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(Research Article)

Anti-ulcer Activity and HPTLC Analysis of *Mangifera indica* L. Leaves

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ABSTRACT

Mangifera indica (Family: Anacardiaceae) is being used in Ayurvedic and indigenous medical systems for the treatment of various diseases including gastric ulcer. Considering the above claims, the present work was undertaken to validate the antiulcer potential of the petroleum ether and ethanol extracts of leaves of M. indica against in vivo aspirin-induced gastric ulcer assay. The petroleum ether (250mg/kg) and ethanol extracts (250mg/kg) of leaves of M. indica plant significantly reduced the ulcer index in the range of P<0.001 and P<0.01 values. Histopathological findings also confirmed the antiulcer activity of M. indica leaves extracts in albino rats. In conclusion, the present study provide preliminary data on the antiulcer potential of M.indica leaves and support the traditional uses of the plant for the treatment of gastric ulcer.

Key Words: *Mangifera indica,* Anacardiaceae, Gastric ulcer, Aspirin, Albino rats, Ulcer index

INTRODUCTION

Peptic ulcer is the most common gastrointestinal disorder in clinical practice. Peptic ulcer is a conglomerate of heterogenous disorders, which manifests itself as a break in the lining of the gastrointestinal mucosa bathed by acid and / or pepsin. Various factors can contribute to the formation of peptic ulcer such as the infection of stomach by *Helicobacter pylori*[1], the frequent use of nonsteroidal anti-inflammatory drugs (NSAIDs)[2] and consumption of alcohol[3]. Duodenal ulcers[4] are more common in adult males. Gastic ulcers occur commonly at old age and in lower socio-economic class of individuals. Although a number of antiulcer drugs such as H_2 receptor antagonists, proton pump inhibitors[5] and cytoprotectants are available for ulceration, all these drugs have side effects and limitations. In recent years, focus on plant research has increased world wide and several studies had showed immense potential of medicinal plants[6]. Herbal medicine deals with plants and plant extracts in treating diseases.

Mangifera indica L. (Family: Anacardiaceae), an important medicinal plant in the Ayurvedic and indigenous medical systems for over 4000 years. Mangoes belong to genus *Mangifera* which consists of about 30 species of tropical fruiting trees in the flowering plant family Anacardiaceae. *M. indica* L. is a large evergreen tree that grows to a height of 10-45 m, dome shaped with dense foliage, typically heavy branched from a stout trunk. The leaves are spirally arranged on branches, linear-oblong, lanceolate-elliptical, pointed at both ends. The inflorescence occurs in panicles consisting of whitish-red or yellowish-green flowers. The fruit is a well known large drupe containing a thick yellow pulp, single seed encased in a hard, compressed fibrous endocarp. Native from tropical Asia and is now found naturalized in most tropical countries[7]. The natural C-glucoside xanthone mangiferin [2-c-β-$_D$-gluco-pyranosyl-1,3,6,7-tetrahydroxyxanthone; $C_{19}H_{18}O_{11}$; Mw, 422.35; melting point, anhydrous 271^oC[8]] has been reported in various parts of *M. indica*: leaves[9], fruits[10], stem bark[11], heartwood[12] and

roots[13]. This pharmacologically- active compound has been reported to have strong antioxidant[14], anti lipid peroxidation, radioprotective[15] , immunomodulation[16], anti-allergic[17], anti-inflammatory and anti-nociceptive[18], antitumour[19], antidiabetic[20], antidegenerative, wound healing, hypotensive, cardiotonic, lipolytic[21], antibone resorption[22], antiviral[23], antibacterial[24], antifungal[25], antiparasitic[26], monoamine oxidase-inhibiting activity[27], hepatoprotective[28] and gastroprotective[29] activities. Various parts of the plant are used as a dentifrice, antiseptic, astringent, diaphoretic, stomachic, vermifuge, tonic, laxative and diuretic and to treat diarrhea, dysentery, anaemia, asthma, bronchitis, cough, hypertension, insomnia, rheumatism, toothache, leucorrhea, haemorrhage and piles. All parts are used to treat abscesses, broken horn, rabid dog or jackal bite, tumour, snakebite, stings, datura poisoning, heat stroke, miscarriage, anthrax, blisters, wounds in the mouth, tympanitis, colic, diarrhea, glossitis, indigestion, bacillosis, bloody dysentery, liver disorders, excessive urination and tetanus. Traditionally the plant is reported to have antiulcer activity[30]. In the present study, an effort has been made to establish the scientific validity to the antiulcer property of the leaves extracts of *M. indica* in aspirin induced ulcer in male albino rats.

