"EVALUATION AND COMPARISON OF MARKETED AYURVEDIC FORMULATIONS IN PEPTIC ULCER''.

[1] Sushant S. Dhandore , [2]Dr. Padma L. Ladda

Student, Associate Professor

Pharmacology

Appasaheb Birnale College of Pharmacy, Sangli India.

ABSTRACT:

The objective of this study was to evaluate the anti ulcer activity of Dadimavaleha liquid and Bhunimbadi kadha in wistar rats, against Pylorus ligation and Ethanol induced model. A daily does of Dadimavaleha liquid (1.31ml/kg P.O) and Bhunimbadi Kadha (2.09 ml/kg P.O) body weight of rats. The Ayurvedic formulations administered orally for 10 days. Omeprazole (20mg/kg P.O) was used as a Standard drug. After administration of both formulations and standard drug in biochemical parameters, Ulcer index, Free acidity, Total acidity, p^H, Gastric volume, Pepsin activity, mucus content was evaluated. All the biochemical parameters showed significant decrease in Dadimavaleha liquid and Bhunimbadi kadha was compare with the control treated group. Omeprazole (20 mg/kg, oral) also produced a significant decrease when compared with the control group. In both formulations are phytochemical analysis revealed the presence of tannins, saponins, flavonoids, carbohydrates and proteins etc. Histopathological studies were conducted to support the antiulcer study.

Keywords- Peptic ulcer, Pylorus ligation, Dadimavaleha , Bhunimbadi kadha.

1. INTRODUCTION:

Peptic ulcer is the most common gastrointestinary disorder in clinical practice.[1]Peptic ulcer is a gastro intestinal disorder due to an imbalance between the aggressive factors like acid, pepsin, Helicobacter pylori and defensive factors like bicarbonate secretion, prostaglandins, gastric mucus, innate resistance of the mucosal cell factors.[2]Peptic ulcer occurs in that part of the gastrointestinal tract which is exposed to gastric acid and pepsin, i.e. the stomach and duodenum. The etiology of peptic ulcer is not clearly known.[3]

Peptic ulcer disease refers to painful sores or ulcers in the lining of the stomach or first part of the small intestine, called the duodenum. Peptic ulcer disease (PUD), also known as a peptic ulcer or stomach ulcer, is a break in the lining of the stomach, first part of the small intestine, or

occasionally the lower esophagus. An ulcer in the stomach is known as a gastric ulcer while that in the first part of the intestines is known as a duodenal ulcer.[4] Approximately 500,000 persons develop peptic ulcer disease in the United States each year.[1]In 70 percent of patients it occurs between the ages of 25 and 64 years The annual direct and indirect health care costs of the disease are estimated at about $10 billion.[5] The most common symptoms are waking at night with upper abdominal pain that improves with eating. Other symptoms include belching, vomiting, weight loss, or poor appetite. Complications may include bleeding, perforation and blockage of the stomach. Bleeding occurs in as many as 15% of people.[4]

Management of peptic ulcer disease continues to evolve because of the emergence of various novel therapeutic agents, advancements in several operative techniques and pharmacological oriented strategies. With the development of various therapies, as well as recognition and understanding of H. pylori infection along with mechanism, the medical management of ulcer has been largely successful. Several drugs are extensively used for the reduction of acidity in peptic ulcer.[6]

The goals of treating peptic ulcer disease are to relieve pain, heal the ulcer and prevent ulcer recurrence. Currently there is no cost effective treatment that meets all these goals. Hence, efforts are to find a suitable treatment from natural product sources as better alternatives for the treatment of peptic ulcer.[7]

2. Methodology:

List of Marketed formulations

Sr. No	Formulations	Company
01.	Dadimavaleha	Sandu Brothers
02.	Bhunimbadi kadha	Baidyanath

A. Procurement of Formulations :

The Formulations were purchased from Fadake ayurvedic medical, Sangli.

B. Calculation of Doses :

The dose calculations were done by using Paget and Barnes, 1964.

C. Experimental Protocol:

Housing of the animals:

All the experiments were carried out using Wistar Albino Rat having weight 180- 200 gm. Rat were kept in polypropylene cages with stainless steel lid. Animals were kept under standard

housing conditions with free access to standard pellets ad libitum. The animals were acclimatized for 7 days prior to experiment. Form B protocol were prepared and submitted to Institutional Animal Ethics committee (IAEC). Approval for animal use was obtained from IAEC prior to experimental study. The experimental protocol ***(IAEC/ABCP/5/2018-19)*** was approved by the IAEC. The procedures involving laboratory animals were in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

D. Experimental Design:

Wistar rats (180 – 200 gm) were divided into following groups –

Table no: 1 Model 1:Pylorus Ligation model.

Sr.No	Group	Treatment	Dose
1	I	control (vehicle)	10ml/kg (P.O)
2	II	Standard (Omeprazole)	20mg/kg (P.O)
3	III	Formulation A (Dadimavaleha liquid)	1.31ml/kg (P.O)
4	IV	Formulation B (Bhunimbadi Kadha)	2.09ml/kg (P.O)

Table no : 2 Model 2: Ethanol induced model.

Sr.No	Group	Treatment	Dose
1	I	control (vehicle)	10ml/kg (P.O)
2	II	Standard (Omeprazole)	20mg/kg (P.O)
3	III	Formulation A (Dadimavaleha liquid)	1.31ml/kg (P.O)
4	IV	Formulation B (Bhunimbadi Kadha)	2.09ml/kg (P.O)

- **Pyloric ligation induced ulcer in rat:**[8,9,10.]

A simple and reliable method for production of gastric ulcer in rat based on ligature of the pylorus has been published by Shay et al. (1945).

Animal was fasted for 24 hr prior to pylorus ligation. The pylorus ligation was carried out 30 min after drug administration. Under light ether anaesthesia abdomen was opened by small incision then stomach removed carefully and pylorus is ligated and the abdominal wall closed by interrupted sutures. Animal was sacrificed at the end of 19 hr after operation. Stomach was dissected out and contents are drained into tube and centrifuged at 1000 rpm for 10min. and

supernatant subjected to analysis for gastric volume, PH& total acidity in gastric juice. The stomach was then cut and open along the greater curvature and the inner surface was examined for ulceration accourding to score number.

- **Ethanol induced ulcer in rat [8]**

  Intra gastric application of absolute ethanol is a reproducible method and considered as risk factor to produce gastric lesions in experimental animal. This model is useful for studying the efficacy of potential drugs or testing agents that have cytoprotective or antioxidant activity. Animal were starved for 24hr. having access to drinking water and ad. libitum. The animals was placed in cages with raised bottom of wide wire mesh in order to avoid cannibalism and caprophagy. Administered test drug orally to the rats 1hr prior to administration of ethanol. 1hr after ethanol administration animals were sacrificed.

For above two models following parameters were measured for evaluation of antiulcer activity.

1. Determination of Total acidity and Free acidity in gastric juice
2. Determination of Ulcer index
3. Determination of Gastric volume & PH
4. Determination of Mucous in gastric content
5. Determination of Pepsin Activity.
6. Histopathological study of stomach.

