Antiulcer activity of Ethanolic Extract of Holoptelea Integrifolia (Roxb.) Leaves: an In vivo Study

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Abstract

The prior

Ulcers can form in either the stomach (gastric ulcer) or duodenum (duodenal ulcer), the inner lining of the stomach and the small intestine. Both types of ulcers fall under the umbrella category of peptic ulcers. Roughly 10% of people as a whole are impacted.

Aim

In vivo study on wistar albino rats to evaluate the "antiulcer activity of Ethanolic Extract of Holoptelea Integrifolia (Roxb.) Leaves" in comparison to the drug ranitidine.

Materials and Methods

The present study used ethanol-induced ulcers in albino rats as a model. The antiulcer effectiveness of EHIL (200, 400 mg/kg p.o. for 7 days) was compared to that of a gold standard drug (Ranitidine). Using an ethanol alcohol caused ulcer model, the ulcer index was developed to quantify the degree of ulceration. The variables included the ulcer index, gastric juice volume, pH, free acidity, and total acidity.

Results

There was a statistically significant ($p<0.01$) and dose-dependent reduction in ulcer index in EHIL-pretreated animals compared to controls (EHIL: 6.98, 6.50, 2.25, 4.15, 4.25, and about 50% ulceration inhibition at 200, 400 mg/kg; ranitidine: about 75% ulceration inhibition).

Conclusion

The study's findings corroborate the folk medicine beliefs that EHIL are more effective against ulceration.

Keywords: Antiulcer effect, Ethanol, Ulcer index

CHAPTER-1

INTRODUCTION

1.1 Human gastrointestinal system

The human gastrointestinal system, or digestive system, is a highly sophisticated network of organs that facilitates the breakdown and absorption of food and the expulsion of waste. It's crucial since it helps provide the body with fuel and important nutrients.[1] Ingestion is the first step in the digestive process, hence the mouth is the entry point for the gastrointestinal system. Chewing and breaking down food with the tongue and teeth helps start the chemical digestion process, which is initiated by the saliva generated by the salivary glands.[2].Swallowing is the process by which food is transported from the mouth to the stomach through the oesophagus, a muscular tube. Once the meal has been ingested, it is carried to the stomach, where digestive acids and enzymes complete the process of digestion. Additionally, food is temporarily stored in the stomach before being passed on to the small intestine.[3]

The small intestine, which includes the duodenum, jejunum, and ileum, is the longest section of the digestive tract. Most digestion and absorption of nutrients take place in the small intestine. Small intestine walls are covered with fingerlike projections called villi and microvilli, which enhance the intestinal surface area and facilitate absorption. Proteins, lipids, and carbs. are digested with the help of pancreatic enzymes and bile from the liver, and the nutrients are absorbed into the circulation.[4,5]

The large intestine, often known as the colon, is where waste and undigested food are sent. The large intestine's primary roles include fluid and electrolyte absorption, as well as faces generation and storage. Beneficial bacteria in the large intestine also help in the production of certain vitamins and further digestion of some undigested material.[6]
When the bowels are empty, the leftover waste is expelled by the anus and rectum, a procedure known as defecation.

1.2 Parts of the human gastrointestinal system

The key parts of the human gastrointestinal system:

1. **Mouth:** The entry point of the digestive system where food is ingested. It contains teeth for mechanical digestion and salivary glands that produce saliva to initiate chemical digestion.[7]
2. **Esophagus:**A muscular tube that, via a series of contractions called peristalsis, moves food from the mouth to the stomach.[8]
3. **Stomach:**A J-shaped digestive organ that takes food from the oesophagus. The stomach produces digestive fluids that further digest meals by secreting enzymes and stomach acid.[9]
4. **Small Intestine:**The longest section of the digestive tract, comprising the jejunum, ileum, and duodenum. It is the primary site of digestion and nutrient absorption.[10]
5. **Large Intestine (Colon):**This is the last part of your digestive system. It forms faeces by absorbing water and electrolytes from undigested food.[11]