MATERIALS AND METHODS

Collection of Plant Material

The leaves of *M. indica* were collected from Maharashtra state, India. The plant material was authenticated by botanist and voucher specimen was deposited in department of Botany, Pune University. The plant material was air dried at room temperature and powdered.

Preparation of the Extract

50gm of powdered leaves were extracted in Soxhlet assembly[31,32,33] with petroleum ether. For ethanol extract, dried and coarsely powdered plant material was extracted separately with ethanol for 48 hours by cold maceration at room temperature and filtered. The extracts were concentrated with the help of rotavapor and the dried mass was kept in a dessicator[34,35,36]. The colour, consistency and percentage yield of extracts were noted (Table 1).

Qualitative Phytochemical Evaluation

Petroleum ether and ethanol extracts were screened for the presence of various secondary metabolites like tannins, alkaloids, glycosides, terpenoids, flavonoids, amino acids and proteins using standard methods[37,38,39].

HPTLC Profile

Chromatography was performed by streaking the extracts in the form of narrow bands of 4 mm and 6 mm apart on high performance thin layer chromatography (HPTLC) plates (Merck, Munchen, Germany) using Hamilton syringe and CAMAG LINOMAT 5 instrument. The sample loaded plates were kept in TLC twin trough developing chamber (after saturation with solvent vapour) with respective mobile phase and the plates were developed in the respective mobile phases (Petroleum ether- Ethyl acetate 9:1, Chloroform-Ethyl acetate 4:6) up to a distance of 90 mm. The developed plates were dried using hot air to evaporate the solvents from the plate. Densitometric scanning was carried out using CAMAG TLC scanner 4 and captured the images at UV 366 nm. Finally the plates were fixed in scanner stage and scanned at 254 nm. The Peak table, Peak display and Peak densitogram was identified[40].

Experimental Animals

Male albino Wistar rats weighing between 150-200 g were used in the present study. They were maintained under standard laboratory conditions in an animal house approved by the committee for the purpose of control and supervision on experiments on animals (CPCSEA) under 12 h light/dark cycle[41,42,43] and controlled temperature (24 ± 1^0C) and fed with commercial pellet diet and water *ad libitum*[44]. All animals were acclimatized to the laboratory environment for atleast one week before the commencement of experiment. The experimental protocol was approved by the Institutional Animal Ethical Committee, Genba Sopanrao Moze College of Pharmacy, Wagholi, Pune, Maharashtra, India.

Dose Selection and Mode of Administration

All the animals fed by oral gavages with the help of feeding tube. The extracts were dissolved in rice bran oil and administered orally at a dose of 250 mg/kg of the body weight. Then Non steroidal Anti-Inflammatory Drug Aspirin used as the ulcerogenic agent at the dose of 200 mg/kg of body weight[45]. Standard anti ulcer drug Omeprazole used at the dose of 20 mg/kg of body weight.

All the animals were put in four groups, each containing 5 rats. The groups were as follows:

Group-I: Control (Aspirin 200 mg/kg) + Rice bran oil
Group-II: Aspirin (200 mg/kg) + Omeprazole (20 mg/kg)
Group-III: Aspirin (200 mg/kg) + Petroleum ether leaves extract
Group-IV: Aspirin (200 mg/kg) + Ethanol leaves extract
After 8 days of dosing, animals were fasted for 24 hours and later aqueous suspension of Aspirin at a dose of 200 mg/kg[46,47] was given orally. The animals were then sacrificed by euthanasia four hours later of Aspirin administration. The stomachs were dissected and examined for ulcers. Gastric tissues were used for histopathological studies.