3. Statistical Analysis

The values are expressed as Mean ± SEM for six Rats in each group. The Statistical Analysis was performed using one way ANOVA followed by Dunnett's test. (Graph pad prism version 8.1).

4. **RESULTS:**

a) PYLORUS LIGATION MODEL.

In present investigation Pylorus ligation was performed by Shay et.al (1945). In the Pylorus ligation model, Gastric ulcer was produced due to over activity of gastric juice. In this method ulcer index, pH, gastric volume, free acidity, total acidity, mucus, pepsin activity were measured to evaluate anti-ulcer activity of marketed formulations.

Table no: 3 Effect of Dadimavaleha and Bhunimbadi kadha on Ulcer Index, Gastric Volume and pH in Pylorus ligation model.

Sr. No.	Treatment Groups	Dose (P.O)	Ulcer Index (Mean ± SEM)	Gastric volume (ml/100gm) & % Decrease in gastric volume	pH and % increase in p^H
1.	Control (DW)	10 ml/kg	16.17±0.333	5.217±0.104	3.45±0.011
2.	Standard (Omeprazole)	20 mg/kg	4±0.182**** (75.26%)	3.15± 0.042**** (39.62%)	6.23±0.0047**** (44.62%)
3.	Dadimavaleha (Formulation A)	1.31 ml/kg	10.42±0.151**** (35.55%)	4.183± 0.197**** (19.81%)	4.63±0.0421**** (25.48%)
4.	Bhunimbadi Kadha (Formulation B)	2.09 ml/kg	8.35±0.183**** (48.36%)	3.867± 0.066**** (25.87%)	5.44±0.1077**** (36.58%)

Significance evaluated by one-way analysis of variance (ANOVA) followed by Dunnett's test control versus all. *<0.05 is considered as criterion for significance. Values are mean ±SEM, (n=6) *Level of significance P<0.05; ****Level of significance P< 0.0001 compared with control.

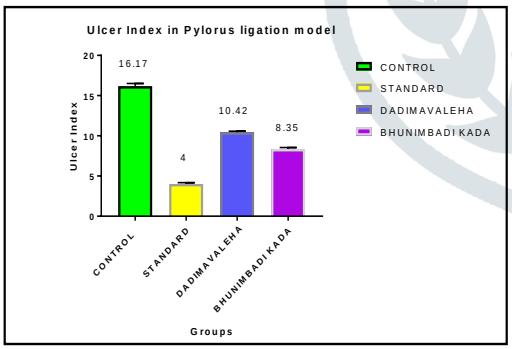


Fig.1: Ulcer Index in Pylorus ligation model

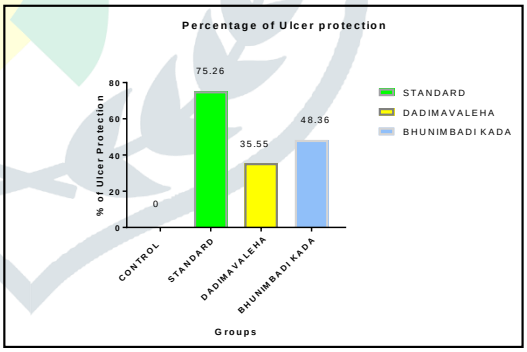


Fig.2: % of Ulcer protection in Pylorus ligation model

Ulcer Index - Pylorus ligation in ulcerated control group had produced ulcer in all animals and the mean ulcer index was (16.17±0.333) indicating the ulcerogenic effect. i.e. Both Formulations of Dadimavaleha & Bhunimbadi kadha showed significant reduction in ulcer index(10.42±0.151) & (8.35±0.183) respectively, compared to control. The results also showed that increase in ulcer protection for Dadimavaleha & Bhunimbadi kadha in model as (35.55%) and (48.36%) respectively, compared to control. while standard Omerpazole also showed significant reduction in ulcer index

(4±0.182), and increase in percentage of ulcer protection (75.26%). These results indicate that Bhunimbadi kadha was demonstrated greater protective ability compared to Dadimavaleha liquid.

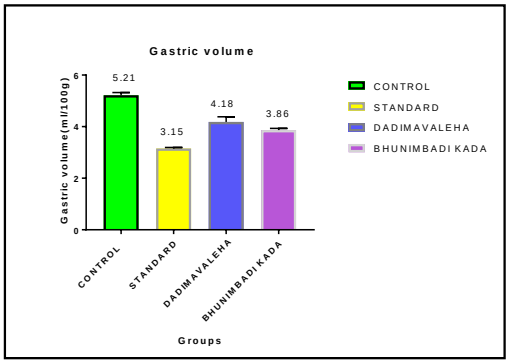


fig.3: Gastric volume in Pylorus ligation model

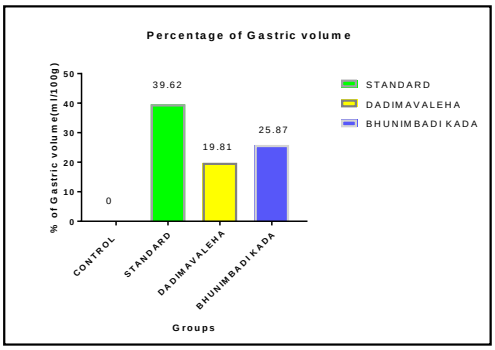


Fig.4: % of Gastric Volume in Pylorus ligation model.

Gastric volume - Pylorus ligation in ulcerated control group had produced ulcer by increasing the gastric volume (5.217±0.104) indicating the ulcerogenic effect. Both Formulations Dadimavaleha (4.183±0.197)(19.81%) &Bhunimbadi kadha (3.867±0.066)(25.87%) respectively, showed statistically significant decrease in gastric volume, as compared to the control group and Bhunimbadi kadha was found more effective than Dadimavaleha liquid.

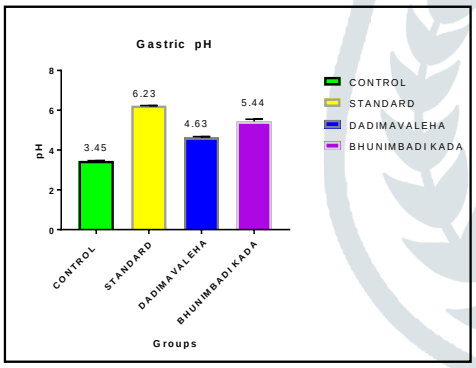


Fig. 5: pH in Pylorus ligation model

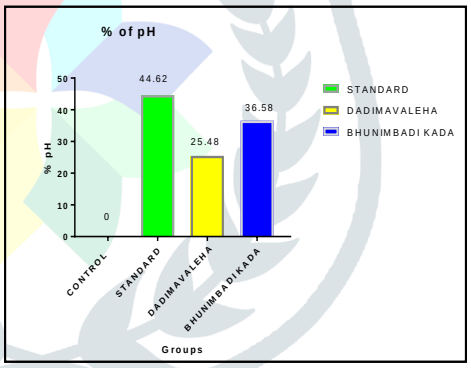


Fig.6: % of pH in Pylorus ligation model.

pH- In ulcerated control group the mean pH was (3.45±0.011) which indicating the ulcerogenic effect. Both Formulations Dadimavaleha & Bhunimbadi kadha showed significant increase in pH, (4.63±0.0421),(5.44±0.1077) respectively as compared to the control group. The percentage increase in pH for Dadimavaleha (25.48%) and Bhunimbadi kadha (36.58%) respectively compared with control which indicates that Bhunimbadi kadha was more effective than Dadimavaleha liquid.

