

Ethnopharmacological Investigation of Ethanolic Extracts of Dual Herbal Combination of *Allium Sativum* and *Lawsonia Inermis*

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Abstract:- The upper section of small intestine and inside lining of stomach both can develop open sores called peptic ulcers. Discomfort of stomach is initial symptom of a peptic ulcer. Peptic ulcers include: Stomach ulcers and Duodenal ulcers. Alzheimer's disease is marked by disturbances in nervous system resulting in protein accumulation. The brain shrinks and weakening cells ends up to cell death. Dementia, which is characterised by a slow loss of memory, reasoning, behaviour, and social skills, is primarily caused by Alzheimer's disease. The study begins by documenting the traditional uses and medicinal properties associated with *Lawsonia Inermis* and *Allium sativum*. This information serves as a foundation for understanding the historical context and traditional knowledge surrounding the herbs. The ethanol extract of *Lawsonia Inermis* and *Allium sativum* is prepared using optimized extraction techniques to ensure the maximum extraction of bioactive compounds. The extract is then examined using phytochemical techniques to see whether different secondary metabolites, including phenolic chemicals, alkaloids, flavonoids, and terpenoids, are present. The results of this study contribute to the field of ethnopharmacology by providing evidence for the traditional use of *Lawsonia Inermis* and *Allium sativum* in combination. The findings shed light on their synergistic effects, supporting their potential as a natural therapeutic option for peptic ulcer and Alzheimer's disease. Further research can build upon these findings to develop novel treatments based on this dual herbs combination.

Keywords:- Antiulcer, Cholinergic, *In vitro* chicken ileum, *Lawsonia* and *Allium*

I. INTRODUCTION

➤ *Peptic Ulcer*

Peptic ulcer is the ulcer caused to the stomach and duodenum. The main reason for the development of peptic ulcer is the imbalance between the protective factor and aggressive factor.

Acid, bile, *H. pylori* are the aggressive factors where as gastric mucus, bicarbonate secretions, Prostaglandin, nitric oxides are the protective factor¹. The majority of medical condition categories are based on the biological origins, such as duodenal and gastric ulcers, which form in the duodenal bulb, which is the area most exposed to gastric acid². Symptoms of peptic ulcer include upper abdominal pain, sleep disturbance due to pain, pain is accelerated by the presence of food in stomach² etc. Bleeding occurs in as many as 15% of cases³.

➤ *Epidemiology*

Recent studies of peptic ulcer has shown that ageing as well as *H. pylori* infections are the reflection of Peptic ulcer disease.

Studies in US shows 4 million people are affected by peptic ulcer. Incidence of the disease is 350000 per year. Gastric ulcer cases are diagnosed more than duodenal ulcer cases. WHO has ranked India 42 in the world in 2020 considering the mortality and morbidity rate of the disease in the country⁴.

➤ *Signs and Symptoms*

- Abdominal pain
- Nausea
- Epigastric pain
- Pain worsened by the presence of food
- burning sensations
- Distressing pain
- vomiting⁵

➤ Pathogenesis of Peptic Disease

As we discussed earlier the main cause of peptic ulcer is the disproportion of aggressive factor and defensive factor. The reason for H. pylori induced ulcer is not yet studied completely. Cytokines are the main mediators of H. pylori infections. Inhibition of Cox 1 enzyme by NSAIDs are the mechanism of NSAID induced ulcer⁷. Cox 1 enzyme is required for the generation of Prostaglandin. Inhibition of the enzyme by NSAIDS causes decreased production of Prostaglandin which is the defensive factor against the peptic ulcer⁸.

➤ Alzheimer's Disease

AD is a neurological disorder characterized by loss of memory. It is mainly affected to the people of age above 60. The patients with AD face difficulty in managing their day to day life. plaque deposition in hippocampus, cortical, subcortical region of brain is one of the cause of AD⁹.

➤ Epidemiology

According to the consensus on 14 WHO regions it was suggested that 26 million people affected with AD every year. The prevalence of disease was increased in the age group of above 60.

Thus the new cases are reporting each year increasing. it is a serious issue. The cases are increased in the regions of china, Africa, Europe, America¹¹.

➤ Signs and Symptoms

- Difficulty in remembering the dates
- Difficult to complete the daily task
- Talking inability
- Walking difficulty
- Not remembering the past recent experience
- Confusion
- Memory loss
- Low concentration¹².