6. **Liver:**An organ in the upper right quadrant of the belly, its bile aiding in the breakdown and absorption of fats. Additionally, it serves an important purpose in detoxification and metabolism.[11]
7. **Gallbladder:**The gall is a tiny organ located under the liver that collects and concentrates bile. When fat digestion is required, it triggers the flow of bile into the small intestine.[12]
8. **Pancreas**: An protease gland that sits below the stomach and supplies the small intestine. It also plays a role in controlling blood sugar by secreting chemicals like insulin and glucagon.[13]
9. **Rectum:**The section of the large intestine that collects waste before it is evacuated.[14]
10. **Anus:**The last departure point of the digestive system from which waste products are expelled.[15]

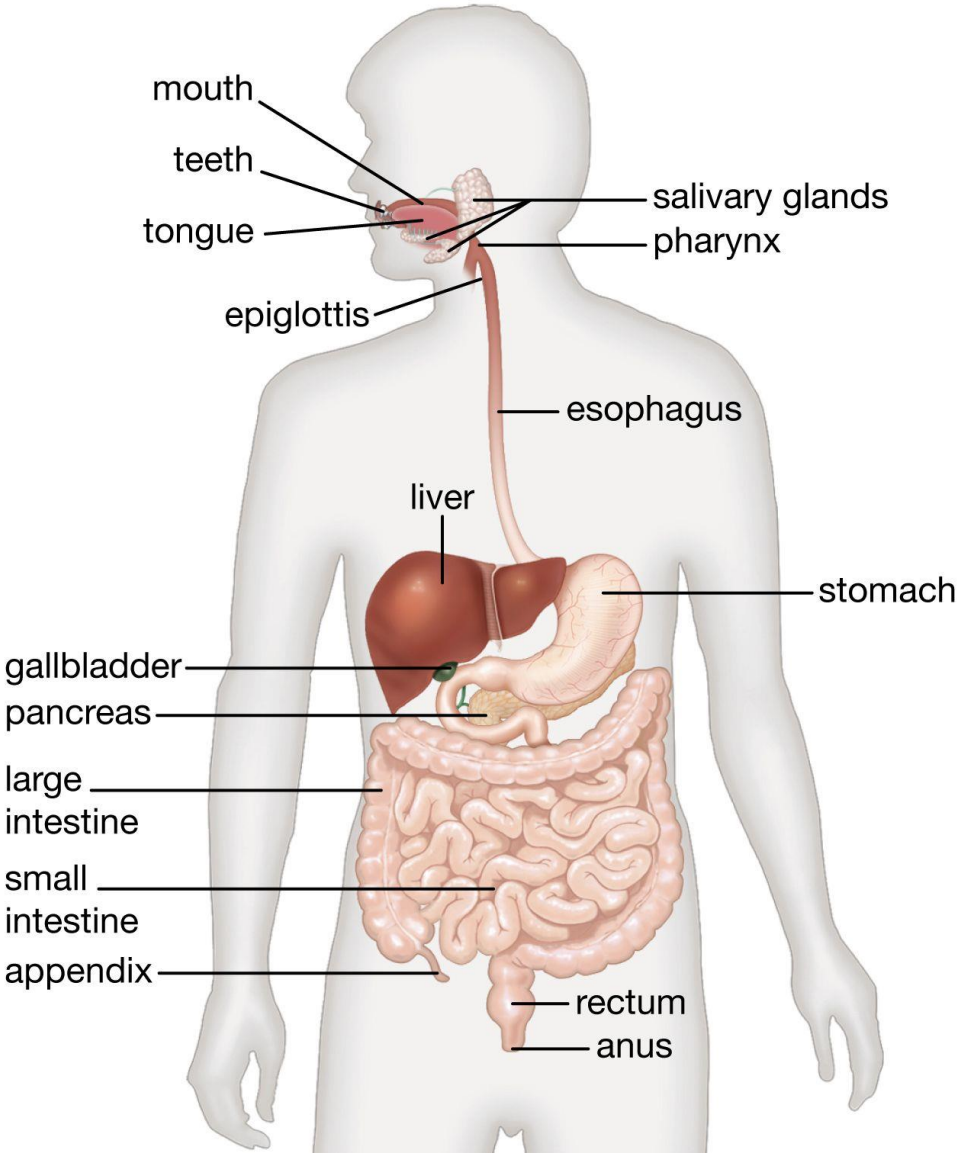


Figure: 1.1 Human gastrointestinal system.[16]