Calculation of Ulcer Score- Ulcer Index
The stomachs were opened along the greater curvature and washed slowly under running tap water. They were put on a glass slide and observed under 10X magnification for ulcers. The ulcers were scored . Mean ulcer score in each group was calculated and was designated as ulcer index and percentage was calculated[48,49,50] as shown in Table 2 using following formula:

% Protection = (C-T/C) X 100

Where C = Ulcer index in control group; T = Ulcer index in treated group

Statistical Analysis
All the values were tabulated and presented in the tables and were expressed as mean ± standard error mean (SEM) of five animals. Significant difference among the means were calculated at the level of P ^{a}<0.001, ^{b}<0.01, ^{c}<0.05 when compared with controls. The statistical significance was calculated using students 't' test.

RESULTS
The results of preliminary phytochemical screening of plant extracts showed presence of tannins, alkaloids, glycosides, steroids and triterpenoids, saponins , coumarins, phenolic compounds and flavonoids (Table 2). The presence of active phytoconstituents may be responsible for antiulcer activity.
HPTLC analysis of *Mangifera indica* extracts of sample solution was spotted as 8-10 mm on the precoated HPTLC silica gel 60F254 plates. The R_f value of the corresponding component as obtained by the software system attached with the instrument is shown in Table-3 and 4. The area corresponds to each peak for the corresponding spot or component in the solution.The HPTLC finger printing of the extracts marked the presence of phytoconstituents(Fig .1 & 2).
Aspirin induced ulceration was found to be (17.5±1.1) in control group(Table 5). The standard drug Omeprazole showed significant activity i.e., P<0.001 Vs control, as it reduced ulcer index to (1.6±0.8). Percentage ulcer protection was found to be 90.8%. PLE has shown significant reduction of ulcer index i.e., P<0.001 Vs control (5.0±1.08^{a}). Percentage ulcer protection for PLE was found to be 71.4%. ELE has shown significant reduction of ulcer index i.e., P<0.01 Vs control. (7.0±1.2^{b}). Percentage ulcer protection for ELE was found to be 60%.In the histopathological examination , stomachs of control rat showed erosion in the upper part of epithelium and RBCs were seen in the eroded portion (Fig .3), stomachs of rats treated with standard drug (omeprazole) showed small erosions with a minimal deviation from normal morphology (Fig .4). Stomachs of rats treated with PLE extract showed small superficial erosion with minimal deviation from normal morphology (Fig.5) and stomachs of rats treated with ELE extract showed superficial erosions with minimal deviations from normal morphology (Fig.6).

DISCUSSION
Peptic ulcer is associated with multipathogenic factors and could be due to disturbances in natural balances between the aggressive factors (acid, pepsin, *H.pylori* , bile salts) and defensive factors (mucous, bicarbonate, blood flow, epithelial cell restoration and prostaglandins)[51-53]. There are several risk factors that may contribute to formation of ulcer in human beings such as stress, chronic use of anti-inflammatory drugs, continuous alcohol ingestion, *H.pylori* infection, Zollinger Ellison syndrome, etc. Generally various non-specific methods are used to restore these imbalances including regular food intake, adequate rest and avoidance of ulcerogenic agents (eg. Tobacco, alcohol and coffee) which are aimed to attenuate and possibly block the gastric acid secretion or to enhance the mucosal defense mechanisms[54]. In addition , there are also drugs, such as pump inhibitors, histamine ($H_{2)}$-antagonists, anticholinergics and antacids, used in the treatment of ulcer[55]. Due to the reported side effects of available antiulcer drugs, focus have been shifted towards medicinal plants which have been known to be amongst the most attractive sources of new drugs giving promising results in treatment of various diseases including gastric and duodenal ulcers[56,57]. It was reported that Mangiferin , a naturally occurring

glucosylxanthone of *Mangifera indica* affords gastroprotection against gastric injury most possibly through the antisecretory and antioxidant mechanisms of action which is consistent in the present study of *Mangifera indica* extracts which were able to prevent formation of ulcers. It has also been reported that the presence of phytoconstituents tannins[58], terpenoids [59], sterols and flavonoids may be responsible for antiulcer activity[60-62]which is in agreement with our findings.

CONCLUSION

The present study indicated that the leaves of *M. indica* possesses anti-ulcer activity in animal models. The anti-ulcer activity is probably due to the presence of bioactive compounds like flavonoids, saponin and tannins. Further studies are required to confirm the exact mechanism underlying the ulcer healing and protecting property of the extract and to identify the chemical constituents responsible for it.