➤ Pathogenesis of Alzheimer Disease

Two important reason for Alzheimer's disease is decreased level of acetylcholine and mutation of APP gene. The above mentioned are primary reason for dementia. secondary reason are inflammation to brain, free radical formation, brain tissue damage etc. plaque deposition in the cortical, subcortical region of brain pave way to dementia¹³.

II. MATERIALS AND METHODS

➤ Chemicals Required

- Ethanol
- Acetic acid
- Aspirin
- Ranitidine
- Tyrodesolution
- Dimethyl sulphoxide

➤ Extraction Procedure

• Extraction of Lawsonia Inermis

Weigh out a sufficient amount of dried and grounded Lawsonia inermis leaves of 50grams. Place the Lawsonia inermis leaves in a thimble and insert it into the Soxhlet extractor. Add the solvent to the round-bottom flask of the Soxhlet extractor. Assemble the Soxhlet extractor and attach the condenser to the top. Turn on the heating mantle or hot plate and begin heating the solvent. As the solvent heats up, it will begin to evaporate and rise up through the Soxhlet extractor. As the solvent reaches the top of the Soxhlet extractor, it will condense in the condenser and drip back down into the round-bottom flask. The solvent will continue to circulate through the Soxhlet extractor, gradually extracting the Lawsonia inermis compounds from the plant material. Allow the extraction to continue for 6 to 12 hours, until maximum color change. Once the extraction is complete, remove the Soxhlet extractor from the heating source and allow it to cool down. Carefully remove the thimble containing the extracted Lawsonia inermis material from the Soxhlet extractor. Evaporate the solvent from the extracted material. Once the solvent has been evaporated concentrated extract of Lawsonia inermis dissolved in dimethyl sulphoxide solution¹⁴.

• Extraction of Allium sativum

Select Soxhlet extractor thimble and fill it with chopped garlic. Pack chopped garlic in thimble with cotton from bottom & upper part. Place the thimble into the Soxhlet extractor and add a suitable solvent, such as methanol to the boiling flask. Heat the solvent to boiling, and then adjust the heat to maintain a gentle reflux around 70 degree (fig 8). Allow the solvent to circulate through the garlic and condense in the condenser, which then drips back into the boiling flask. Continue the extraction for several hours or until the solvent in the boiling flask becomes clear. Once the extraction is complete, remove the thimble from the Soxhlet extractor. Evaporate the solvent from the extracted. Once the solvent has been evaporated, concentrated extract of garlic was dissolved in dimethyl sulphoxide solution¹⁵.

III. PHARMACOLOGICAL STUDY

A. Combination effect of ulcer protective activity on chicken ileum Aspirin induced ulcer:

Aspirin was used as ulcerogenic agent. The chicken ileum was cut into 5 -6cm long segments. The segments were opened with mucous upward and washed and stretched on the dish containing tyrode solution. They are divided into

- Group 1 ; control ; Treated with 10ml normal saline
- Group 2: Standard ; Treated with 1 mg ranitidine in 10ml tyrode solution
- Group 3: Test group
- ✓ Test 1: 0.1mg of lawsonia inermis in 10 ml of tyrodesolution
- ✓ Test 2: 0.1mg of allium sativum IN 10ml of tyrode solution

- ✓ Test 3 :100micro gram per ml of both in 1:1 ratio

After 30 min to all add 1ml aspirin solution

- Group 4; Treated with 10ml of aspirin solution

➤ *Ethanol Induced Ulcer;*

Ethanol was used as ulcerogenic agent. The chicken ileum was cut into 5 -6cm long segments. The segments were opened with mucous upward and washed and stretched on the dish containing tyrode solution. They are divided into

- Group 1 ; control ;Treated with 10ml normal saline
- Group 2: Standard ; Treated with 1 mg ranitidine in 10ml tyrode solution
- Group3:Test group

- ✓ Test 1: 0.1mg of lawsonia inermis in 10 ml of tyrode solution

- ✓ Test 2: 0.1mgof allium sativum IN 10ml of tyrode solution

- ✓ Test 3 :100micro gram per ml of both in 1:1 ratio

After 30 min to all add 1ml ethanol

- Group 4;Treated with ethanol solution

➤ *Acetic Acid Induced Ulcer;*

Acetic acid was used as ulcerogenic agent. The chicken ileum was cut into 5 -6cm long segments. The segments were opened with mucous upward and washed and stretched on the dish containing tyrode solution. They are divided into

