in either the duodenum or stomach in the ratio of 4:1 each of the two main types may be acute or chronic [2]. A stomach is a bag of muscle which crushes food with pepsin and HCL acid. Too much pepsin and acid may damage the lining of the stomach, causing an ulcer [3]. The lifetime risk for developing a peptic ulcer is approximately 10% [4]. They resulted in 301,000 deaths in 2013 down from 327,000 deaths in 1990 [5]. Although mortality rates from peptic ulcer disease are low, the high prevalence and the resulting pain, suffering, and expense are very costly [6].There are enormous chemical agents available for the treatment of peptic ulcers, but proclaim serious side effects. Herbal drugs have preserved their importance due to relatively less toxicity, better cultural acceptability, better compatibility with human body, lesser adverse effects, economical, effective and easy availability. *Cynodon dactylon*, *Ocimum sanctum*, *Glycyrrhiza glabra*, *Ficus religiosa* are some of the plants which show antiulcer activity [7]. *Pisonia grandis* R.Br (Nyctaginaceae) is widely distributed through India from Himalayas down to Ceylon and is a widespread evergreen tree commonly known as 'Leechai kottai keerai'[8].The plant is used traditionally as an anti-fungal and anti-rheumatic [9]. Leaves are useful in chronic rheumatism, wound healing and also used as vegetable/spinach [10-12]. *Pisonia grandis* R.Br have numerous bio active compounds includes Pinnatol, Allantion, β-Sitosterol, α-Spinasternol, β-Sitosterol glucoside, Octocosanal Dulcitol, Flavonoids and Quercetin [13]. The different parts of *Pisonia granids* R.Br are extensively used by the trial's in the preparation of several folk medicines. It is extensively used in Indian traditional medicine as an anti-diabetic, anti-inflammatory, wound healing, diuretic, analgesic, filariasis, dysentery, constipation, abdominal discomfort and rheumatic disorders [14].

MATERIALS AND METHODS

The leaves of *Pisonia granids* R.Br were collected from local source from Tamilnadu. Color. Odor, taste, shape, size and texture of the leaf material were estimated by visual and sensory evaluation.

Preparation of *Pisonia granids* R.Br leaf extract:

The plant material was washed under running tap water and dried in shade for 3 weeks. Dried leaves were coarsely powdered and passed through sieve of mesh size no:22. 400g of coarse powder was extracted with

hydroalcohol (30:70) in Soxhlet apparatus at a temperature not exceeding 60°C. The extract was stored at 0-4°C for further analysis. Ther percentage yield was calculated by using following formula.

$$\text{Percentage yield (\%W/W)} = \frac{\text{Weight of extract obtained (g)}}{\text{Weight of plant material used}} \times 100$$

Preliminary Phytochemical Analysis:

HEPG was subjected to preliminary phytochemical screening for the presence and absence of phytoconstituents like Phenols, Carbohydrates, Sterols, Proteins, Flavonoids, Gums and Mucilage, Glycosides, Oxalate, Tannins, Saponins, Alkaloids, Phytate, Ascorbic acid and Terpens [15].

Experimental animals:

Healthy Wistar rats of either sex weighing 180 to 250g were used for this study. The protocol for the evaluation of antiulcer and toxicity study was approved by Institutional Animal Ethical Committee. The IAEC number is IAEC/XLIX/03/CLBMCP/2016. The animals were housed six per cages maintained under standard conditions (12h/12h light and dark) at 22±2°C. They were fed with standard rat pellet and water ad libitum.

Acute toxicity study:

OECD guidelines 423 were followed to carry out acute toxicity study at dose level of 2000mg/kg. This study was carried out by administering the test solutions orally to rats, at the dose level of 2000mg/kg for 14days, to check whether the test solution has any toxic effects, signs and symptoms of toxicity were observed for next 48 hours. No toxicity or death was observed in the experimental rats when they were subjected to toxicity study [16].