1.5 Peptic Ulcer

Peptic ulcers are sores or open wounds that originate in the stomach or duodenum (the first section of the small intestine). It develops when the digestive tract's protective lining breaks away, exposing vulnerable tissues to the harmful effects of stomach acid and digestive enzymes.[39]

Helicobacter pylori (H. pylori) infection and long-term use of nonsteroidal anti-inflammatory medicines (NSAIDs) are the two most common causes of peptic ulcers. Because NSAIDs irritate the lining of the stomach and duodenum, and because H. pylori decreases this mucus layer, both increase the risk of ulcers and bleeding.[40]

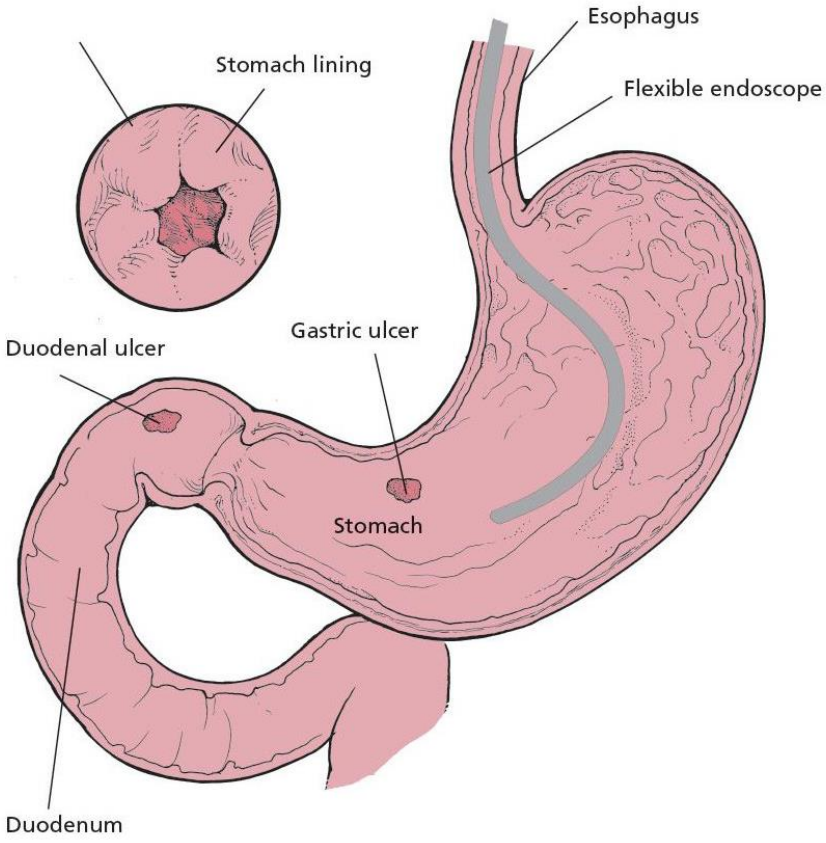


Figure: 1.2 Peptic ulcer.[41]

1.6 Types of Peptic ulcers

The location and an etiology of a peptic ulcer determines which sub type it falls under. Gastric and duodenal ulcers are the most common forms of peptic ulcers.