- Group 1 ; control ;Treated with 10ml normal saline
- Group 2: Standard ; Treated with 1 mg ranitidine in 10ml tyrode solution
- Group3:Test group

- ✓ Test 1: 0.1mg of lawsonia inermis in 10 ml of tyrode solution

- ✓ Test 2: 0.1mgof allium sativum IN 10ml of tyrode solution Test 3 :100micro gram per ml of both in 1:1 ratio

After 30 min to all add 1ml ethanol

- Group 4; control ; Treated with acetic acid solution

B. Cholinomimetic Activity

Cholinomimetic activity of 1:1 combination of Allium sativum and Lawsonia inermis using isolated chicken ileum

➤ *Procedure*

Fresh chicken intestine was taken out and put into a beaker with modified Tyrode solution that was kept at 37°C with aeration. Identification and cutting into 2-3 cm lengths of the ileo-caecal junction were done. At both ends, loops were carefully made without cutting off the lumen. The preparation was mounded in a modified Tyrode solution-containing organ bath to provide aeration.

Recording of DRC Time cycle: 3 minutes Base line:30 seconds

Contact time: 45 seconds Relaxation periods:1 minutes

The drum was started and base line was recorded.

Concentration of 0.2, 0.4, 0.8 mL of Acetylcholine was added and record the contraction of tissue. Then the Combination of Allium sativum and Lawsonia inermis (1:1) and Concentration of 0.2,0.4, mL of Acetylcholine was added and recorded.Record the individual response of Allium sativum & Lawsonia inermis

IV. RESULT

➤ *Aspirin Induced Ulcer*

Control Group:The chicken ileum showed no obvious evidence of injury or ulcers in thecontrol group. Aspirin Group: Increasing exposure of chicken ileum with aspirin resulted in the development of visible ulcers on the surface of the ileum.

First hour exposure: least ulcer were seen on the surface of chicken ileum.

2nd-hour exposure: At the end of 2 hours, small, discrete ulcers started to appear on the surface of the ileum.3rd-hour exposure: After 3 hours of aspirin treatment, the ulcers became larger and more pronounced compared to the 2nd-hour group

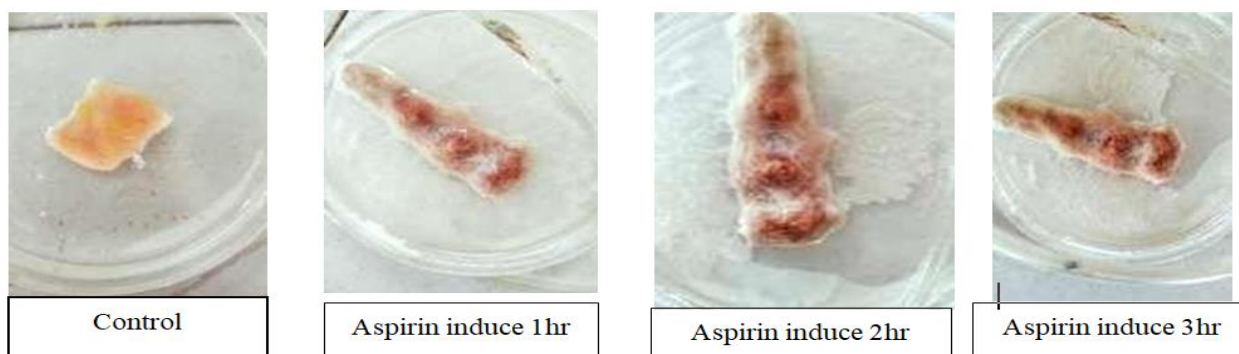


Fig 1 Aspirin Induced Chicken Ileum

• *Ulcer Protective Activity of Lawsonia Inermis*

1st-hour exposure: Lawsonia inermis treatment after 1 hour of aspirin exposure showed no ulcerformation. 2nd-hour exposure: Lawsonia inermis treatment at the end of 2 hours demonstrated a moderate in ulcersize

3rd-hour exposure: Lawsonia inermis treatment after 3 hours of aspirin exposure exhibited a severeulcer formation.