Experimental Gastric Ulcers:

Indomethacin Induced Gastric ulcer

Grouping of Animals:

Group I: Control animal treated with normal saline

Group II: Indomethacin (40mg/kg p.o) induced ulcer

Group III: Indomethacin (40mg/kg p.o) induced ulcer and treated with Omeprazole (20mg/kg p.o)

Group IV: Indomethacin (40mg/kg p.o) induced ulcer and treated with HEPG (200mg/kg p.o)

Group V: Indomethacin (40mg/kg p.o) induced ulcer and treated with HEPG (400mg/kg p.o)

Procedure:

Group I was treated with normal saline. Group II was treated with Indomethacin (40mg/kg p.o) on 14th day. Group III was treated with Omeprazole (20mg/kg p.o) 30min prior to induction of gastric ulcer on the 14th day and group IV and V were treated with HEPG 200mg/kg p.o and HEPG 400mg/kg

p.o respectively for 14days. After fasting for 24hours, the gastric ulcer was induced to all the groups using indomethacin (40mg/kg p.o) except group I and sacrificed 4hours after treatment [17]. The stomach was cut open along with the greater curvature and the contents drained into small beaker, centrifuged and subjected to assess antiulcer activity. The inner surface of stomach was examined for ulcer index. Parameters of Percentage inhibition of ulcer, SOD, CAT, Total protein, SGOT and SGPT were then performed.

Pylorus Ligation Induced Gastric ulcer

Grouping of Animals:

Group I: Control animal treated with normal saline

Group II: Pylorus ligation induced ulcer

Group III: Pylorus ligation induced ulcer and treated with Omeprazole (20mg/kg p.o)

Group IV: Pylorus ligation induced ulcer and treated with HEPG (200mg/kg p.o)

Group V: Pylorus ligation induced ulcer and treated with HEPG (400mg/kg p.o)

Procedure:

Group I was treated with normal saline. Group II was treated with pylorus ligation on 16th day. Group III was treated with pylorus ligation and omeprazole (20mg/kg p.o) administered 30min prior to the test on 16th day. Group IV and V were treated with (HEPG) 200mg/kg and 400mg/kg p.o respectively for 14days. Group II, III, IV and V were fasted for 24hours, care being taken to avoid coprophagy. On 16th day pylorus ligaiton was performed. Rats were anaesthetized with the help of anaesthetic ether; the abdomen was opened by a small midline incision below the xiphoid process. Pylorus ligation of the stomach was slightly lifted out and ligated, avoiding traction to the pylorus or damage to its blood supply [18]. The stomach was replaced carefully and the abdominal wall was closed by interrupted sutures. Rats were sacrificed by an over dose of anaesthetic ether after 6 hours of pylorus ligation. The abdomen was opened, cardiac end of the stomach was dissected out and the contents were drained into a glass tube. The inner surface of stomach was examined for ulcer index. Parameters of Percentage inhibition of ulcer, Free acidity, Total acidity, Gastric volume, SGOT and SGPT were then performed.

Physical parameters:

Ulcer index [19]

Ulcer index is measured by using following formula: UI = UN + US + UP × 10-1

Where,

UI = Ulcer index, UN = Average of number of ulcer per animal

US = Average of severity score, UP = Percentage of animal with ulcers

Scoring of ulcer

0 = Normal coloured stomach, 0.5 = Red colouration, 1 = Spot ulcer

1.5 = Haemorrhagic streaks, 2 = Ulcers ≥ 3 but ≤ 5, 3 = Ulcers > 5

Percentage inhibition [19]

Percentage inhibition of ulceration is calculated as below:

Percentage Inhibition = (UI negative control – UI treatment) / UI negative control × 100

Biochemical parameters:

Stomach contents were drained in small beaker for the estimation of Free acidity [20], Total acidity [20], Gastric volume [20]. Stomach tissue homogenate prepared for the estimation of SOD [21], CAT [22] and Total protein [23]. Animals were sacrificed and blood was collected for the estimation of SGOT [24], SGPT [24].