1.6.1Gastric Ulcers:

Peptic ulcers of the stomach lining are known as gastric ulcers. Due to an imbalance between the protective elements of the stomach lining and the harmful effects of stomach acid and digestive enzymes, many conditions manifest as open sores or lesions.[42]

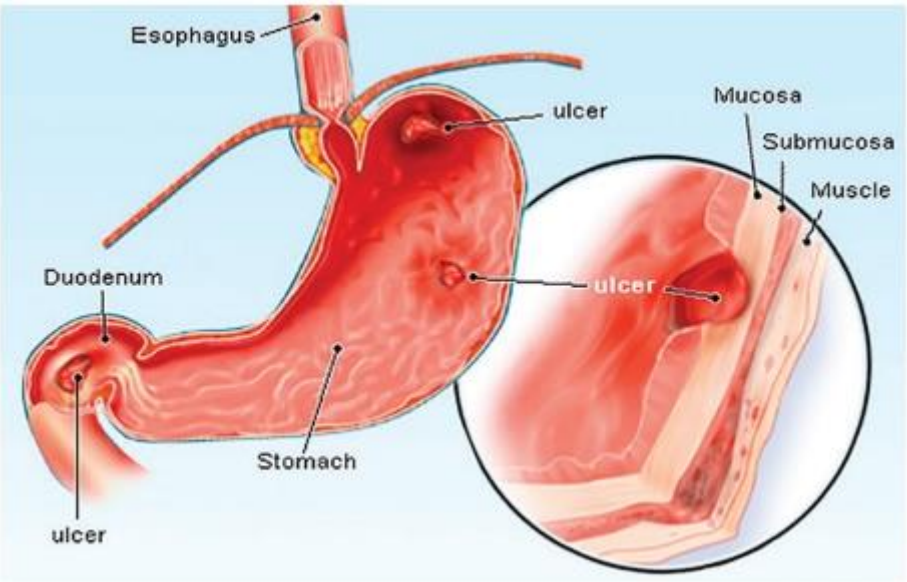


Figure: 1.3 Gastric ulcer.[42]

Causes: Infection with Helicobacter pylori (H. pylori) bacteria and long-term use of nonsteroidal anti-inflammatory medicines (NSAIDs) are the leading causes of stomach ulcers. Damage from stomach acid is made more likely by H. pylori infection because the stomach's protective mucus layer is weakened. NSAIDs have been linked to stomach irritation and ulcer development.[43]

Symptoms: Pain that is described as burning or gnawing in the upper abdomen is the hallmark of gastric ulcers. Eating, particularly on an empty stomach, might increase the discomfort, while eating or taking an antacid can briefly alleviate it. Other symptoms can include nausea, vomiting, bloating, early satiety (feeling full quickly), and unintended weight loss.[44]

Diagnosis: Gastric ulcers can be diagnosed through various methods, including upper endoscopy, which allows direct visualization of the stomach lining. A flexible tube containing a camera is introduced orally into the stomach during this surgery. To check for H. pylori infection or to rule out other diseases, a biopsy may be done.[45]

Treatment: Gastric ulcers are treated with a mix of medication and dietary and lifestyle changes. Medication options to treat acid reflux include proton pump inhibitors (PPIs) and histamine receptor blockers (H2 blockers). If H. pylori infection is present, antibiotics are used to treat it. Lifestyle changes, such as quitting smoking, avoiding NSAIDs, and adopting a healthy diet, can also aid in the healing process.[46]

Complications: Complications from untreated gastric ulcers include bleeding, perforation (a hole in the stomach lining), and obstruction of the gastric outlet (blockage of the stomach outlet).These complications require immediate medical attention.[47]

1.6.2 Duodenal Ulcers

Peptic ulcers of the duodenum, the first section of the small intestine, are known as duodenal ulcers. Due to an imbalance between protective and harmful substances in the gastrointestinal system, they are characterised by open sores or lesions in the duodenal mucosa.