Table No. 4 : Effect of Dadimavaleha & Bhunimbadi kadha on Total and Free Acidity Gastric Mucus, Pepsin activity in Pylorus ligation model.

Sr. No.	Treatment Groups	Dose (P.O)	Total Acidity (mEq/L/100g) and % ↓ in Total acidity	Free Acidity (mEq/L/100gm) and %↓ in Free Acidity	Gastric juice mucus(mg/ml) % ↑ in Gastric mucus.	Pepsin activity (µ/ml) %↓ in Pepsin
1.	Control (DW)	10 ml/kg	73±0.816	59±0.856	44.81± 0.316****	77.34± 0.273****
2.	Standard (Omeprazole)	20 ml/kg	52±0.365**** (28.76%)	34±0.365**** (42.37%)	109.9± 0.393**** (59.22%)	50.54± 0.357**** (34.65%)
3.	Dadimavaleha (Formulation A)	1.31 ml/kg	61.62±1.30**** (15.57%)	46.67±1.33**** (20.89%)	93± 1.506**** (52.95%)	58.65± 1.44**** (24.16%)
4.	Bhunimbadi Kadha (Formulation B)	2.09 ml/kg	59±0.966**** (15.58%)	41.5±0.763**** (29.66%)	100.2± 0.600**** (55.27%)	55.83± 1.014**** (27.81%)

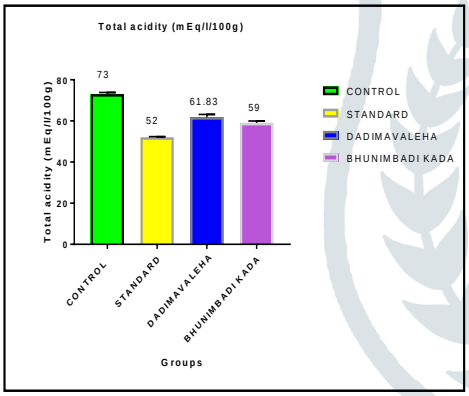


Fig.7: Total Acidity in Pylorus ligation model.

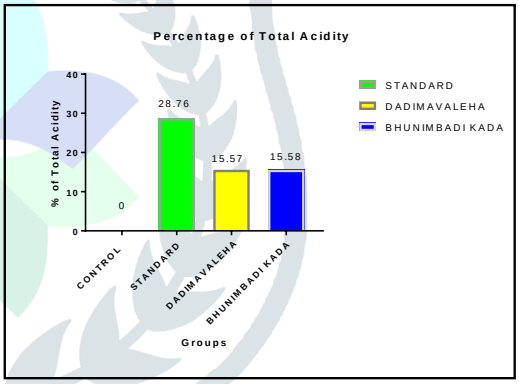


Fig.8: % of Total acidity in Pylorus ligation model.

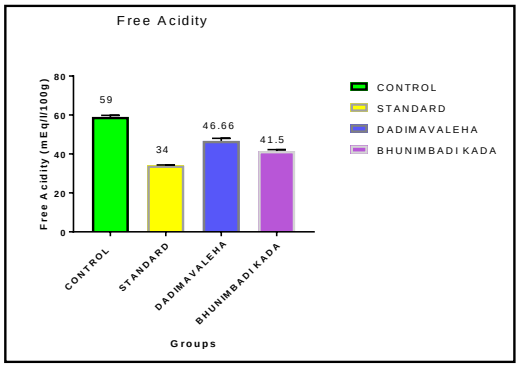


Fig. 9 Free Acidity in Pylorus ligation model.

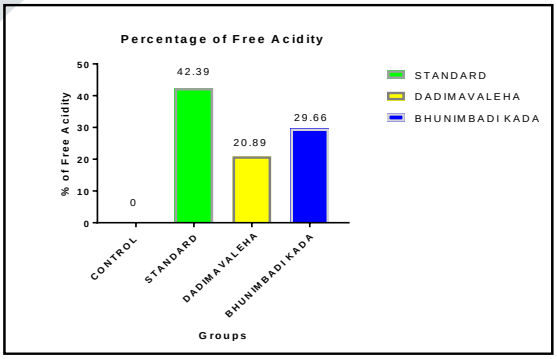


Fig.10: % of Free acidity in Pylorus ligation model.

Total Acidity and Free acidity- The mean of total acidity (73±0.816) and free acidity (59±0.856) was found in control group. The mean and percentage of total acidity (61.62±1.30) (15.57%) & free acidity

(46.67±1.33) (20.89%) were observed in Dadimavaleha and in Bhunimbadikadha (59±0.966)(15.58%) and (41.5±0.763)(29.66%) respectively. The percentage decrease in total acidity and free acidity for both formulations showed significant antiulcer activity.

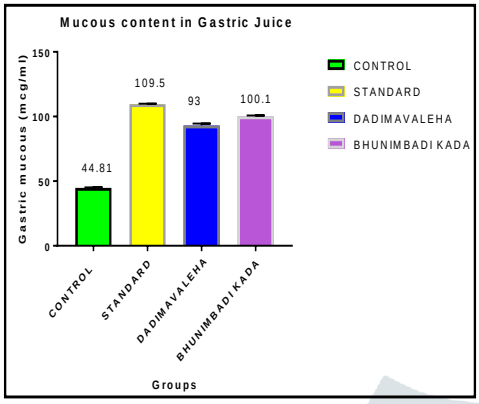


Fig.11: Mucus content in Gastric juice Pylorus ligation model.

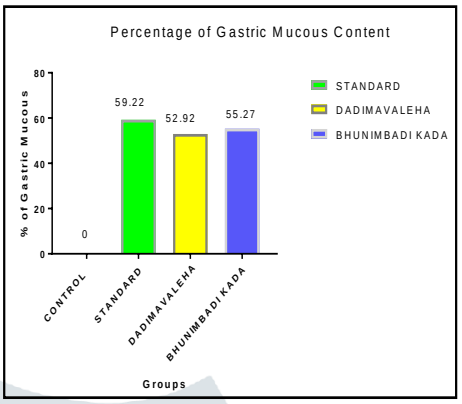


Fig.**12: % of Gastric mucus content in Pylorus ligation model.**

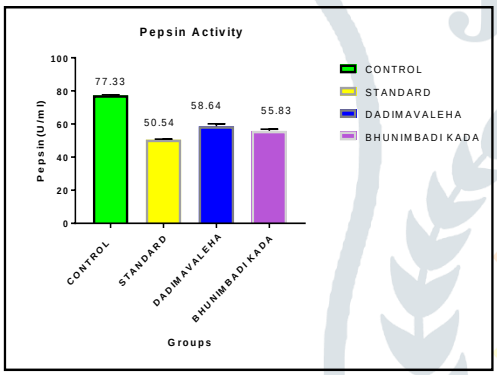


Fig. 13 Pepsin activity in Pylorus ligation model.