RESULTS

Phytochemical investigation:

Hydroalcoholic Extract of Pisonia grandis R.Br showed the presence of phenols, carbohydrates, proteins, flavonoids, glycosides, tannins, saponins, terpens and showed the absence of phenols, sterols, gums and mucilage, oxalate, alkaloids, phytate and ascorbic acid.

Acute oral toxicity study:

There was no considerable change in body weight before and after treatment and no sign of toxicity was observed. (Table 1)

Indomethacin Induced Gastric ulcer:

There was significant increase in Ulcer index in group II, IV ($P<0.001$), III, IV ($P<0.01$) when compared to group I. There was significant decrease in Ulcer index in group III, IV, V ($P<0.001$) when compared to group II. There was significant decrease in Percentage inhibition of ulcer in group II, III, IV, V ($P<0.001$) when compared to group I. There was significant increase in Percentage inhibition of ulcer in group III, IV, V ($P<0.001$) when compared to group II. There was significant decrease in SOD in group II, IV ($P<0.001$), III ($P<0.05$), V ($P<0.01$) when compared to group I. There was significant increase in SOD in group III, IV, V ($P<0.001$) when compared to group II. There was significant decrease in CAT in group II, III, IV, V ($P<0.001$) when compared to group I. There was significant increase in CAT in group III, V ($P<0.001$), IV ($P<0.05$) when compared to group II. Results shown in Table 2.

There was significant increase in Total protein in group II, IV ($P<0.001$), III, V ($P<0.05$) when compared to group I. There was significant decrease in Total protein in group III, V ($P<0.001$), IV ($P<0.05$) when compared to group II. There was significant increase in SGOT in group II, IV

(P<0.001), III, V (P<0.05) when compared to group I. There was significant decrease in SGOT in group III, IV, V (P<0.001) when compared to group II. There was significant increase in SGPT in group II (P<0.001), III, V (P<0.05), IV (P<0.01) when compared to group I. There was significant decrease in SGPT in group III, V (P<0.01), IV (P<0.05) when compared to group II. Results shown in Table 3.

Pylorus Ligation Induced gastric ulcer:

There was significant increase in Ulcer index in group II, IV (P<0.001), III, IV (P<0.01) when compared to group I. There was significant decrease in Ulcer index in group III, IV, V (P<0.001) when compared to group II. There was significant decrease in Percentage inhibition of ulcer in group II, III, IV, V (P<0.001) when compared to group I. There was significant increase in percentage inhibition of ulcer in group III, IV, V (P<0.001) when compared to group II. There was significant increase in Free acidity in group II (P<0.001), III (P<0.05), IV, V (P<0.01) when compared to group I. There was significant decrease in Free acidity in group III (P<0.01), IV (P<0.05), V (P<0.01) when compared to group II. There was significant increase in Total acidity in group II, IV (P<0.001), III, V (P<0.05) when compared to group II. Results shown in Table 4.

There was significant increase in Gastric volume in group II, IV (P<0.001), III, IV (P<0.05) when compared to group I. There was significant decrease in Gastric volume in group III, IV, V (P<0.001) when compared to group II. There was significant increase in Total protein in group II, IV (P<0.001), III, V (P<0.01) when compared to group I. There was significant decrease in Total protein in group III, IV, V (P<0.001) when compared to group II. There was significant increase in SGOT in group II, IV (P<0.001), III, V (P<0.05) when compared to group I. There was significant decrease in SGOT in group III, IV, V (P<0.001) when compared to group II. There was significant increase in SGPT in group II, IV (P<0.001), III, V (P<0.05) when compared to group I. There was significant decrease in SGPT in III, IV, V (P<0.001) when compared to group II. Results shown in Table 5.