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Table-1 : Percentage yield of petroleum ether and ethanol leaves extract of *Mangifera indica*

S.No	Extract	Colour	Odour	Consistency	% Yield
1.	PLE	Dark green	Characteristic	Viscous	20.6
2.	ELE	Dark green	Characteristic	Viscous	21.3

Table-2: Phytochemical screening of petroleum ether and ethanol leaves extracts of *Mangifera indica*

S.No	Phytoconstituents	Petroleum ether leaves extract	Ethanol leaves extract
1	Tannins	-	+
2	Alkaloids	-	+
3	Cardiac glycosides	+	+
4	Steroids	+	+
5	Carbohydrates	-	+
6	Saponins	+	+
7	Flavonoids	-	+
8	Anthraquinones	-	+
9	Proteins	-	-
10	Terpenoids	+	+
11	Coumarins	-	+
12	Phenolic compounds	-	+

(+) sign indicates presence of phytoconstituent in the extract
(-) sign indicated absence of phytoconstituent in the extract

Table-3: HPTLC profile of *Mangifera indica* petroleum ether extract

Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %	Assigned substance
1	0.06	0.1	0.09	373.5	71.27	0.17	29.8	13584.5	80.32	Unknown*
2	0.17	29.8	0.18	33.7	6.43	0.19	22.6	512.4	3.03	Unknown*
3	0.32	26.1	0.33	28.4	5.42	0.35	18.5	830.9	4.91	Unknown*
4	0.54	1.8	0.56	12.0	2.30	0.57	4.5	168.1	0.99	Unknown*
5	0.59	6.6	0.61	10.5	2.00	0.64	0.2	346.8	2.05	Unknown*
6	0.84	0.1	0.87	34.8	6.63	0.90	1.5	1038.1	6.14	Unknown*
7	0.95	7.3	0.96	14.5	2.76	0.97	11.9	218.6	1.29	Unknown*
8	0.97	11.9	0.97	16.7	3.19	0.99	0.3	213.7	1.26	Unknown*

Rf : Retention Factor

Table-4 : HPTLC profile of *Mangifera indica* ethanol extract

Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %	Assigned substance
1	0.11	22.2	0.11	22.8	3.83	0.12	2.1	166.9	0.55	Substance 5
2	0.18	0.0	0.22	25.0	4.21	0.25	1.0	505.7	1.65	Substance 4
3	0.61	14.9	0.75	492.4	82.87	0.85	19.8	28797.7	94.6	Substance 1
4	0.96	6.4	1.00	54.0	9.09	1.01	14.6	1112.8	3.64	Substance 2

Table-5 : Effects of *Mangifera indica* leaves extracts in Aspirin induced ulcers in rats

Group	Ulcer index	% Ulcer healing
Control	17.5+1.1	-
Omeprazole	1.6+0.8[a]	90.8%
PLE	5.0+1.08[a]	71.4%
ELE	7.0+1.2[b]	60%

Values are mean ± SEM of five animals in each group P[a]<0.001 Vs Control, [b]<0.01 Vs Control, [c]<0.05 Vs Control, using students t test.