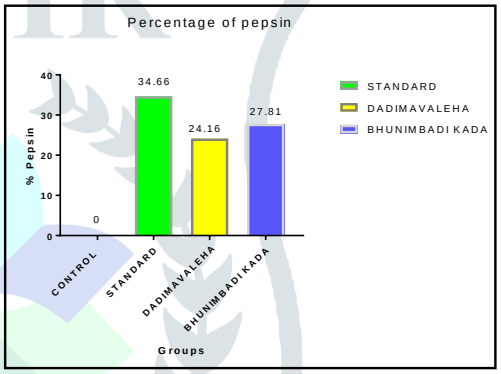
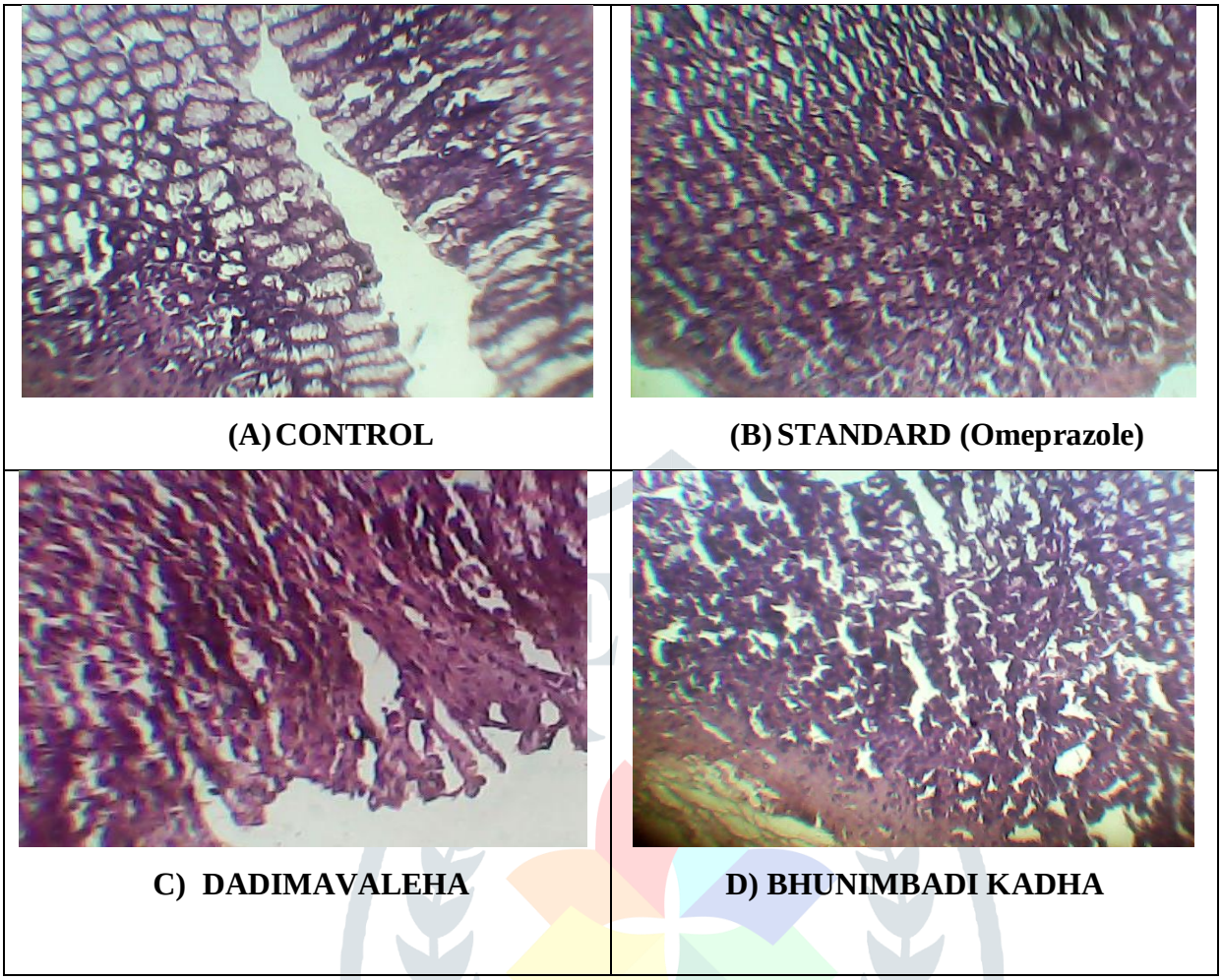


Fig.14: % of Pepsin in Pylorus ligation model.

Mucus –In ulcerated control group, the mean mucus content was found (44.81±0.316) indicating the ulcer. Observed increase in mean mucus content in Formulations Dadimavaleha (93±1.506) &Bhunimbadi kadha (100.2±0.600) compared to the control group. We also found percentage increase in mucus for Dadimavaleha (52.95 %) and Bhunimbadi kadha (55.27%) respectively. Thus more protective effect was observed in Bhunimbadi kadha formulation.

Pepsin activity- In ulcerated control group, we found mean pepsin activity was (77.34±0.273). Both Formulations Dadimavaleha & Bhunimbadi kadha showed significant decrease in pepsin activity (58.65±1.44) (55.83±1.014), respectively as compared to the control group .We also observed the percentage decrease for Dadimavaleha (24.16%) and Bhunimbadi kadha (27.81%). Hence, result indicates that Bhunimbadi kadha was effective than Dadimavaleha in decreasing pepsin activity.

Histopathology of Stomach in pylorus ligation induced ulcer model.



(A) CONTROL

(B) STANDARD (Omeprazole)

C) DADIMAVALEHA

D) BHUNIMBADI KADHA

Fig. no.15:Histopathological photographs of marketed Ayurvedic formulations.

Histopathology of normal stomach as well as treated groups was shown in above figures. The Control group rat shows damage in gastric mucosa with hemorrhages, edema & inflammatory cells infiltration in the submucosal layer. Dadimavaleha, Bhunimbadikadha& Omeprazole treated groups showed less mucosal damage to epithelium as compared to control. Formulations treated groups showed significant regeneration of mucosal layer and significantly prevented the hemorrhages, edema and severity of damage to mucosal epithelium as compared to control.

b) Ethanol Induced ulcer model.

Table no:5 Effect of Dadimavaleha & Bhunimbadi kadha on Ulcer Index, Gastric Volume and pH Ethanol induced model.

