Journal of Scientific and Innovative Research 2021; 10(3): 76-80
Available online at: www.jsirjournal.com

Research Article

ISSN 2320-4818
JSIR 2021; 1(3): 76-80

Received: 19-09-2021
Accepted: 03-10-2021

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Experimental evaluation of preventive action of baladimandura in gastric ulcer based on histopathological reports

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Abstract

Background: Peptic ulcer diseases constitute a major disease that affects the Gastro Intestinal tract. Gastric ulcers are one among the types of Peptic ulcers in which the ulcers are manifested in the lining of gastric mucosa. *Annadrava shoola* can be correlated with gastric ulcer due to its similarity in symptomatology. Baladimandura is a drug of choice in the management of Amlapitta and Parinamashoola mentioned in Rasakamadhenu. **Aims & Objectives:** To evaluate the gastric ulcer preventive action of Baladimandura in pyloric ligated albino rats through the histopathology examination of stomach tissue. **Methodology:** 24 wistar strain albino rats were grouped into 4; all the rats were free access to food and water ad libitum along with standard and test drug to the respective groups for 8 days. On 9th day all the rats were kept for fasting and 10th day pyloric ligation performed followed by sacrificing the rats for taking the stomach tissue for histopathology examination. **Results:** By comparing the histopathology report of all the rats the test group showed no ulcer formation. However slight inflammation was observed in the test drug group. **Discussion & Conclusion:** Gastric ulcers are manifested when the gastric mucosal barrier fails to prevent the entry of excess HCL into the cells. Baladimandura acts as Amlapitta hara, Parinama shoola hara and as a powerful ulcer preventive drug due to its gastro protective action.

Keywords: *Annadrava shoola*, Mucosal barrier, Peptic ulcer.

INTRODUCTION

Acharya Madhava has explained *Annadrava shoola* [1] as a condition in which the pain abdomen starts either after the food has been digested, during its digestion, or before it has been digested; it neither subsides by the use of salutary or un salutary substances nor by taking food or by remaining without food. In such condition the pain will not relieve as long as the jarat pitta (digestive juice) not expelled out by vomiting. *Annadrava shoola* can be correlated with gastric ulcer on the basis of similarities in the signs and symptoms.

Gastric ulcers [2] are one of the troubling ailments of Gastro Intestinal tract falls under the category of peptic ulcers in which the ulcers are developed in the lining of stomach. Disruption of the mucosal integrity of the stomach and / or duodenum due to an active inflammation, leading to a local defect or excavation is termed as Peptic ulcer. They form when digestive juices damage the walls of Gastro-intestinal tract. The gastric mucosal barrier protects the gastric mucosa from damage caused by the excessive secretion of HCl (autodigestion).

Baladimandura [3] is a herbo-mineral formulation mentioned in Rasakamadhenu for Amlapitta and Parinamashoola. As Parinamashoola occurs sometimes as a secondary manifestation to Amlapitta, the drug was chosen to evaluate its ulcer preventive action in gastric mucosa. The formulation is also mentioned in Rasayogasagara [4]. The key ingredient of Baladimandura is Mandura bhasma, and the herbal ingredients are being Bala (*Sida cordifolia* Linn.), Satavari (*Asparagus recemosus* Willd.), Eranda (Ricinus communis Linn.), Yava (*Hordeum vulgare* Linn.), Jeeraka (*Cuminum cyminum* Linn.), Pippali (*Piper longum* Linn.), Twak (*Cinnamomum zeylanicum* Blumme), Ela (*Elleteria cardamomum* Maton), Patra (*Cinnamomum tamala* Nees), Nagakeshara (*Mesua ferrua* Linn.) and Guda (Jaggary).

MATERIALS & METHODS

A total of 24 Wistar strain albino rats weighing between 200-250 g of either sex were selected from the SDM Centre for Research in Ayurveda and Allied Sciences Udupi for the animal study and grouped into 4 (6 rats in each group). The study was started after getting the approval from the Institutional Animal Ethical Clearance Committee (Ref no: SDMCAU/ACA/49/AEC24/2018-19) dated 25/03/2019.

Table 1: Grouping of the animals

Group no.	Group	No. of rats	Drug
1	Normal control	6	Normal water
2	Pyloric ligation control	6	Normal water
3	Standard group	6	Ranitidine + 0.5% CMC + water
4	Test group	6	Baladi Mandura+0.5% CMC+ water

Methodology

All the four groups had free access to food and water ad libitum for the first 8 days along with standard and test drug administered to the respective groups. On the 9th day, after the administration of standard and test drug to the respective groups, all the rats were kept for fasting (free access to water ad libitum) for around 36-40 hours by placing them in a metabolic cage to prevent coprophagy. On the 10th day after dosing to the respective groups, the pylorus was ligated by following the method of Shay *et al*. (1945). Later the stomach tissue washed and stored in formalin solution for histopathology examination.