Table 1: Acute oral toxicity studies of HEPG (OECD 423 guidelines)

Sl. No	Treatment Group	Dose	Weight of Animal in 'g' Before test	Weight of Animal in 'g' After test	Signs of toxicity	Onset of toxicity	Duration
1	HEPG	2g/kg	200	200	No	Nil	14 days
2	HEPG	2g/kg	200	200	No	Nil	14 days
3	HEPG	2g/kg	230	230	No	Nil	14 days

Table 2: Effect of HEPG on Ulcer index, % inhibition of ulcer, SOD and CAT in Indomethacin induced gastric ulcer

Group	Ulcer Index	% Inhibition of ulcer	SOD (mmol/min/mg/ tissue)	CAT (Moles of H_2O_2 consumed/min)
I	0.0±0.0	100±0.0	91±1.06	41.83±0.79
II	8.45±0.3a***	0.0±0.0a***	21.67±0.8a***	15.83±1.01a***
III	2.75±0.18a**b***	72.39±0.45a***b***	83.1±0.88a*b***	29.1±0.7a***b***
IV	4.03±0.14a***b***	57.67±0.2a***b***	62.17±1.5a***b***	19.6±0.9a***b*
V	3.25±0.08a**b***	68.7±0.35a***b***	78.8±0.79a**b***	26.6±1.4a***b***

Table 3: Effect of HEPG on Total protein, SGOT and SGPT in Indomethacin induced gastric ulcer

Group	Total protein (g/dl)	SGOT (U/L)	SGPT (U/L)
I	327±1.92	130.3±2.52	55.6±1.14
II	474±1.38a***	269±1.67a***	93±1.4a***
III	351.7±1.85a*b***	141.8±1.92a*b***	69.8±2.18a*b**
IV	405.5±1.52a***b*	209.3±1.62a***b***	79.1±1.04a**b*
V	345.7±1.17a*b***	142.8±1.7a*b***	71±1.14a*b*

Table 4: Effect of HEPG on Ulcer index, % inhibition of ulcer, Free acidity and Total acidity in Pylorus ligation induced gastric ulcer

Group	Ulcer Index	% Inhibition of ulcer	Free acidity (mEq/L)	Total acidity (mEq/L)
I	0.0±0.0	100±0.0	11.05±0.17	32.9±0.30
II	15.53±0.22a***	0.0±0.0a***	25.2±0.30a***	63.9±0.39a***
III	4.77±0.12a**b***	64.7±0.28a***b***	15.8±0.35a*b**	45.38±0.17a*b***
IV	11.67±0.20a***b***	40.78±0.38a***b***	19.9±0.40a**b*	55.8±0.25a***b*
V	6.93±0.20a**b***	62.07±0.30a***b***	17.83±0.25a**b**	42.95±0.40a*b***

Table 5: Effect of HEPG on Gastric volume, Total protein, SGOT and SGPT in Pylorus ligation induced gastric ulcer

Group	Gastric volume (ml)	Total protein (g/dl)	SGOT (U/L)	SGPT (U/L)
I	2.23±0.081	352±1.39	104.3±1.60	65.3±1.47
II	6.492±0.129a***	651.3±1.9a***	235.2±1.13a***	162±1.52a***
III	5.9±0.089a*b***	384±1.2a**b***	134.8±1.01a*b***	80.8±1.35a*b***
IV	5.05±0.156a***b***	467±2.55a***b***	210.8±1.95a***b***	113.8±1.7a***b***
V	3.6±0.092a*b***	392.3±1.6a**b***	139.2±2.52a*b***	83.6±1.11a*b***

The values are expressed as mean ± SEM of 6 animals;

Comparisons were made between:

a. Group I vs Group II, III, IV,V is considered as “a”
b. Group II vs Group III, IV, V is considered as “b”

Statistical significance test for comparison was done by One way ANOVA followed by Dunnett’s test.

Symbols represent statistical significance p*<0.05, p**<0.01, p***<0.001.