Sr. No.	Treatment Groups	Dose (P.O)	Ulcer Index (Mean± SEM) and %Ulcer Protection	Gastric volume (ml/100gm) and % Decrease in Gastric volume	pH and % Increase in pH
1.	Control (DW)	10 ml/kg	15±0.2582	6.067±0.055	3.572±0.025
2.	Standard (Omeprazole)	20 gm/kg	4.33±0.1667**** (71.13%)	3.417±0.047**** (43.72%)	6.147±0.0071**** (41.85%)
3.	Dadimavaleha (Formulation A)	1.31 ml/kg	10.2±0.1528**** (32.00%)	2.55±0.125**** (57.92%)	4.117±0.1138**** (12.87%)
4.	BhunimbadiKadha (Formulation B)	2.09 ml/kg	8.35±0.1232**** (44.33%)	2.017±0.083**** (66.83%)	4.233±0.0714**** (15.60%)

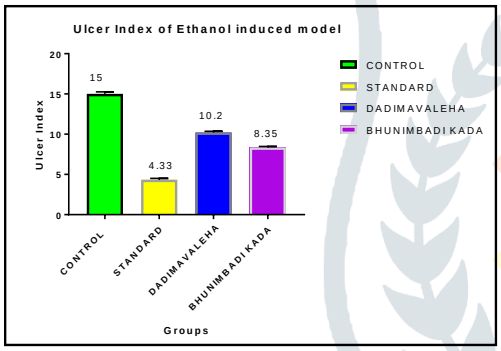


Fig.15 Ulcer Index in Ethanol induced model.

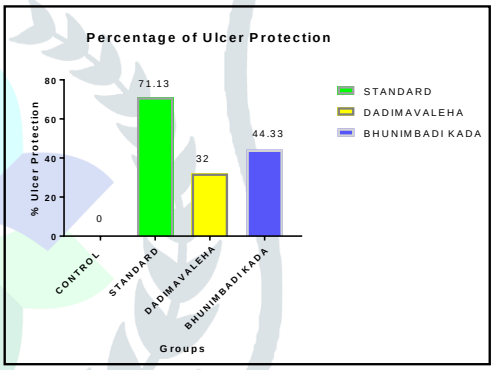


Fig.16: % of Ulcer protection in Ethanol induced model

Ulcer Index- Ethanol induced model in ulcerated control group had produced ulcer in all animals and the mean ulcer index was (15±0.2582) indicating the ulcerogenic effect. i.e. Both Formulations of Dadimavaleha & Bhunimbadi kadha showed significant reduction in ulcer index(10.2±0.1528) & (8.35±0.1232) respectively, compared to control. The results also showed that increase in ulcer protection for Dadimavaleha & Bhunimbadi kadha as (32%) and (44.33%) respectively, compared to control. while standard Omerpazole also showed significant reduction in ulcer index (4.33±0.1667), and increase in percentage of ulcer protection (71.13%). Thus Bhunimbadi kadha was demonstrated greater protective ability compared to Dadimavaleha liquid.

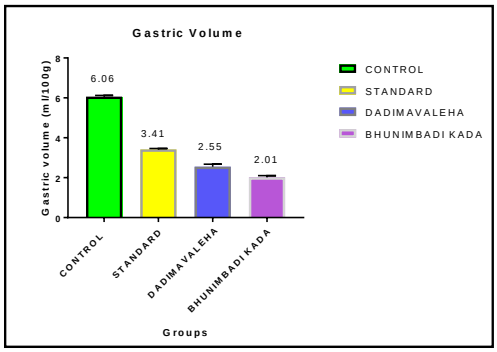


Fig.17: Volume of Gastric juice in Ethanol induced model.

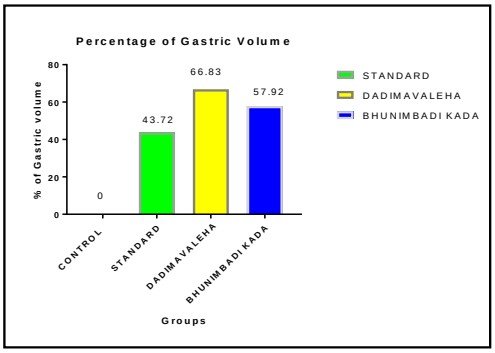


Fig.18: % of Gastric Volume in Ethanol induced model.

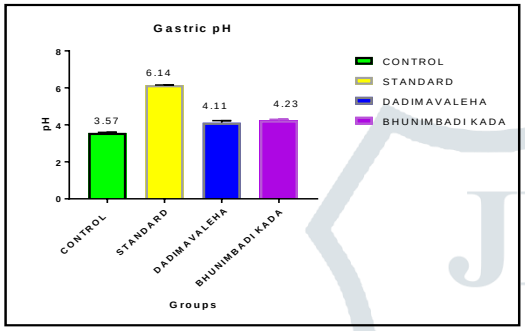


Fig.19. p^H of Ethanol induced model.

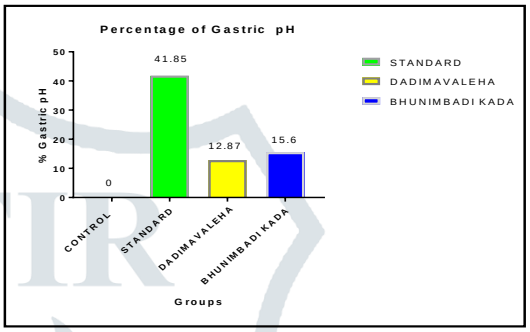


Fig.20:% of p^H in Ethanol induced model.

Gastric volume - Ethanol induced in control group had produced ulcer by increasing the gastric volume (6.067±0.055) indicating the ulcerogenic effect. Both Formulations Dadimavaleha (2.55±0.125)(57.92%) & Bhunimbadi kadha (2.017±0.083)(66.83%) showed statistically significant decrease in gastric volume, as compared to the control group. Bhunimbadi kadha was found effective than Dadimavaleha liquid.

pH - In ulcerated control group the mean pH was(3.572±0.025) indicating the ulcerogenic effect. Both Formulations Dadimavaleha & Bhunimbadi kadha showed significant increase in pH, (4.117±0.1138),(4.233±0.714) respectively, as compared to the control group. The percentage increase in pH for Dadimavaleha(12.87%) and Bhunimbadi kadha (15.60%) respectively, which indicates that Bhunimbadi kadha was more effective than Dadimavaleha liquid.

Table no. 6: Effect of Dadimavaleha and Bhunimbadi kadha on Total and Free Acidity, Gastric Mucus and Pepsin activity in Ethanol induced model.

Sr. No.	Treatment Groups	Dose (P.O)	Total Acidity (mEq/l/100g) and % ↓ in Total acidity	Free Acidity (mEq/l/100) and % ↓ in Free Acidity	Gastric mucus (mg/ml) % ↑in Gastric mucus	Pepsin activity (µ/ml) % ↓ in Pepsin
1.	Control (DW)	10 (ml/kg)	69.5±0.22	49.5±0.42	52.22±0.316	79.82±0.275
2.	Standard (Omeprazole)	20 (mg/kg)	49.17±0.47**** (29.25%)	36.5±0.42**** (26.26%)	141.9±0.257***** (63.19%)	48.71±0.244***** (38.97%)
3.	Dadimavaleha (Formulation A)	1.31 (ml/kg)	65.33±1.40**** (6.04%)	45.17±1.35***** (8.74%)	116.8±1.558***** (55.29%)	60.67±0.666***** (23.99%)
4.	Bhunimbadi Kadha (Formulation B)	2.09 (ml/kg)	59±0.577**** (17.64%)	40.5±0.56**** (18.18%)	122.3±1.43**** (57.30%)	51.57±0.292***** (35.93%)

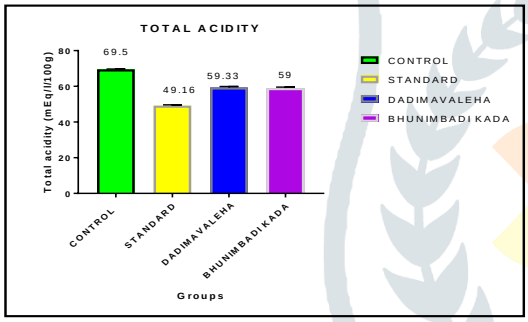


Fig.21: Total Acidity in Ethanol induced model.