Histopathology procedure

A fragment of glandular part of stomach was transferred to 10% formalin and sent to a commercial laboratory of slides. The slides with sections obtained were scanned through Trinocular Carl Zeiss's microscope (Germany) under different magnifications. Changes in the cytoarchitecture were noted down.

Procedures followed to prepare Histopathological slides

Fixation

The tissues were excised out immediately after sacrificing the animals, cleaned of extraneous tissues, cut into pieces of appropriate thickness and were transferred to 10% formalin solution. The tissues were allowed to remain in it till they are taken up for processing.

Tissue processing

The tissue processing involves dehydration, clearing and infiltration of the tissue with paraffin. The usual dehydrating agent is ethyl alcohol; acetone and isopropyl alcohol can also be used. Following dehydration tissue was transferred to paraffin solvent, which is miscible with the dehydrating agent as well. These are known as clearing agent such as chloroform and xylene. The tissue were thoroughly washed by placing them under running tap water and then passed through a series of following solvents as per schedule for dehydration, clearing and paraffin infiltration.

Table 2: Solvents and duration taken for tissue processing

Solvents	Duration
Alcohol 70%	20 min
Alcohol 80%	20 min
Alcohol 90%	20 min
Alcohol 95%	20 min
Iso propyl alcohol	20 min
Acetone (2 changes)	20 min
Chloroform (3 changes)	20 min
Melted paraffin wax (600c), (2 changes)	30 min

Next the tissues were embedded in paraffin wax to prepare tissue blocks, which are oriented so that sections are cut in desired plane of the tissue. Tissue blocks were fixed to a metal object holder after trimming them to suitable size.

Section cutting

The tissue section of the 5-6 µm thickness were cut with the help of Spencer type rotating microtone and floated in a water bath between 50-550c for 30 minutes and then they were mounted on clear glass slides with a drop of Mayer's egg albumin dried on hot plate at 500c for 30 minutes.

Staining: After fixing the section on the slide, the sections were stained by serially placing them in the following reagents.

Table 3: Reagents and duration taken for staining and sections

Reagents	Duration
Xylol (2 changes)	3 min
Acetone	3 min
Alcohol 95%	3 min
Running water	3 min
Haematoxylin stain	3 min
Running water ash	20 min
Eosin working solution	2 min
Alcohol (2 changes)	3 min
Acetone (2 changes)	3 min
Xylol (2 changes)	3 min

After passing through all the above reagents and stains, the slides were covered with D.P.X (Diphenyl phthalein xylene) and cover slip were placed. Care was taken to avoid the air bubble formation during mounting the slides. The slides were viewed under binocular research Carl-Zeiss's microscope Germany) at various magnifications to note down the changes in the microscopic features of the tissue studies.

RESULTS

The histopathology of stomach tissue of control, pyloric ligation control, standard and therapeutic groups were analysed and the results are depicted in the table no: 4,5,6,7 respectively. The images of histopathology of stomach of each group are shown in the figures 1, 2, 3 and 4.

Table 4: Results of histopathology of control group (C)

Group and rat no.	Mucosal layer	Sub-mucosal layer	Muscular layer	Remarks
C1	No changes	No changes	No changes	Normal cells
C2	No changes	No changes	No changes	Normal cells
C3	No changes	No changes	No changes	Normal cells
C4	No changes	No changes	No changes	Normal cells

Table 5: Results of histopathology of pyloric ligation control group (PC)

Group and rat no.	Mucosal layer	Sub-mucosal layer	Muscular layer	Remarks
PC 1	Mild acute inflammatory cells seen.	Mild acute inflammatory cells seen.	Mild acute inflammatory cells seen.	Inflammation
PC2	Mild ulcerative acute inflammatory cells seen in small area	Moderate acute inflammatory cells with congested blood vessels seen	Mild acute inflammatory cells seen.	Inflammation and ulceration
PC3	No changes	Mild Congested blood vessels seen	No changes	Mild Inflammation
PC4	Mild acute inflammatory cells seen.	Moderate acute inflammatory cells with congested blood vessels and edema seen	Mild acute inflammatory cells seen.	Inflammation

Table 6: Results of histopathology of standard group (S)