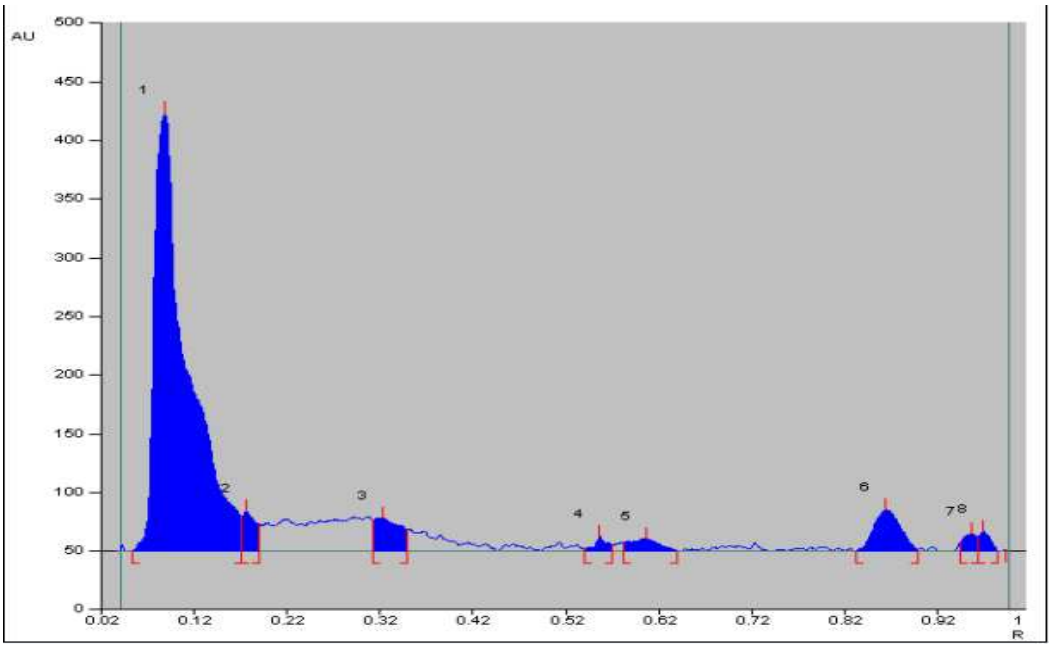

Fig.1 : Chromatogram of petroleum ether extract.