Here are some key points about duodenal ulcers:

Causes: Helicobacter pylori (H. pylori) infection and the use of nonsteroidal anti-inflammatory medicines (NSAIDs) are the two most common triggers of duodenal ulcers (NSAIDs). Duodenal lining defences are compromised by H. pylori infection, rendering the lining more vulnerable to harm from stomach acid and digesting enzymes. NSAIDs can also irritate the duodenal lining and contribute to ulcer formation.[48]

Symptoms: Duodenal ulcers are characterised by a burning or gnawing discomfort in the upper abdomen, especially in the hours between meals and first thing in the morning. Eating or using antacids may help ease the discomfort. Bloating, nausea, vomiting, and unexpected weight loss are among other specific signs.[49]

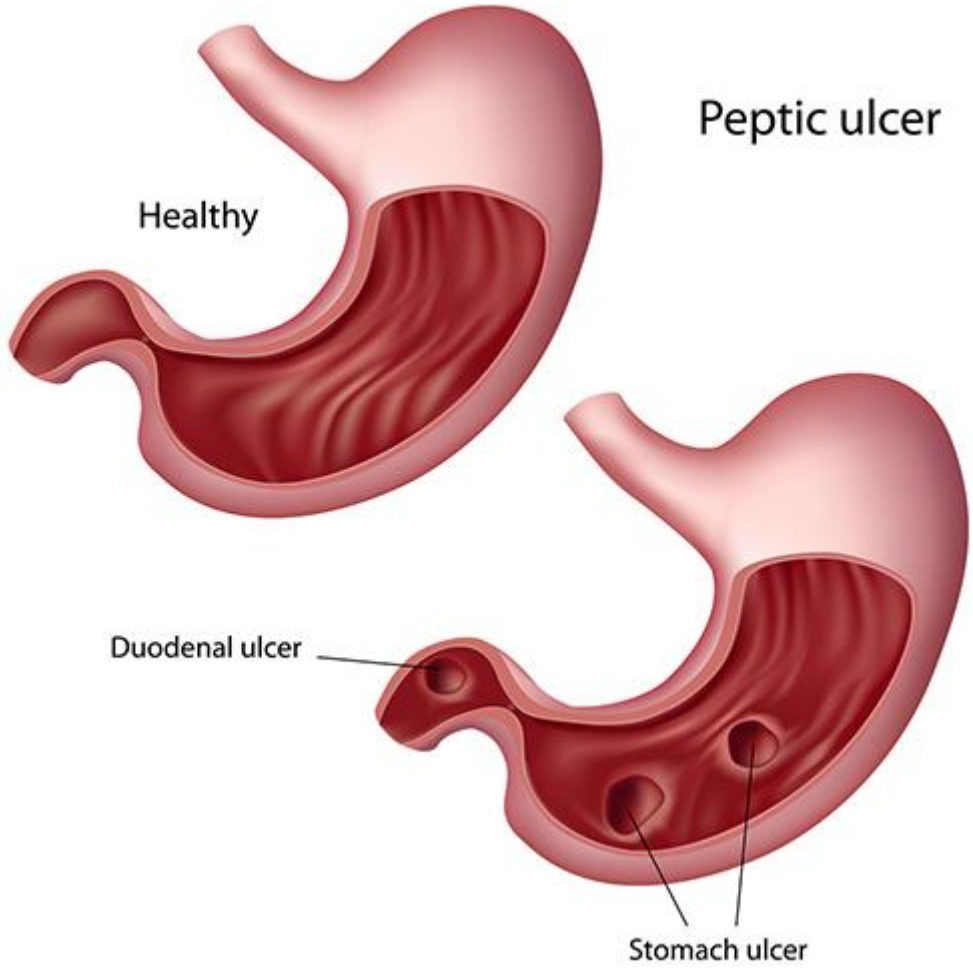


Figure: 1.4 Duodenal ulcers.[49]

Diagnosis: Upper endoscopy is only one of several diagnostic tools for duodenal ulcers. The ulcer is observed and a biopsy sample is taken by inserting a flexible tube with a camera through the mouth and into the duodenum. Infection with H. pylori may also be checked for through blood, breath, or stool tests.[50]