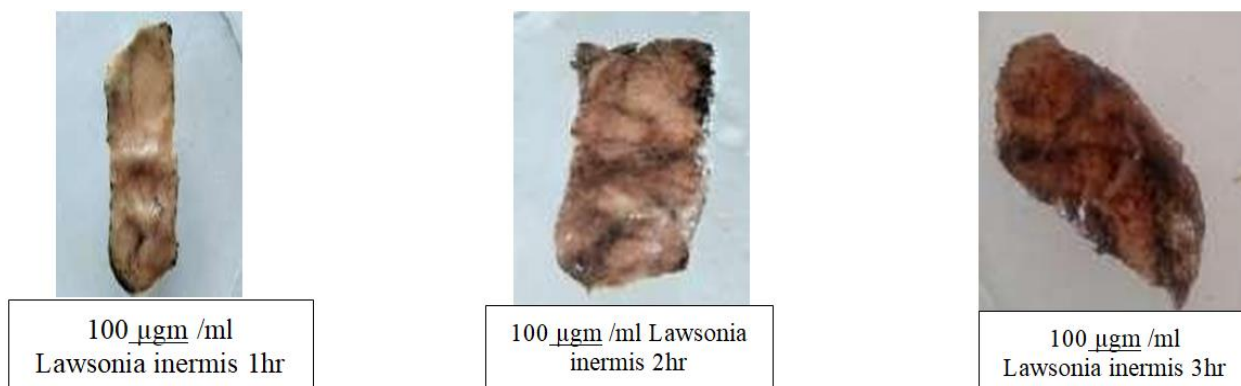


Fig 2 Ulcer Protective Activity of Lawsonia Inermis

• *Ulcer Protective Activity of Allium*

1st-hour exposure: Allium sativum treatment following 1 hour of aspirin exposure shows no ulcer. 2nd-hour exposure: After two hours, the allium sativum treatment shows significant ulcer formation

3rd-hour exposure: Allium sativum treatment after 3 hours of aspirin exposure exhibited a severeulceration.

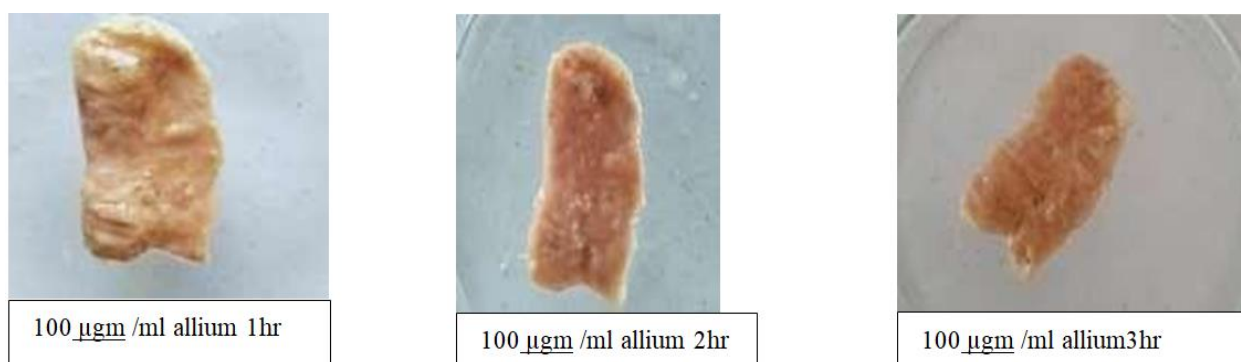


Fig 3 Ulcer Protective Activity of Allium Sativum Extract

• *Combination of Lawsonia Inermis and Allium Sativum:*

1st-hour exposure: In synergistic treatment following 1 hour of aspirin exposure shows noulcer.2nd-hour exposure: After two hours, treatment significantly no ulcer formation isobserved.3rd-hour exposure: after 3hour treatment only there shows significant ulceration