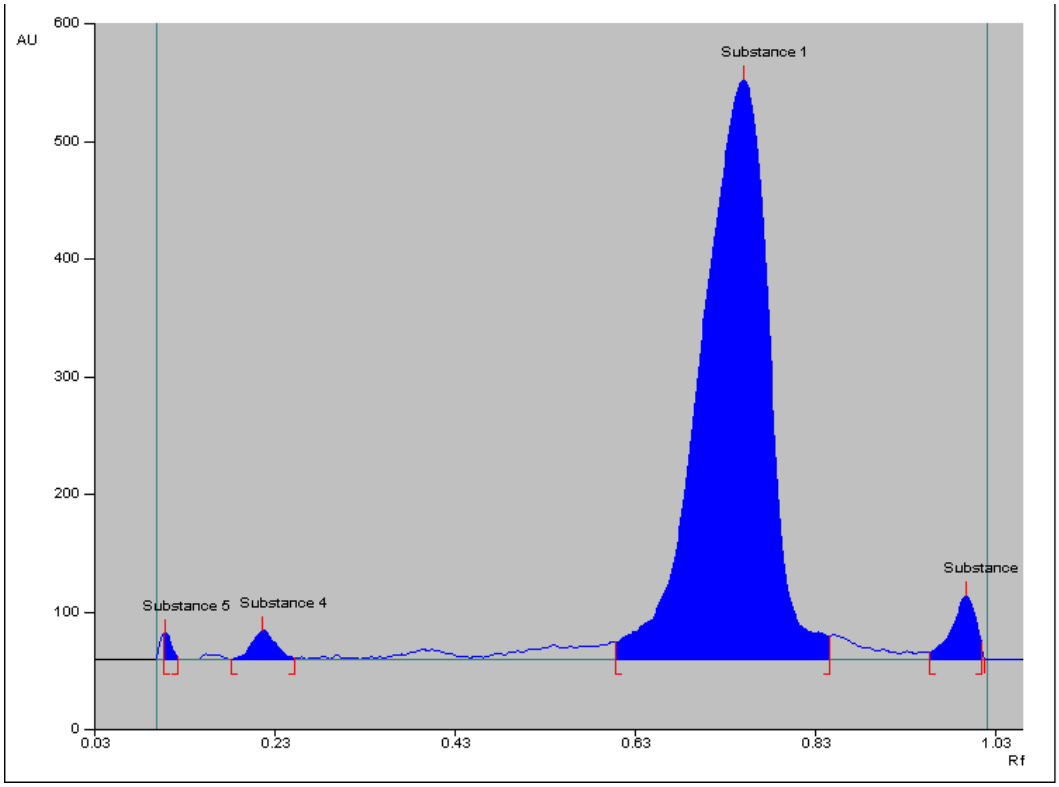

Fig .2: Chromatogram of ethanol extract

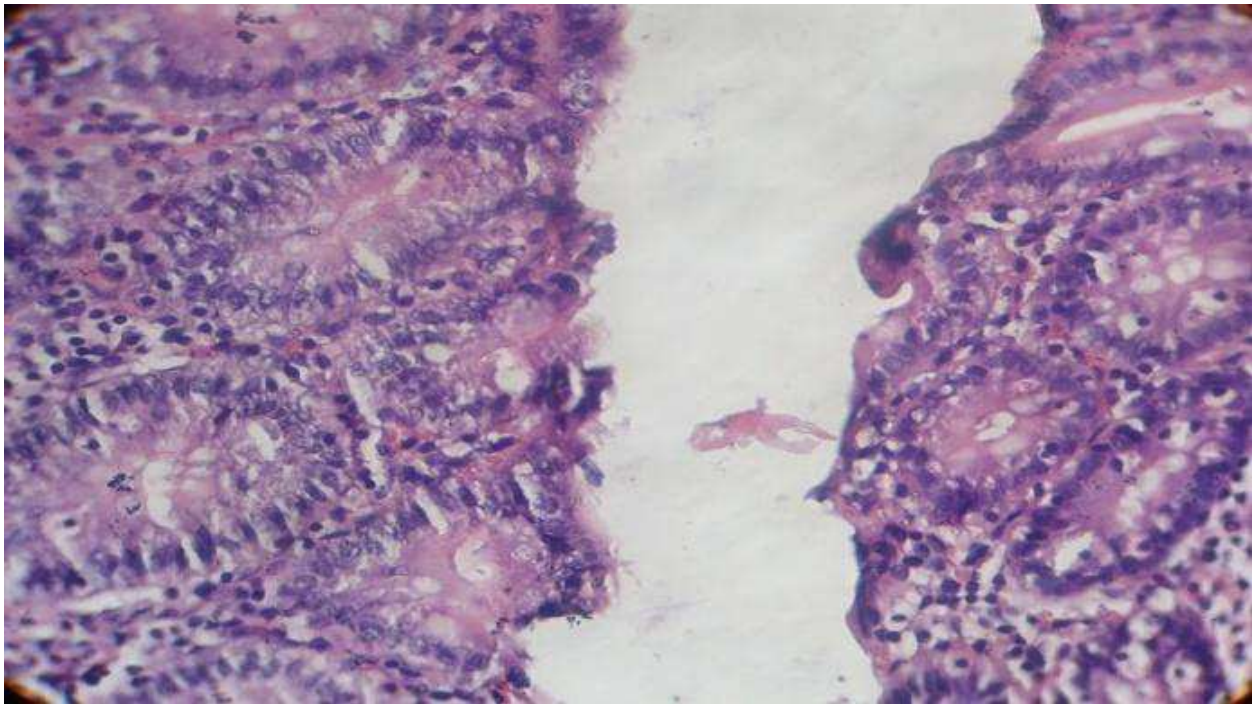

Fig .3. Stomach of control rat showing erosion in the upper part of epithelium with RBCs in eroded portion