Treatment: Duodenal ulcers are treated with a mix of medicines and dietary and lifestyle changes. Medication options to treat acid reflux include proton pump inhibitors (PPIs) and histamine receptor blockers (H2 blockers). If H. pylori infection is present, antibiotics are used to treat it. A balanced diet, less stress, and no nonsteroidal anti-inflammatory drugs (NSAIDs) may all speed healing.[51]

Complications: If left untreated, duodenal ulcers can lead to complications such as bleeding, perforation (a hole in the duodenal wall), or obstruction due to scarring and narrowing of the duodenal passage. These complications require immediate medical attention.[52]

1.7 Causes of peptic ulcers

When the lining of the stomach, upper small intestine, or oesophagus begins to break down and bleeds, this is called a peptic ulcer. Helicobacter pylori is a bacterium that is the leading cause of peptic ulcers (H. pylori). However, other factors can contribute to the development of peptic ulcers. Here are some of the main causes:

- **Helicobacter pylori (H. pylori) infection**: Inflammation and a thinning of the stomach's protective mucus layer are the results of H. pylori infection. This bacterium is a major cause of peptic ulcers.[53]
- **Nonsteroidal anti-inflammatory drugs (NSAIDs):**Peptic ulcers are more likely to occur with regular or extended use of nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin, ibuprofen, naproxen, or prescription NSAIDs. These medications inhibit the production of prostaglandins, which help protect the stomach lining.[54]
- **Excessive stomach acid production**: Ulcers form when the stomach's protective lining is worn away by stomach acid, which may happen under certain situations. Hypercalcemia and the very uncommon Zollinger-Ellison syndrome both involve abnormally high blood calcium and gastrin levels.[55]
- **Smoking:** Smoking cigarettes and using tobacco products can increase the risk of peptic ulcers and delay their healing. Smoking interferes with the protective mechanisms of the stomach lining and impairs blood flow, slowing down the healing process.[56]
- **Alcohol consumption**: Drinking too much alcohol may cause irritation and erosion of the stomach lining, which can lead to ulcer development. Alcohol also stimulates acid production in the stomach, further increasing the risk.[57]
- **Stress:** While stress itself may not directly cause peptic ulcers, it can aggravate the symptoms and delay the healing process. Chronic stress can affect the body's ability to repair damaged tissues and weaken the immune system, making it more susceptible to H. pylori infection.[58]

1.8 Symptoms of Peptic ulcers

Different symptoms, and how long they last, may be caused by peptic ulcers. Peptic ulcers are characterised by a variety of symptoms.

- **Abdominal pain:**Pain that is dull, burning, or gnawing in the upper abdomen is the primary sign of peptic ulcers. The pain might be sharp or dull, and it can occur anywhere from the navel to the breastbone.[59]
- **Heartburn:** Many people with peptic ulcers experience a burning sensation or discomfort in the chest, often referred to as heartburn. This sensation may worsen when lying down or on an empty stomach.[60]
- **Indigestion:**Indigestion, characterised by fullness, bloating, or pain after eating, may be a symptom of peptic ulcer disease. Some people may also experience nausea or belching.[60]
- **Loss of appetite**: Peptic ulcers can lead to a decreased appetite, as the pain and discomfort associated with the ulcers may make it difficult to eat.[61]
- **Unintended weight loss:** In some cases, peptic ulcers can result in unintended weight loss. This is often due to the loss of appetite and reduced food intake.[62]

- **Nausea and vomiting:**Nausea and vomiting may be associated with peptic ulcers. Vomiting may be more common when the ulcer is located in the stomach.[63]
- **Dark or bloody stools**: Bleeding ulcers can result in the presence of blood in the stool. Stools may appear black and tarry (melena) or have bright red blood, indicating fresh bleeding.[64]
- **Fatigue**: Peptic ulcers induce chronic blood loss, which may result in anaemia and its associated symptoms of fatigue, weakness, and dizziness.[65]