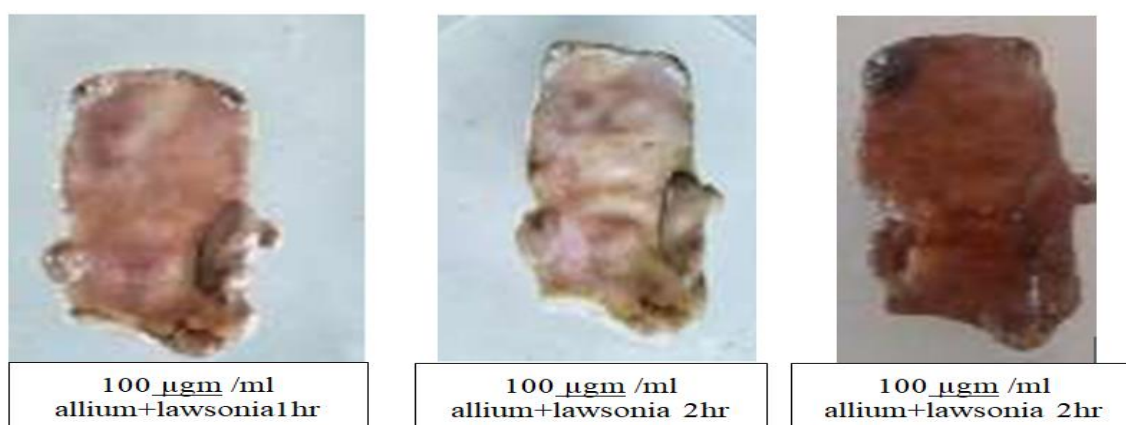


Fig 4 Combination Effect of Lawsonia and Allium extracts

• *Ethanol Induced Ulcer*

At 1st hour The ethanol-exposed chicken ileum showed only little ulcers. There were only a few small, superficial erosions and no considerable disturbance of the mucosal layer. At 2nd hour The severity of the ulcers caused by ethanol increased . The mucosal layer displayed more pronounced disruption, and deeper ulcerations were seen in several ileal regions. At 3rd hour The chicken ileum displayed the most extensive ulceration after being exposed to ethanol. There was severe destruction to the mucosal layer, and the ileum was covered with big, deep ulcers.



Fig 5 Ethanol Induced Chicken Ileum

• *Ulcer Protective Activity Of Lawsonia Inermis*

At 1st hour The ethanol-exposed chicken ileum shows few superficial erosion. At 2nd hour The ethanol exposed chicken ileum shows more eroded mucosal layer. At 3rd hour The chicken ileum shows severe destruction to the mucosal layer.



Fig 6 Ulcer Protective Activity of Lawsonia Inermis Extract

• *Ulcer Protective Activity of Allium*

At 1st hour The ethanol-exposed chicken ileum shows no superficial erosion. At 2nd hour The ethanol exposed chicken ileum shows few eroded mucosal layer. At 3rd hour The chicken ileum shows severe destruction to the mucosal layer.

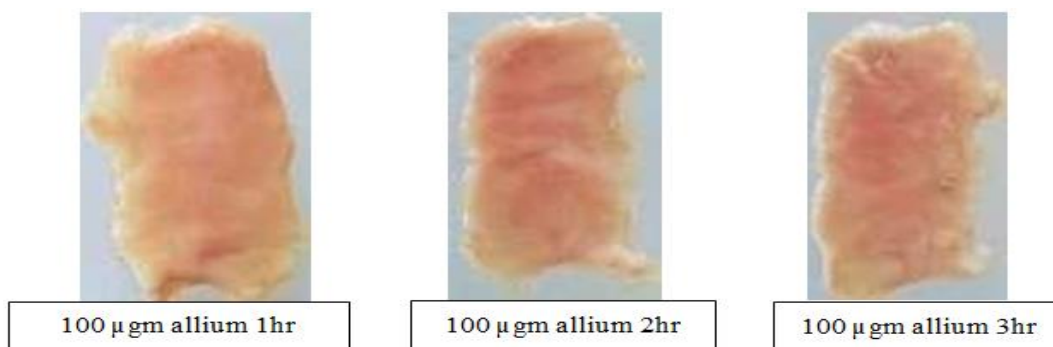


Fig 7 Ulcer Protective Activity of Allium Extract

• *Combination Effect of Lawsonia Inermis and Allium Sativum*

At 1st hour The ethanol-exposed chicken ileum shows no superficial erosion. At 2nd hour The ethanol exposed chicken ileum shows no eroded mucosal layer. At 3rd hour The chicken ileum shows few destruction to the mucosal layer.