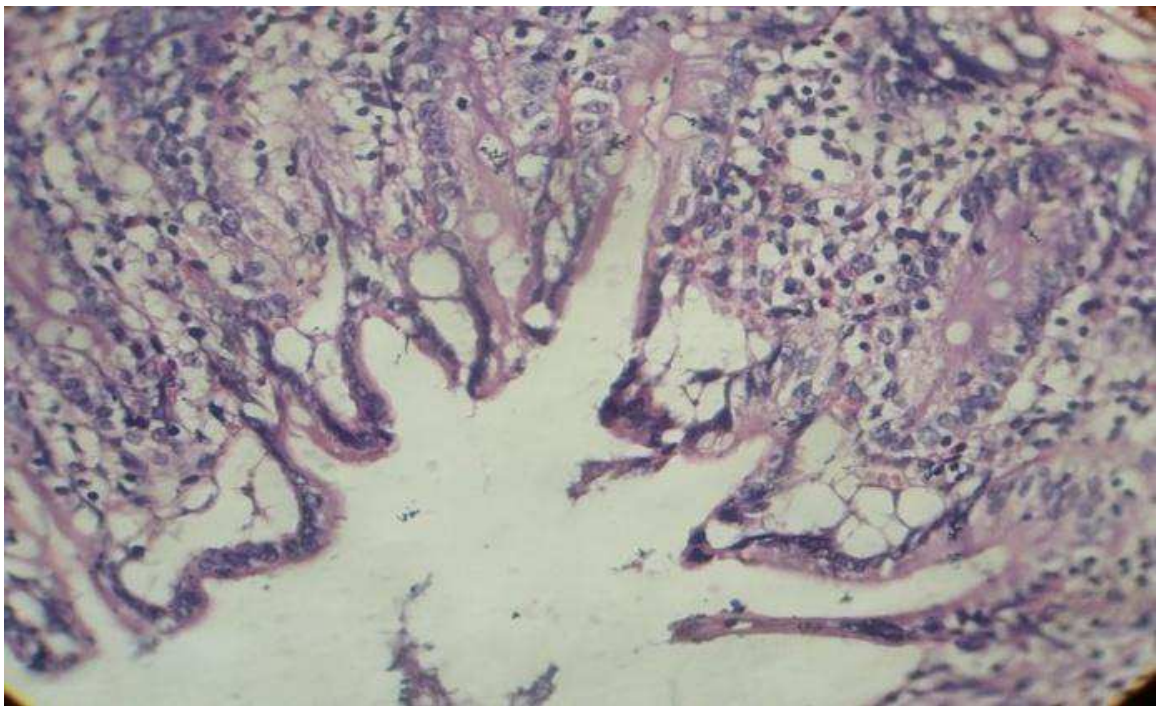

Fig .4 : Stomach of rat treated with omeprazole showing small erosions with minimum deviation from normal morphology