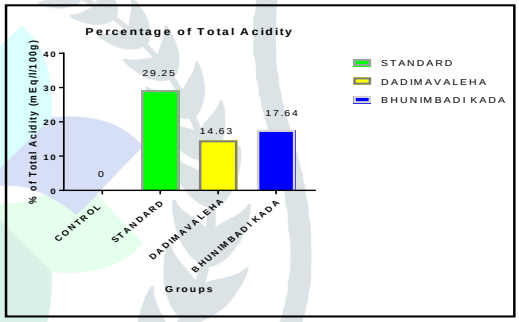


Fig.22: % of Total acidity in Ethanol induced model.

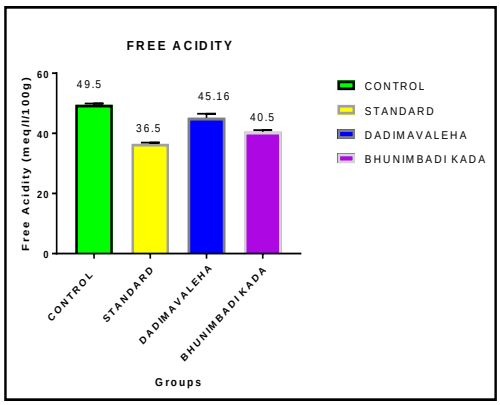


Fig.23: Free Acidity in Ethanol induced model.

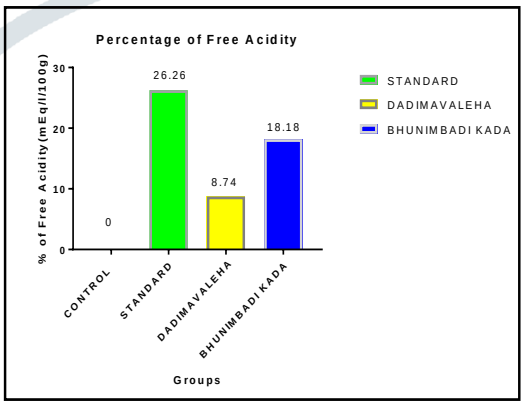


Fig.24: % of Free acidity in Ethanol induced model.

Total Acidity and Free acidity- The mean of total acidity (69.5±0.22) and free acidity (49.5±0.42) was found in control group. The total acidity (65.33±1.40) (6.04%), & free acidity (45.17±1.33)

(8.74%) observed in Dadimavaleha while in Bhunimbadi kadha (59±0.577) (17.64%) and (40.5±0.56)(18.18%) respectively. The percentage decrease in total acidity and free acidity for both formulations showed significant antiulcer activity.

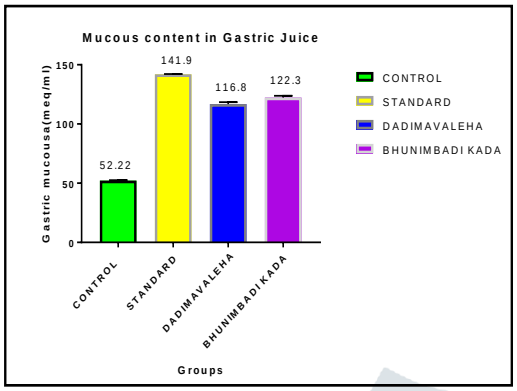


Fig.25: Mucus content in Gastric Juice Ethanol induced model.

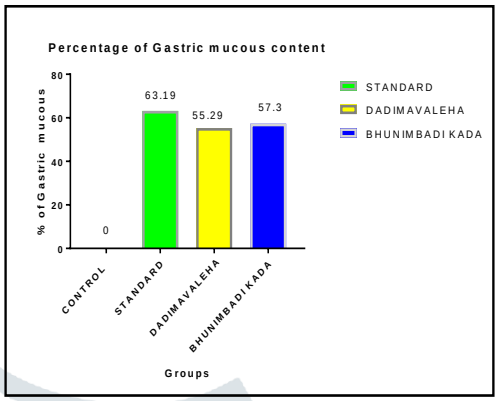
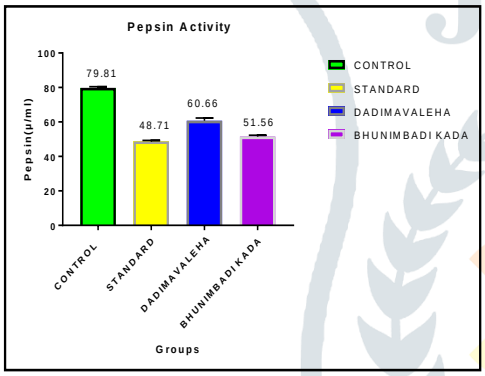


Fig.26: % of Gastric mucus content in Ethanol induced model.



Pepsin activity in Ethanol induced model.

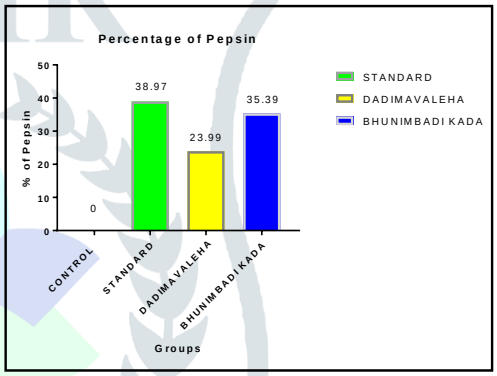


Fig.27: Fig.28: % of Pepsin in Ethanol induced model.

Mucus - In control group, the mean mucus content was found (52.22±0.316) indicating the ulcer. Obsreved increase in mean mucus content in both Formulations Dadimavaleha (116.8±1.558) &Bhunimbadi kadha (122.3±1.43)compared to the control group .We also found percentage increase in mucus for Dadimavaleha (55.29 %) and Bhunimbadi kadha (57.30%). Thus more protective effect was observed in Bhunimbadi kadha formulation.

Pepsin activity - In ulcerated control group, we found mean pepsin activity was (79.82±0.273). Both Formulations Dadimavaleha (60.67±0.666) &Bhunimbadi kadha (51.57±0.292) showed significant decrease in pepsin activity, as compared to the control group. We also observed the percentage decreases for Dadimavaleha (23.99%) and Bhunimbadi kadha (35.93%). Hence, result indicates that Bhunimbadi kadha was effective than Dadimavaleha by decreasing pepsin activity.

Histopathology of Stomach in Ethanol induced ulcer model.