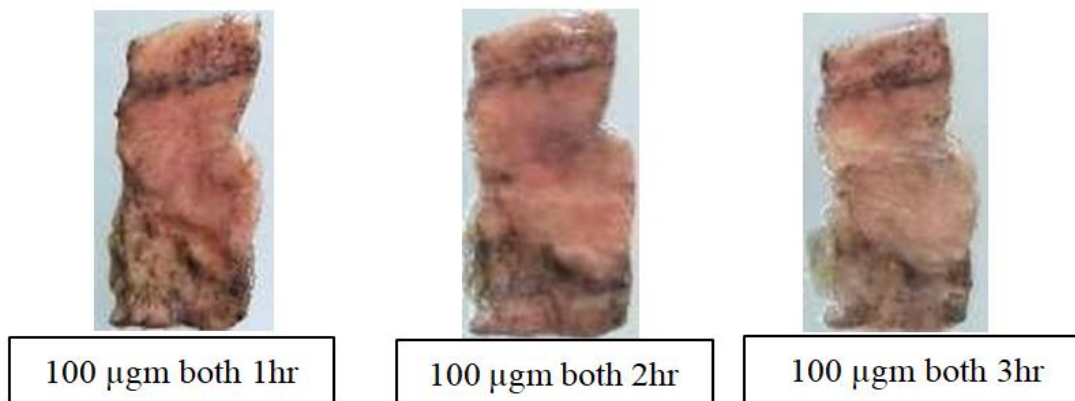


Fig 8 Combination Effect of Lawsonia Inermis and Allium Sativum

• *Acetic Acid Induced Ulcer*

At 1st hour The acetic acid -exposed chicken ileum showed significant ulceration with minimum disruption of mucosal layer. At 2nd hour The severity of the ulcers caused by acetic acid increased. The mucosal layer get more eroded. At 3rd hour The chicken ileum shows severe ulceration with extensive erosion of mucosal layer.



Fig 9 Acetic Acid Induced Chicken Ileum

• *Ulcer Protective Activity of Lawsonia Inermis*

At 1st hour The Lawsonia treated chicken ileum shows no erosion or disruption. At 2nd hour The lawsonia exposed chicken ileum shows eroded mucosal layer. At 3rd hour The chicken ileum shows severe destruction to the mucosal layer.



Fig 10 Ulcer Protective Activity of Lawsonia Inermis Extract

• *Ulcer Protective Activity of Allium*

At 1st hour The allium-exposed chicken ileum shows no surface changes. At 2nd hour The Allium treated chicken ileum shows few eroded mucosal layer. At 3rd hour The chicken ileum shows severe mucosal eroded and major disruption of surface.

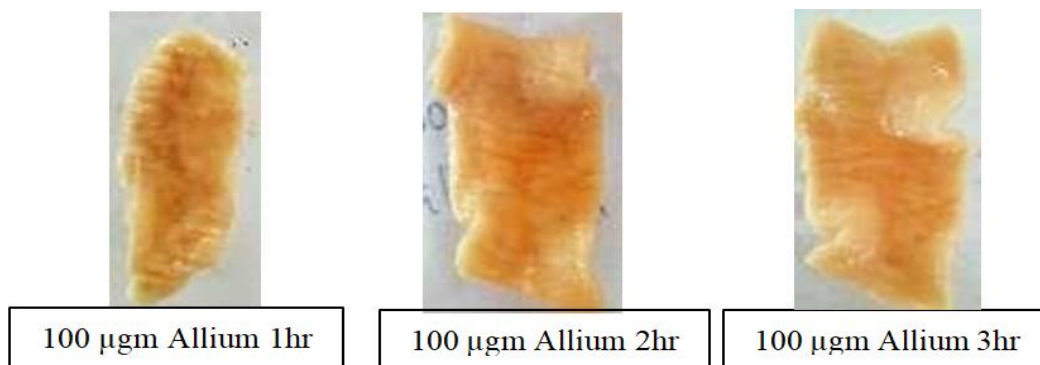


Fig 11 Ulcer Protective Activity of Allium Extract

• *Combination effect of Lawsonia and Allium Extracts*

At 1st hour The Acetic acid chicken ileum shows no superficial erosion. At 2nd hour The acetic acidexposed chicken ileum shows few eroded mucosal layer. At 3rd hour the chicken ileum shows few destruction to the mucosal layer.