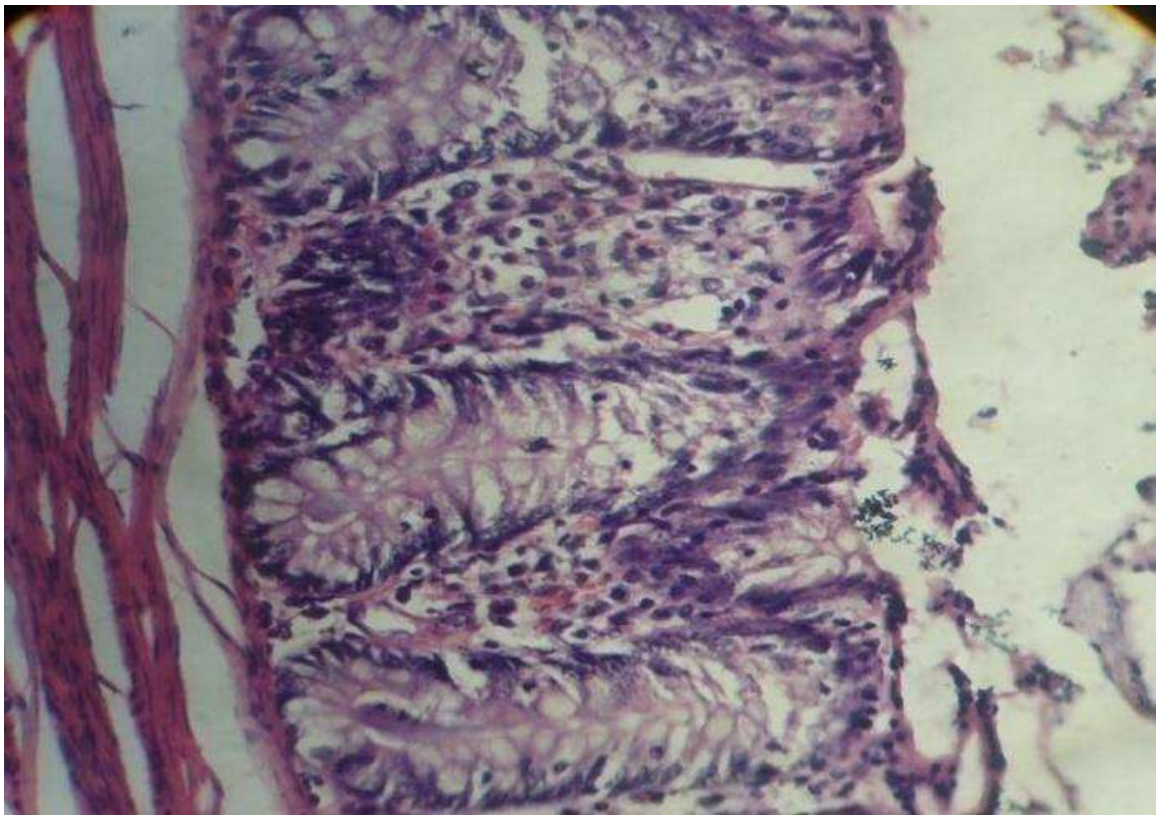

Fig .5 : Stomach of PLE treated rats showing small superficial erosion with minimum deviation from normal morphology

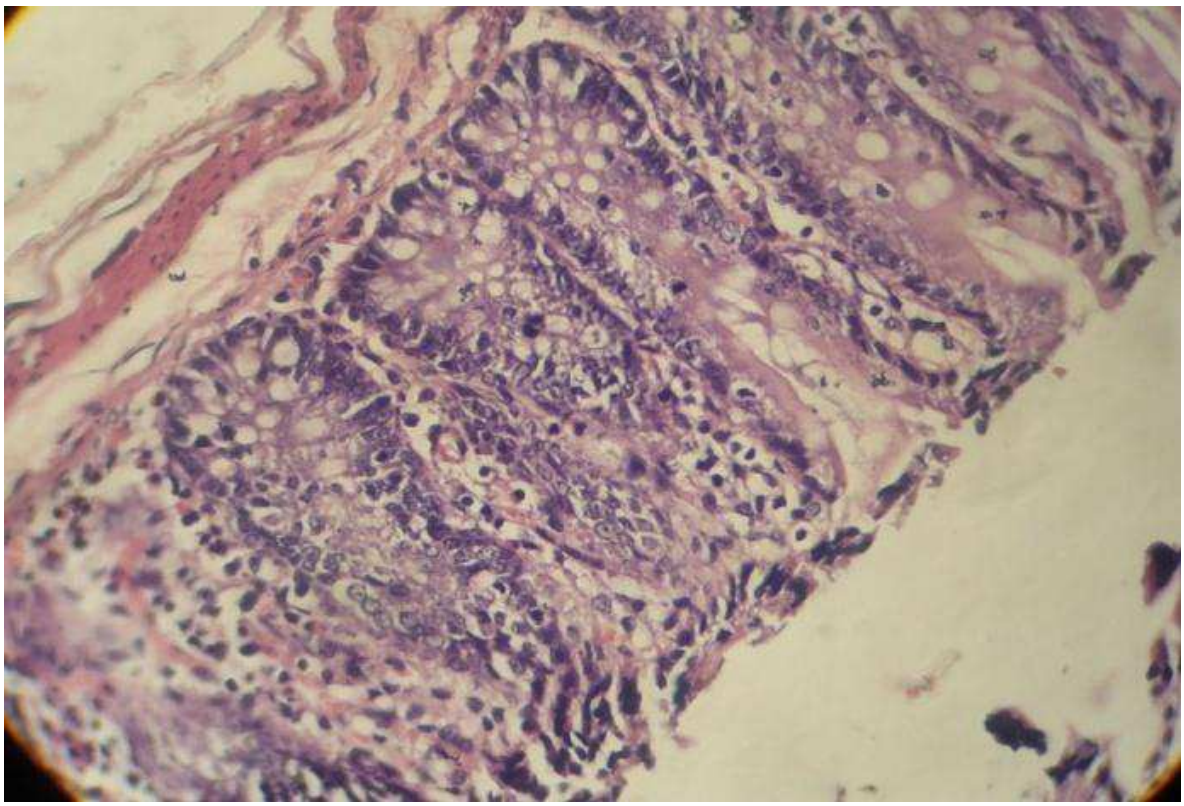

Fig .6 : Stomach of rat treated with ELE showing superficial erosions with minimum deviations from normal morphology

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