Figure 1: Histopathological slides of different groups are shown below (Indomethacin induced gastric ulcer model)

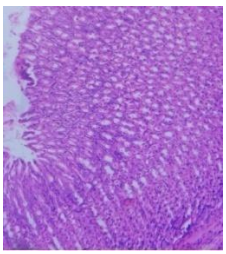
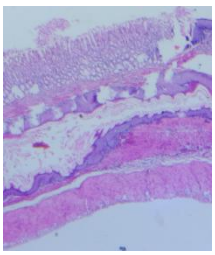
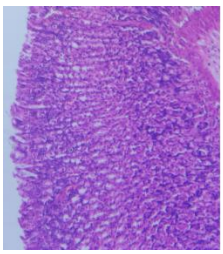
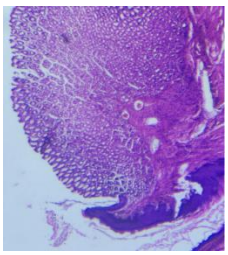
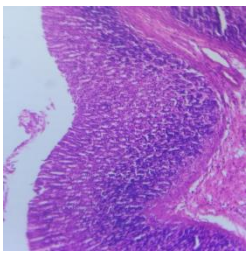
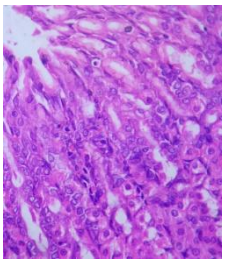
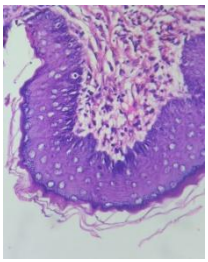
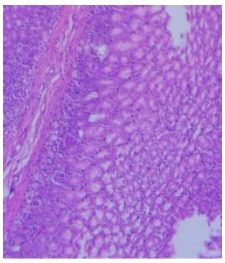
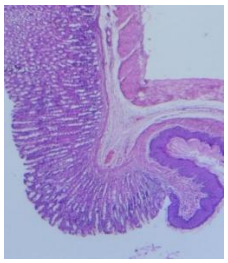
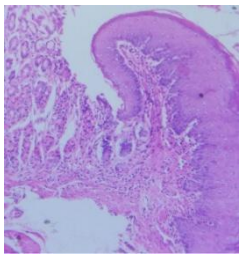
Group I	Group II	Group III	Group IV	Group V
				

Figure 2: Histopathological slides of different groups are shown below (Pylorus ligation induced gastric ulcer model)

Group I	Group II	Group III	Group IV	Group V
				

DICUSSION AND CONCLUSION

Peptic ulcer is the most common GIT disorder in the present day life of the industrialized and civilized world. It is a chronic inflammatory disease characterized by ulceration in the regions of upper gastrointestinal tract where parietal cells are found which secrete hydrochloric acid (HCL) and pepsin. Various factors can contribute to the formation of gastric ulcer such as the infection of stomach by *H.pylori*, use of NSAIDs, stress, smoking and consumption of alcohol.

The current medicinal treatment of peptic ulcer is generally based on the inhibition of gastric acid secretion by histamine H_2 antagonists, proton pump inhibitors, antacids and anticholinergics as well as on acid independent therapy provided by sucralfate and colloidal bismuth subcitrate [25]. However, the majority of these drugs produce adverse reactions, such as hypersensitivity, arrhythmia, dry mouth, impotence, gynecomastia and hematopoietic changes [26]. For examples, H_2 receptor antagonists (e.g. Cimetidine) may cause gynecomastia in men and galactorrhea in women [27], proton-pump inhibitors (e.g. omeprazole and lansoprazole) may cause nausea, abdominal pain, constipation and diarrhea, antacids may cause constipation, aluminium toxicity, hypocalcaemia and stones [28].