Fig 12 Combination Effect of Lawsonia and Allium Extracts

• *Ulcer Protective Activity of Ranitidine*

✓ *Ulcer Protective Activity of Ranitidine in Aspirin*

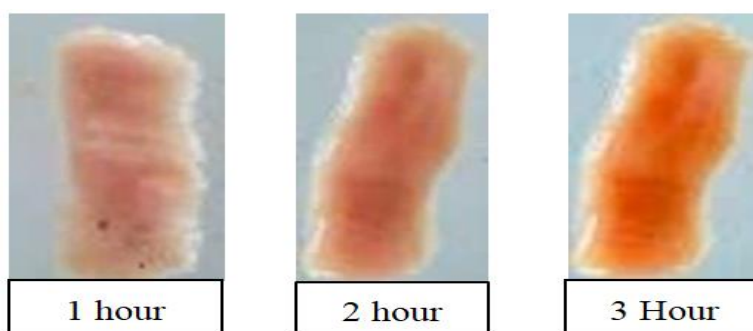


Fig 13 Ulcer Protective Activity of Ranitidine in Aspirin

✓ *Ulcer Protective Activity of Ranitidine in Ethanol*



Fig 14 Ulcer Protective Activity of Ranitidine in Ethanol

✓ *Ulcer Protective Activity of Ranitidine in Acetic Acid*

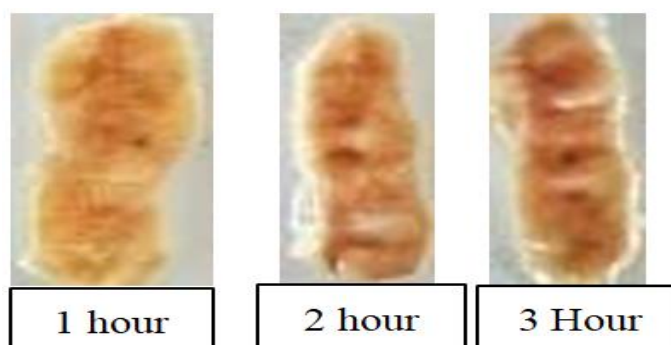


Fig 15 Ulcer Protective Activity of Ranitidine in Acetic Acid

➤ *Ulcer Protective Activity Of Ranitidine*

In the ranitidine treated chicken ileum no any ulcer is formed in any of the case. In case of aspirin, Ethanol ,acetic acid induced chicken ileum the ranitidine protected the mucosal layer fromulcer. As the hours increases no prominent change occurs to the chicken ileum.Thus the standard ranitidine is protecting the ileum from ulcer.

➤ *Using an Isolated Chicken Ileum, Impact of Lawsonia Inermis and Allium Sativa on CRC of Ach.*

According to findings below Allium sativa had cholinomimetic effects, while the Lawsonia inermis and mix of two herbal extracts Results did not demonstrate the same effect.

The existence of cholinergic impairments doesn't explain the neuropathology of the brain seen in Alzheimer's disease.

The clear evidence of cholinergic neuron degradation, on the other hand, suggests a new therapy option for Alzheimer's disease symptoms.

The levels of ACh in the cortex and hippocampus area of Alzheimer's patients were shown to be lower¹⁶.

The present approach that has been discovered to provide symptomatic relief involves the administration of cholinesterase inhibitors, which decrease AChE and lead to ACh breaking down at the cholinergic synapse.

An opportunity which is helpful for novel treatment agent for Alzheimer's disease due to their antioxidant activity and inhibition of acetylcholine esterase¹⁷.