1.9 Gastric and duodenal juices

1.9.1 Gastric Juice: The stomach's gastric glands secrete gastric juice. The primary components are HCl, pepsinogen (an inactive version of the enzyme pepsin), and mucus.The gastric juice has several functions, including:

1. **Protein digestion:**Pepsin, the major enzyme in gastric juice, digests proteins into simpler building blocks called peptides. When exposed to the stomach's acidic environment, pepsinogen is converted into pepsin.[66]
2. **Activation of enzymes:** Gastric acid activates pepsinogen to its active form, pepsin. Pepsin then helps initiate the digestion of proteins.[67]
3. **Disinfection**: The high acidity of gastric juice helps kill many ingested microorganisms, preventing their entry into the intestines.[68]
4. **Mucus production**: The mucus in gastric juice helps protect the stomach lining from the corrosive effects of gastric acid, preventing damage to the stomach wall.[69]

1.9.2 Duodenal Juice: The first section of the small intestine, called the duodenum, contains glands that secrete duodenal juice. It's vital for balancing out the stomach acid that chyme (partially digested food) carries into the duodenum. [70] The key components of duodenal juice include:

1. **Bicarbonate ions**: Duodenal juice contains bicarbonate ions, which help neutralize the acidity of the chyme coming from the stomach. This neutralization is important to create an optimal pH environment for the enzymes in the small intestine to function effectively.[71]
2. **Enzymes**: Enzymes including pancreatic amylase, lipase, and proteases are found in duodenal juice and aid in the breakdown of carbs, lipids, and proteins.[72]
3. **Mucus production**: Similar to gastric juice, mucus in duodenal juice helps protect the lining of the duodenum from the acidic and aids in the smooth movement of digested food along the intestines.[73]

1.10 Helicobacter pylori

Helicobacter pylori (H. pylori) is a stomach-colonizing bacteria that has a significant role in the pathogenesis of a number of gastrointestinal disorders. Here are some key roles of H. pylori:

- **Peptic Ulcers**: Peptic ulcers are open sores that grow on the lining of the stomach or the upper section of the small intestine, and H. pylori infection is significantly linked to their development. When the stomach's defences are downed by bacteria, stomach acid and digestive enzymes may eat away at the mucosa and cause an ulcer to emerge.[74]