Indomethacin is a non-selective COX-1/COX-2 inhibitor, which leads to decrease in prostaglandin E_2 synthesis. PGE_2 and I_2 are predominantly synthesized by the gastric mucosa and are known to inhibit the secretion of gastric acid, stimulate the secretion in the gastric epithelial cells is also stimulated by the prostaglandin. It is well known that inhibition of prostaglandin synthesis, which is essential for mucosal integrity and regeneration, will trigger the mucosal lining damage [29]. Extensive damage to the gastric mucosa by indomethacin leads to increase neutrophils infiltration into the ulcerated gastric tissue. These neutrophils, which are a major source of inflammatory mediators, inhibit gastric ulcer healing by mediating lipid peroxidation through the release of highly cytotoxic and tissue damaging reactive oxygen species such as superoxide, hydrogen peroxide and myeloperoxidase derived oxidants [30].

The decrease level of SOD and CAT in indomethacin induced group may be due to the increase generation of reactive free radicals which can create an oxidative stress in the cell [31]. As SOD converts the reactive superoxide radical to H_2O_2 which CAT further convert it into water and oxygen, which if not scavenged by CAT, can cause LPO by the generation of hydroxyl radicals and tissue damage. In the present study, HEPG showed increase level of SOD and CAT which indicates antioxidant activity of HEPG.

It is observed that HEPG reduces ulcer index and increased formation of ulcer inhibition compared to indomethacin induced group which suggests the possible role of HEPG in strengthening of gastric mucosa. The increase in the total protein level of the gastric juice in a pylorus ligated groups indicates the damage to the gastric mucosa as a result if which plasma protein leaks into gastric juice. HEPG treated groups showed significant reduction in protein concentration, which indicates strengthening of the gastric mucosa, therefore it prevents the entry of plasma protein into gastric juice. It is also observed that liver enzymes such as SGOT and SGPT levels are increased which is due to the damage of gastric mucosa in the ulcer induced models, whereas it showed in SGOT and SGPT levels are decreased in HEPG treated groups indicates antiulcer activity.

The pylorus ligated rat model is used (Shay rat) for the production of acute ulcers in the fore stomach. The activation of the vago-vagal reflex by stimulation of pressure receptors in the antral gastric mucosa in pylorus ligation model is believed to increase gastric tonus and secretion. Digestive effect of the accumulated gastric juice is believed to be responsible for producing ulcers in the pylorus ligated rats. Pylorus ligated ulcers are thought to be caused due to increase in presence of acid and pepsin in the stomach. The essential criteria, which determine the status of mucosal defense barrier against the offensive assault of acid-pepsin is the quality and quantity of gastric mucus secretion. Increase in mucus secretion, bicarbonates and prostaglandin synthesis by the gastric mucosal cells can prevent gastric ulceration by several mechanisms including reduction of the stomach wall friction during peristalsis, alter mucosal blood flow and acting as an effective barrier to the back diffusion of hydrogen ions [32-34].

HEPG treated groups showed significant decrease in total acidity, free acidity and gastric volume which indicates both gastric secretory and gastric cytoprotectives effect. The increase in the total protein level of the gastric juice in a pylorus ligated groups indicates the damage in gastric mucosa as a result of which plasma protein leaks into gastric juice. HEPG treated groups showed significant reduction in protein concentration, which indicates strengthening of the gastric mucosa, therefore it prevents the entry of plasma protein into gastric juice [35]. It is also observed that liver enzymes such as SGOT and SGPT level are increased which indicates injury caused to stomach tissue, cell membrane

gets damaged these enzyme leak into blood stream causing damage to the gastric mucosa in the ulcer induced model whereas it showed in SGOT and SGPT levels are decreased in HEPG treated groups indicates antiulcer activity.

Omeprazole is a proton pump inhibitor which has been widely used as an acid inhibitor agent for the treatment of disorders related to gastric acid secretion for about 15years [36]. Omeprazole inhibits acid secretion by acting on the hydrogen-potassium exchanger (H^+, K^+ - ATPase) for the apical plasma membrane of the gastric mucsoa [37]. Omeprazole is highly selective for the proton pump and undergoes catalyzed conversion into active form within the acid forming space. The active inhibitors react with SH (thiol) group of the proton pump, resulting in inhibition of acid formation [38]. The HEPG treated groups showed antiulcer activity comparable to omeprazole.