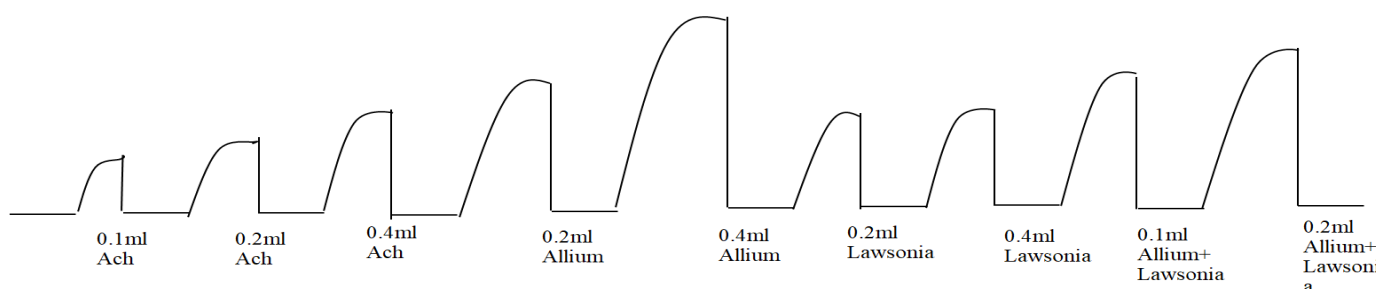


Fig 16 Using an Isolated Chicken Ileum, Impact of Lawsonia Inermis and Allium Sativa on CRC of Ach

V. DISCUSSION

The antiulcer properties of Lawsonia inermis and Allium sativum were investigated in this study. The current study's findings suggest that Lawsonia inermis and Allium sativum have an antiulcer impact on aspirin-induced ulcers.

The presence of flavonoid, alkaloid, proteins, amino acids, and terpenoids, as well as fixed oil and glycosides, is shown by early phytochemical evaluation of whole plant extracts.

The antiulcer efficacy of ethanol extracts of Lawsonia inermis and Allium sativum on aspirin-induced anti-ulcer research is studied. According to the findings of these studies, ethanol extracts of Lawsonia inermis and Allium sativum exhibit antiulcer properties.

About 90% of the basal, food-driven, and hormonally mediated stomach acid, which is repeatedly produced by gastrin, histamine, parasympathomimetic medications, and vagal stimulation, is dramatically reduced when ranitidine is administered as an H2 receptor blocker. Ranitidine works by blocking the histamine-mediated c-AMP dependent pathway to reduce gastric secretion. Patients with duodenal ulcers were induced to produce specific mimics of gastric mucus by ranitidine.

The control group's ethanol-induced ulcers were easier to see and distinguish from those in the intestinal segments treated with ranitidine, where ulceration was noticeably diminished. The control group's intestinal segment margins

were visibly degraded upon closer inspection. In the treated group, there was only one ulcer compared to 3 in the control group. Ranitidine reportedly offers significant protection in ulcer sites and the surrounding region, respectively.

Table 1 Antiulcer Activity of Lawsonia Inermis and Allium Sativum

Hr.	Control(Aspirin, Ethanol, Aceticacid)	Test(Lawsonia inermis andAllium sativum)	Standard (Ranitidine)
1	3 2 1	1	0
2	3 2 2	2	0
3	4 3 3	2	1

A variety of approaches are being utilised to estimate medication anti-ulcer activity. All of the approaches are based on the premise of causing ulcers with ulcerogenic drugs such as NSAIDS (aspirin, indomethacin, and so on), alcohol, or pylorus- ligation. The rats were then sacrificed and the stomach and small intestine were examined for the existence of lesion. Regardless of the manner of generating ulcers, all procedures include the death of rats. As a result, the technique chosen may be expanded and used to examine the anti-ulcer effect of medicines and plants. However, this in-vitro study cannot prove the actual pathophysiology of ulcers.

This alternative technique, however, may be recommended to researchers for qualitative results. Once good results are obtained, in vivo study can begin. This approach can also be used to study how drugs affect wound healing. As a result, It is possible to advise using the investigated in vitro method in research investigations to lessen stress and suffering in rats while avoiding sacrifice.

VI. SUMMARY AND CONCLUSION

The current study made a good effort to evaluate the ulcer-preventive properties of a herbal mixture (Allium sativum and Lawsonia inermis) in an isolated chicken ileum.

Finally our findings suggest that the combination of herbs protected the mucosal layer from ulcer formation for more hours than the individual extract. Here the individual extract produce ulcer within 1 or 2 hours whereas the combination of herbal extract protected the ileum from ulcer for more than 2 hours.

The presence of bioactive chemicals is responsible for this increased activity in both extracts that act synergistically to promote protection of gastric mucosa.

In cholinomimetic activity, our study shows that the combination of herbal extracts did not show significant to the standard whereas the Allium sativum shows significant cholinomimetics activity as that of the standard.

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