Group and rat no.	Mucosal layer	Sub-mucosal layer	Muscular layer	Remarks
S1	Mild acute inflammatory cells seen.	Moderate acute inflammatory cells with congested blood vessels seen	Mild acute inflammatory cells seen.	Mild Inflammation No ulcer
S2	Mild acute inflammatory cells seen.	Moderate acute inflammatory cells with congested blood vessels seen	Mild acute inflammatory cells seen.	Mild Inflammation No ulcer
S3	Mild acute inflammatory cells seen.	Mild acute inflammatory cells with moderate congested blood vessels seen	No acute inflammatory cells found.	Mild Inflammation No ulcer
S4	Mild acute inflammatory cells seen.	Moderate acute inflammatory cells with congested blood vessels seen	Mild acute inflammatory cells seen.	Mild Inflammation No ulcer

Table 7: Results of histopathology of trial group (T)

Group and rat no.	Mucosal layer	Sub-mucosal layer	Muscular layer	Remarks
T1	Mild acute inflammatory cells seen.	Moderate acute inflammatory cells with mild congested blood vessels seen	Mild acute inflammatory cells seen.	Mild Inflammation No ulcer
T2	Mild acute inflammatory cells seen.	Moderate acute inflammatory cells with mild congested blood vessels seen	Mild acute inflammatory cells seen.	Mild Inflammation No ulcer
T3	No acute inflammatory cells found.	Mild acute inflammatory cells with congested blood vessels seen.	No acute inflammatory cells seen.	Mild Inflammation No ulcer
T4	Mild acute inflammatory cells seen.	Mild acute inflammatory cells with congested blood vessels seen.	Mild acute inflammatory cells seen.	Mild Inflammation No ulcer

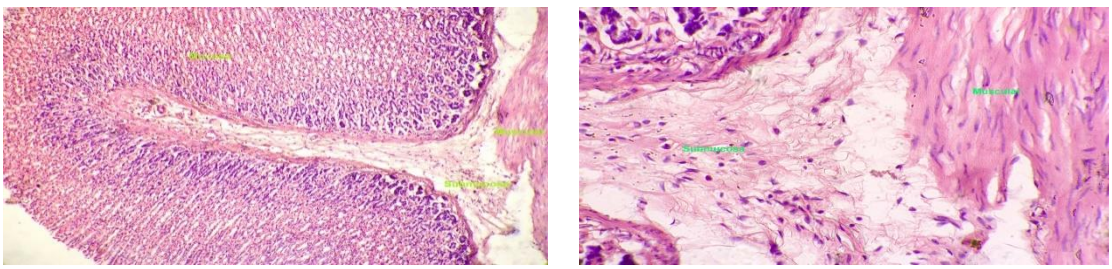

Figure 1: Histopathology of stomach of normal control group (Normal cytoarchitecture)

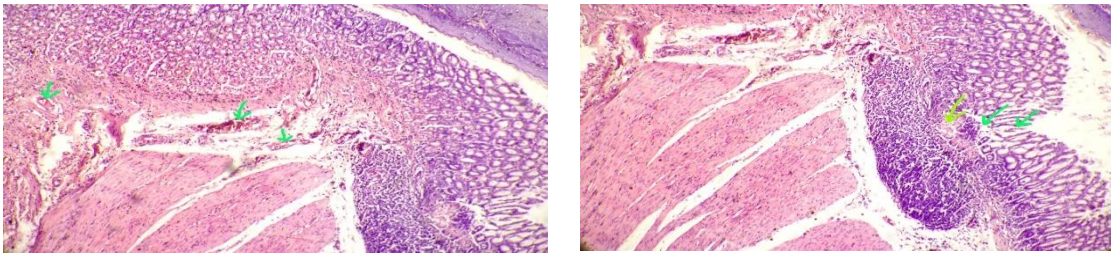

Figure 2: Histopathology of stomach of pyloric ligation control group showing congested blood vessels, ulcerative mucosa and necrosis.

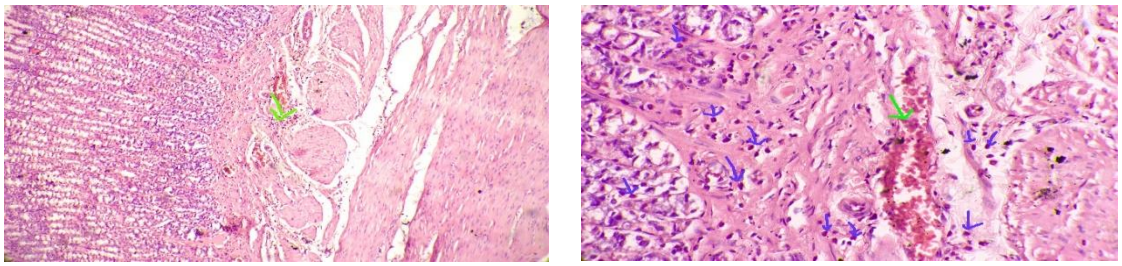

Figure 3: Histopathology of stomach of standard group showing mild and acute inflammatory changes with no ulcer.