In conclusion, the present study provided preliminary data for the first time that the leaf of *Pisonia grandis* R.Br possesses significant anti-ulcer activity in animal models. It has a gastric antisecretory and acid neutralizing effect that are comparable to standard drug omeprazole. The anti-ulcer activity is probably due to the presence of bioactive compounds like flavonoids and sterols. These compounds protect and strengthen the mucosal barrier which may be responsible for the antiulcer activity. The histopathological studies suggested that no haemorrhage, inflammation and congestion of the stomach were seen in HEPG treated group which indicate the healing of the ulcer in the stomach. Further studies are required to confirm the exact molecular level mechanism underlining the ulcer healing and protecting property of the extract and to identify the chemical constituents responsible for it.

ACKNOWLEDGEMENT

We are very thankful to the Department of Pharmacology, Principal and Management of C.L. Baid Metha College of Pharmacy for providing the facilities to conduct the research.

REFERENCE

1. Tripathi KD. Essentials of Medical Pharmacology, “Gastrointestinal drugs”, 2008; 6:627-638.
2. Harsh Mohan. “Text book of pathology”, 2010; 6:550-554.
3. WWW.disable-world.com/health/digestive/stomach-ulcers.php.
4. Snowden FM. “Emerging and reemerging disease: a historical perspective”. *Immunol. Rev.* 2008; 225(1):9-26.
5. GBD 2013 Mortality and Cause of Death, Collaborators, “Global, regional and national age-se specific all-cause and cause specific mortality for cause of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013”. Lancet. 17 December 2014.
6. Kaur DJ, Rana AC, Sharma NG, Herbal Drugs with Antiulcer Activity, Journal of Applies Pharmaceutical Science 02 (03); 2012: 160-165.

7. Schlesinger PK, Robinson B, Layden TJ. Epidemiology consideration in peptic ulcer disease. Journal of the Association for Academic Minority Physicians 1992;3(3):70-77.
8. Khare CP. Indian Medicinal Plants. Springer publications Pvt Ltd, New Delhi:2007; 502-503.
9. Krtikar KR and Basu BD Indian Medicinal Plants. International book distributors sellers & publishers, Dehradun, 1984;VoII, PP.1561-1564.
10. Asima Chatterjee and Satyesh Chandra Prakashi, The Treatise an Indian medicinal Plants, National institute of science communication, CSIR, New Delhi, 1984; 4:114.
11. Manogaran E. National symposium on emerging trends in Indian medicinal plants: 2002; 10-12.
12. The Wealth of India-An Encyclopedia of Indias, Raw material Resources. 1969;Edn 1, VIII.
13. Natarajan RK, Ragothaman P, Velachamy G, Balakrishna K. Chemical Examination of *Pisonia grandis* R.Br Bulletin of Medico-ethno botanical research, 1990; 11(4): 110-111.
14. Will McClatchy. The ethno Pharmacopoeia of Rotuma. Journal of Ethno pharmacology, 50(3): 147-156.
15. Pradheesh G, Suresh S and Alexramani V. Phytochemical and GC-MS analysis of methanolic extract of *Pisonia grandis* R.Br. International Journal of Chemical Sciences, 2015; 13(3): 1295-1304.
16. OECD Guidelines for the testing of chemicals. Test no.423:A.
17. Rainsford KD, Whitehouse MW. Biochemical gastroprotection from acute ulceration induced aspirin and related drugs. Biochemical pharmacology, 1980; 29: 1281-1289.
18. Shay H, Komarov SA, Fels SE, Meranze D, Grunstein M, Siplet. H. Gastroenterology, 1945; 5:43-61.
19. Dashputrel NL, Naikwade NS. Evaluation of Anti-ulcer activity of Methanolic extract of Abutilon indicum Linn leaves in experimental rats. International Journal of Pharmaceutical Sciences and Drug Research 2011;3(2):97-100.
20. Dashputrel NL, Naikwade NS. Evaluation of Anti-ulcer activity of Methanolic extract of Abutilon indicum Linn leaves in experimental rats. International Journal of Pharmaceutical Sciences and Drug Research 2011;3(2):97-100.
21. Poonam Kakkar, Ballabh Das, Viswanathan PN. A modified spectrophotometric assay of superoxide Dismutase. Indian Journal of Biochemistry and Biophysics 1984 April; 21: 130-132.
22. Sinha AK. Colorimetric assay of catalase. Analytical biochemistry. 1972 Jun 1;47(2):389-94.
23. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. Journal of biological chemistry 1951;193:265-75.