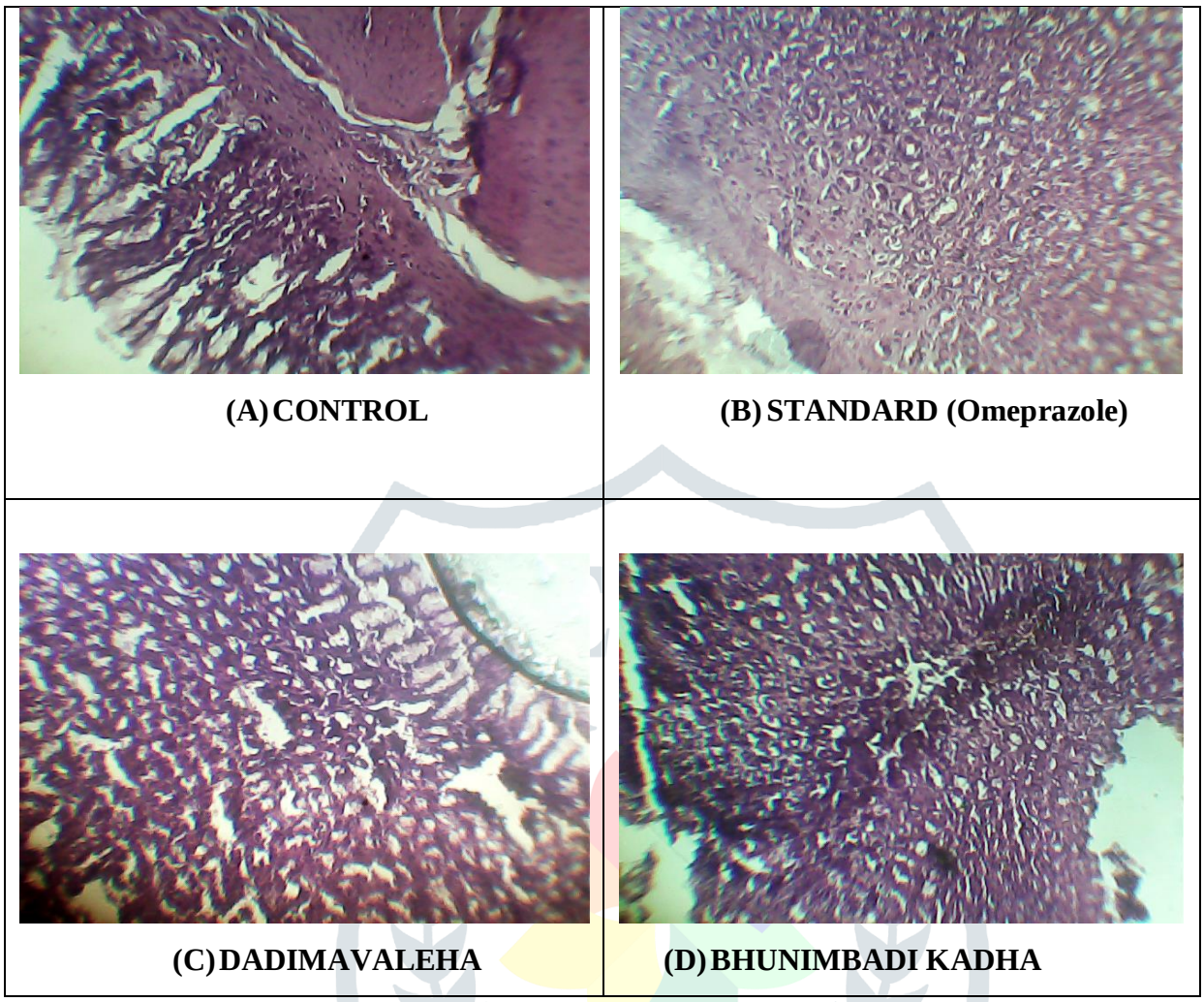


Fig. no. 6.2.15: Histopathological Photogrphs of marketed Ayurvedic formulations.

Microscopicalchange of ethanol induced model were shown in fig. no 30. Histopathological changes in control showed the degeneration , hemorrhage ,edematous appearance of the gastric tissue, where as Dadimavaleha, Bhunimbadi kadha& Omeprazole treated groups showed regeneration of mucosal layer and substantial prevention of the formation of hemorrhage and edema. Hence both formulations showed anti-ulcer activity.

5. DISCUSSION-

An ulcer is defined as disruption of mucosal integrity of the stomach and/or duodenum leading to a local defect or excavation due to active inflammation.[11] Although H. pylori is present in the GI tract of 50% of adult population, only 10-20 % of latter develop DU.[12] Peptic ulcer is very common in the United state with 4 million individuals (new cases and recurrences) affected per year.[1]Approximately 500,000 persons develop peptic ulcer disease in the United States each year. In 70 percent of patients, it occurs between the ages of 25 and 64 years[13]. Early observations showed that peptic ulcer was more common among the population of South India than North India.[7]

The goals of treating peptic ulcer disease are to relieve pain, heal the ulcer and prevent ulcer recurrence.[6]Currently there is no cost effective treatment that meets all these goals. hence, efforts are taken to find a suitable treatment from natural product sources as better alternatives for the treatment of peptic ulcer. However, there is no scientific evidence on antiulcer effect of these two marketed ayurvedic formulations Dadimavaleha and Bhunimbadi kadha against traditional claims so far. Hence, the present study was conducted to evaluate and compare the anti-ulcer activity of Ayurvedic formulations.

Formulation A (Dadimavaleha) contains :-

Punicagranatum, Myristicafragrans, Cinnamomumtamala, Cinnamomumverum, Syzygium - aromaticum, Zingiberofficinale, Ficusreligiosa.

Formulation B (Bhunimbadikadha) contains :-

Tinosporacordifolia, Coriandrumsativum, Annonasquamosa, Symplocosracemosa, Holarrhena - antidysenterica, Mellifera, Woodfordiafruticosa, Sidacordifolialinn, Aeglemarmelos, Tinospora - cordifolia, Holarrhenapubescens, Cyperusscariosus.

The phytochemicals reported in these plants of formulations are alkaloids, Glycosides, Steroids, Flavonoids, Phenolic compounds, Triterpinoids, Saponins, Amino acids, Vitamin E, Proteins, etc.[14] In the present study, Pylorus ligation and ethanol induced models were used to evaluate and compare antiulcer activity of Marketed Ayurvedic Formulations Dadimavaleha (Formulation A) and Bhunimbadi kadha (Formulation B). All the models have been reported to be reproducible and reliable in evaluating the antiulcer activity.[14] Two Ayurvedic formulations viz. Formulation A (Dadimavaleha) in a dose of 1.31 ml/kg and Formulation B (Bhunimbadi kadha) in a dose of 2.09 ml/kg used for evaluation and comparison of antiulcer activity.