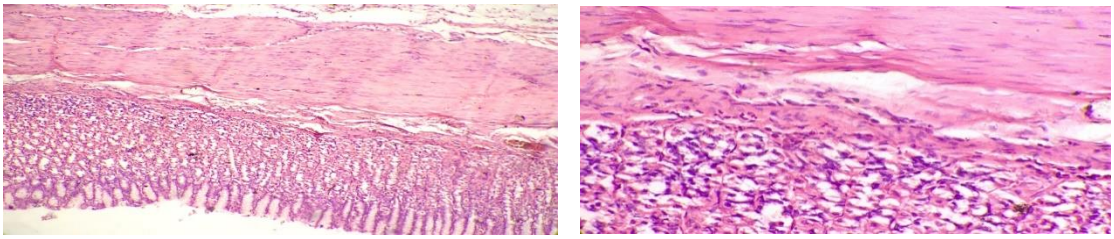

Figure 4: Histopathology of stomach of test group showing absence of inflammation with no ulcer.

DISCUSSION

The stomach tissue sections of normal control group showed thick mucosa, sub-mucosa and muscular layer. The mucosa has a columnar lining which dips to numerous gastric pits. Numerous gastric glands are also present. This data suggested the normal cytoarchitecture of stomach.

In all the groups most of the tissue sections showed acute inflammatory cells like eosinophil in all the layers with congested blood vessels. The ulcerative mucosa with necrosis accompanied by chronic inflammatory infiltrate and neutrophils in muscularis mucosa of pyloric ligation control group suggests the chronicity of ulceration. In both standard and test drug group there was no ulcer or erosion seen. This suggests the ulcer preventive action of Baladimandura within 8 days of administration. T3 showed slight reduction in inflammatory cells compared with PC group. These inflammatory changes due to eosinophil cells could be because of the cut injury during the procedure of pyloric ligation.

Vata dosha has a predominant role in the manifestation of any kind of shoola [5]. However, in the manifestation of *Annadrava shoola* all the three doshas plays a major role. The drugs such as Bala Shatavari and Ela are having vata-pitta hara action [6], Eranda act as tridoshashamaka [7] and all the other ingredients acts as either vata-kapha or pitta kapha nashaka. With all these combined actions the drug Baladimandura reduces the tridosha. The madhura rasa and sheeta veerya properties of most of the ingredients favor the action in reducing the excessive pitta dosha and thereby increase the mucosal secretion and thus prevented the ulceration.

Moreover, various research studies have been conducted on the actions of all the above mentioned drugs, which are contributing to the present study. Bala is proven to have anti-inflammatory action [8], anti-oxidant action [9] and wound healing property [10]. Shatavari has been proved to have anti-ulcer and anti-secretory activities in pyloric ligation induced gastric ulcers in rats [11]. Eranda taila (Castor oil) has anti-ulcer action and was proved experimentally [12]. The gastro protective effect of Cardamom and Elettaria cardamom was proven experimentally in rats [13]. Hence, with all these actions Baladimandura act as gastro protective drug by inhibiting the acid secretion and also by strengthening the gastric mucosa and thus prevent the ulcer formation. A clinical study on Baladimandura showed a significant result in Amlapitta by reducing various parameters of the disease [14].

Mandura bhasma is the key ingredient of Baladimandura which acts mainly as pitta shamaka and indicated in Shopha [15] (Inflammatory conditions). Hence it acts as an anti-inflammatory drug with respect to Shophahara action. Iron is absorbed in the body by the small intestine in the form of ferrous (Fe_2^+ irons). Here Baladimandura reduces the gastric p^H and makes a suitable environment for the iron absorption by the small intestine. Thus it may eradicate the iron deficiency anemia caused due to either bleeding peptic ulcer or by H. pylori associated chronic gastritis.

CONCLUSION

The Histopathological examination of pyloric ligated stomach tissues of albino rats were analysed to study the ulcer preventive action of Baladimandura. The test drug group showed a mild to moderate acute inflammatory cells in the mucosal, sub-mucosal and muscular layers of stomach, however there was no ulcer or corrosion seen.

Annadrava shoola is a disease of annavaha srotas and it may develop as a secondary manifestation to Amlapitta. Baladimandura is a herbo-mineral formulation mentioned in Rasakamadhenu indicated for Amlapitta and Parinamashoola. Due to the synergistic action of all the ingredients of Baladimandura it helps in strengthening the gastric mucosal barrier, neutralizes the gastric contents and there by prevented the ulcer formation.

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