24. Reitman S, Frankel S. A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. American journal of clinical pathology 1957 Jul 1;28(1):56-63.
25. Bighetti AE, Antonio MA, Kohn LK, Rehder VL, Foglio MA, Possenti A, Vilela L, Carvalho JE. Antiulcerogenic activity of a crude hydroalcoholic extract and coumarin isolated from Mikania laevigata Schultz Bip. Phytomedicine. 2005 Jan 10;12(1-2):72-7.
26. Chan FK, Leung WK. Peptic-ulcer disease. The Lancet. 2002 Sep 21;360(9337):933-41.
27. Feldman M, Burton ME. Histamine2-receptor antagonists: standard therapy for acid-peptic diseases. New England Journal of Medicine. 1990 Dec 13;323(24):1672-80.
28. Reilly JP. Safety profile of the proton-pump inhibitors. Am. J. Health Syst. Pharm. 1999; 56(23): S11-S17.
29. Maria AOM, Franchi AM, Wendel GH, Gimeno M, Guzman JA, Giordano OS, Guerreiro E. Gastric cytoprotective activity of dehydroleucodine in rats. Role of prostaglandins. Biological and Pharmaceutical Bulletin. 1998; 21: 335–338.
30. Cheng CL, Koo MW. Effects of Centella asiatica on ethanol induced gastric mucosal lesions in rats. Life sciences. 2000 Oct 13;67(21):2647-53.
31. Sairam K, Rao CV, Babu MD, Kumar KV, Agarwal VK, Goel RK. Antiulcerogenic effect of methanolic extract of Emblica officinalis: an experimental study. J Ethanopharmacology 2002; 82:1-9.
32. Shay H, Komarov SA, Fels SE, Meranze D, Grunstein M, Siplet H. Gastroenterology 1945;5:43-61.
33. Baggio CH, Freitas CS, Rieck L, Marques MC. Gastroprotective effects of a crude extract of Baccharis illinita DC in rats. Pharmacological Research. 2003 Jan 1;47(1):93-8.
34. Rachchh MA, Jain SM. Gastroprotective effect of Benincasa hispida fruit extract. Indian journal of pharmacology. 2008 Nov;40(6):271-275.
35. Jain SM, Parmar NS, Santani DD. Gastric antiulcer activity of calcium channel blockers in rats. Indian Journal of Pharmacology 1994; 26:29-34.
36. Li X, Anderson TB, Ahlstom M, Weidolf L. Comparison of inhibitory effects of proton pump inhibiting drugs omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole on human cytochrome P450 activites. Drug metabolism and disposition. 2004 Aug 1;32(8):821-7.
37. Satoh HI, Inatomi NO, Nagaya HI, Inada IK, Nohara AK, Nakamura NO, Maki YO. Antisecretory and antiulcer activities of a novel proton pump inhibitor AG-1749 in dogs and rats. Journal of Pharmacology and Experimental Therapeutics. 1989 Feb 1;248(2):806-15.

38. Nagaya H, Inatomi N, Nohara A, Satoh H. Effects of the enantiomers of lansoprazole (AG-1749) on H^+ /K^+ - ATPase activity in canine gastric microsomes and acid formation in isolated canine parietal cells. Biochemical pharmacology. 1991 Oct 24;42(10):1875-1878.