PYLORUS LIGATION MODEL-

Pylorus ligation induced ulcers are due to auto digestion at the gastric mucosa and breakdown of the gastric mucosal barrier. In case of pyloric ligation, ulcer formation is mainly due to increase in gastric hydrochloric acid secretion and or the stasis at the gastric juice and stress.[15] In the present study, in pylorus ligation induced gastric ulcer model, Dadimavaleha and Bhunimbadikadha treated group has shown significant reduction in gastric volume, total acidity, Free acidity & ulcer index along with significant increase in gastric pH thus indicating anti-secretory mechanism involved in the formulations for their anti-ulcerogenic activity. These finding are in line with those observed by previous investigators. Chandan N.G.& et.al.[14]

In pylorus ligation model, the ulcer index found in control group is and the present study showed decrease in ulcer index and percentage of ulcer protection compared with control in Dadimavaleha (↓35.55%) &Bhunimbadikadha(↓48.36%) & Omeprazole (↓75.26%) . Antiulcer activity in Pylorus-ligation model is evident from its significant increase in the gastric pH in drug treated animals. The percentage increase pH is found in Dadimavaleha (↑25.48%) &Bhunimbadikadha (↑36.58%) while Omeprazole (↑44.62%) as compared with control group. This finding signifies that formulations possesses a gastroprotective effect.

Dadimavaleha & Bhunimbadi kadha treated animals significantly inhibited the formation of Pylorus-ligated ulcers in the stomach and also decreased acid concentration, therefore it is suggested that Dadimavaleha & Bhunimbadi kadha can suppress gastric damage induced by aggressive factors. Non-steroidal anti-Inflammatory drugs like Aspirin cause gastric mucosal damage by decreasing prostaglandin levels through inhibition of prostaglandin synthesis.[16] In the present research, the significant reduction in basal gastric secretion and complete inhibition of ulcers by Dadimavaleha & Bhunimbadi kadha after pylorus ligation which suggested that its cytoprotective mechanism of action on the gastric mucus. Thus it may be responsible for the direct reduction of gastric secretion through one or more possible mechanism. Gastric acid secretion is regulated by many factors including anxiety effect in the central nervous system. Vagal activity, irritant receptors and histaminergic and gastrinergic neurotransmissions including the proton pump.[17] The results clearly demonstrated that Dadimavaleha & Bhunimbadi kadha inhibited the aggressive factors and gastric acid secretions. The antiulcerogenic effect of these may be related to its antisecretory action because acid is major factor in the development of peptic ulcer . The results obtained for the present studies indicates that Dadimavaleha & Bhunimbadi kadha has anticholinergic and vagolytic activity. However, certain antiulcer drug increase the amount of gastric mucus secretion in the gastric mucosa. The mucus consists of mucin-type glycoproteins, which can be detected by amounts of alcian blue binding.[17]

The possible mechanism of gastric mucousal protection by Dadimavaleha & Bhunimbadi kadha may be partly due to the reinforcement of resistance of the mucosal barrier by a protective coating. The antiulcer effect was also supported by a decrease in aggressive factor like pepsin and an increase in defensive factor like mucin. The decrease in the pepsin content of gastric juice by Dadimavaleha & Bhunimbadi kadha, this also suggests an increase in the gastric mucus, acting as coating and protective barrier on the gastric mucosa. A significant increase in the mucus content and decreases total pepsin content in rats was found similar as reported by Srivastava, et. al.[18]

ETHANOL INDUCED ULCER MODEL-

Ethanol induced gastric ulcers have been widely used for the evaluation of gastro protective activity. Ethanol is metabolized in the body and releases superoxide anion and hydroperoxyl free radicals. It was reported to stimulate the formation of leukotrienes C4 (LTC4), mast cell secretory products and reactive oxygen species resulting in the damage of rat gastric mucosa. It has been found that oxygen derived free radicals are implicated in the mechanism of acute and chronic ulceration in the gastric mucosa and scavenging these free radicals can play an appreciable role in healing these ulcer.[14] In our study, Dadimavaleha & Bhunimbadi kadha significantly decreased the gastric volume, free and total acidity, ulcer index, gastric lesion and ulcer severity. Ulcer index, which is attributed to different parameters like number of ulcers, ulcer severity was decreased by Dadimavaleha & Bhunimbadi kadha showed a significant decrease in the gastric volume when compared with the control group, this enumerates its activity as an anti-secretory agent.

Ulcer index was used for the analysis as ulcer formation is directly related to factors such as gastric volume, free and total acidity, mucus content.[41]The present study showed decrease in ulcer index and percentage of ulcer protection in Dadimavaleha(↓32.00%) & Bhunimbadi kadha(↓44.33%) &standard Omeprazole (↓71.13%). Dadimavaleha & Bhunimbadi kadha produces a decrease in the ulcer index compared to control group. There was increase in pH as well as percentage increase in Dadimavaleha as (↑12.87%) &Bhunimbadikadha (↑15.60%) while in Omerpazole (↑41.85%) as compared with control group.We found percentage increase in mucus content, in Dadimavaleha&Bhunimbadikadhais (↑55.29%) and (↑57.30%) respectively while in Omeprazole(↑63.19%). The mucus content was statistically significantly increase in treated group, when compared with control group. The Pepsin activity as well as percentage decrease in treated group as when compared with control group.

Histopathological results demonstrated that Formulations treated groups showed significant regeneration of mucosal layer and significantly prevented the hemorrhages, edema and severity of damage to mucosal epithelium as compared to control which suggest that both formulations have cytoprotective effect. Literature review of revealed that the different constituents like flavonoids, tannins, terpenes, steroids, Saponins, alkaloids and glycosides have been reported that they are responsible for anti ulcer activity.[13] These constituents which are also present in the composition of our marketed formulations, that may be responsible for their antiulcer activity. Flavonoids are though to increase mucosal Prostaglandin content, decrease histamine secretion from mast cell by inhibition of histidine decarboxylase, inhibition H.pylori growth, act as free radical scavengers and inhibit H^+ /K^+ – AT pase. Sapponins may activate mucous members protective factors & tannins render the outermost layer of mucosa less permeable, for instance, to chemical irritation.[16]

The biochemical study and histopathological finding observed in two models which are employed in this study reveals that both Formulation showed antiulcer effect that justify the traditional usage of this to treat peptic ulcer. However B (Bhunimbadi kadha) is highly effective as compared to Formulation A (Dadimavaleha). The following reasons might be responsible for significant antiulcer activity of Formulation B (Bhunimbadi kadha).

- The dose of formulation B (Bhunimbadi kadha) (2.09 ml/kg) is more than the formulation A (Dadimavaleha) (1.31ml/kg).
- The formulation B (Bhunimbadi kadha) is contains more number of plant extracts in its composition as compared to formulation A (Dadimavaleha) .

Formulations Bhunimbadikadha exhibited more significant anti-ulcer activity compared to Dadimavaleha liquid against both pylorus ligation and ethanol induced gastric ulcer in rats. The various phytoconstituents present in the Formulations might contribute to the anti ulcer activity.

6. CONCLUSION-

The results of the present study conclude that marketed formulation Dadimavaleha liquid and Bhunimbadi kadha demonstrate a significant antiulcer activity against Pylorus ligation and Ethanol induced model in rats by both reduction in gastric acid secretion and gastric cytoprotection. The presence of various phytoconstituents in the formulations might be responsible for gastric ulcer protection. Therefore, this study validates its antiulcer use in market.

However Bhunimbadikadha has suggested more potent antisecretory and significant antiulcer effects in comparison to Dadimavaleha liquid.and may be beneficial in the treatment of gastric lesions to treat peptic ulcer. Further investigations on isolations of specific phytochemicals and elucidation of the mechanism of action are recommended in future.

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