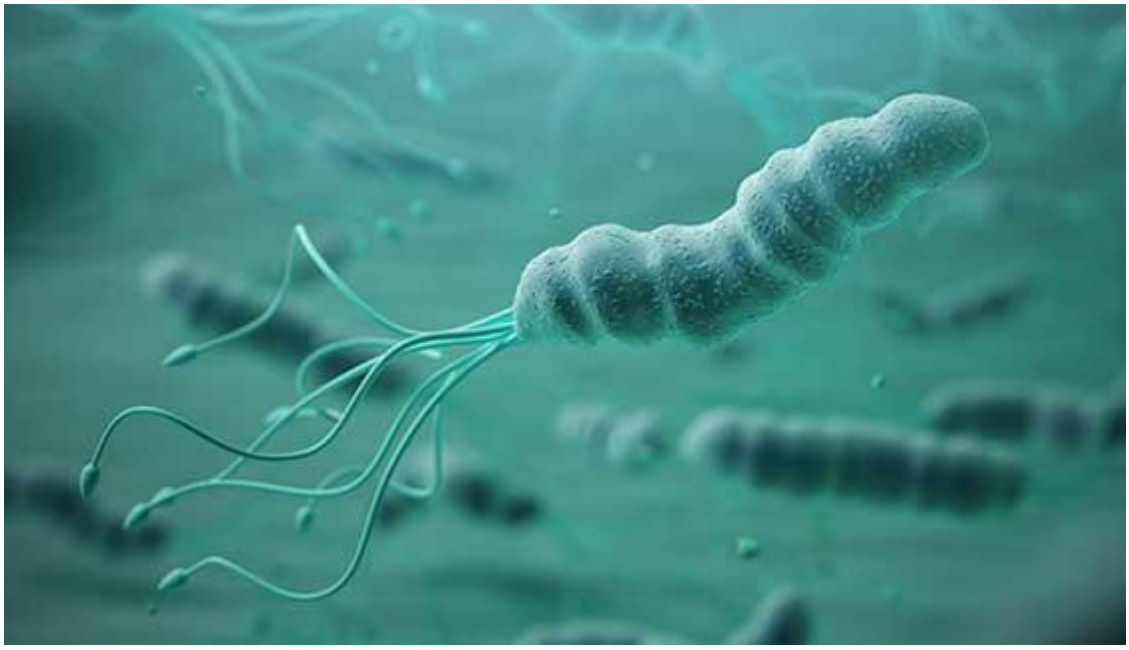


Figure: 1.5 Helicobacter Pylori.[75]

1.11 Peptic ulcers complications

Several issues might arise from peptic ulcers if they are not treated or managed properly. Peptic ulcers often lead to the following complications:

- **Bleeding Ulcer:** Peptic ulcers can erode blood vessels in the stomach or duodenal wall, leading to bleeding. Melena, or black, tarry stools, may be a sign of a bleeding ulcer, as may the presence of bright red blood in the stool. Severe bleeding may result in vomiting blood (hematemesis) or signs of anemia, such as fatigue and weakness.[76]
- **Perforation:** In some cases, peptic ulcers can penetrate completely through the stomach or duodenal wall, causing a perforation. This leads to the leakage of stomach acid and digestive juices into the abdominal cavity, resulting in a condition known as peritonitis. A perforation is a life-threatening condition that need immediate surgical attention.[78]
- **Gastric Outlet Obstruction:**Gastric outlet blockage occurs when chronic inflammation and scarring from peptic ulcers reduce or block the stomach's aperture. This leads to symptoms such as persistent vomiting, bloating, and feeling full after consuming small amounts of food.[79]
- **Gastrointestinal Obstruction:** Peptic ulcers located in the duodenum can sometimes cause strictures or scarring that can lead to partial or complete blockage of the small intestine. This can result in symptoms like abdominal pain, bloating, nausea, and vomiting.[80]
- **Increased Risk of Gastric Cancer:**Helicobacter pylori is a major cause of peptic ulcers, and long-term infection with this bacteria is linked to an increased risk of developing stomach cancer. Although H. pylori infection does not often lead to cancer, having an ulcer may raise the risk even more.[81]

1.12 Diagnosis of peptic ulcers

Evaluation of the patient's medical history, a physical examination, and diagnostic testing are the usual components of a peptic ulcer diagnosis. The following are some of the most typical diagnostic procedures for peptic ulcers:

1. **Medical History and Physical Examination:** The doctor will take a detailed medical history, including symptoms such as abdominal pain, indigestion, and any factors that may contribute to ulcer development (e.g., smoking, NSAID use). They will also perform a physical examination to assess for any signs of complications or related conditions.[82]
2. **Endoscopy**: Esophagogastroduodenoscopy (EGD) is a commonly used diagnostic procedure for peptic ulcers. Endoscopy is the examination of the esophagus, gastric, and duodenal linings by a thin, flexible tube with a camera (endoscope) inserted via the mouth. This allows direct visualization of any ulcers or other abnormalities.[83]
3. **Biopsy:** During endoscopy, the doctor may take small tissue samples (biopsies) from any suspicious areas. For the purpose of diagnosing H. pylori infection or ruling out other illnesses, such as stomach cancer, these biopsies are submitted to a laboratory for further analysis.[84]
4. **Urea Breath Test:**The H. pylori bacteria may be detected using this non-invasive test. The patient consumes a carbon isotope-labeled fluid. Labeled carbon dioxide is exhaled and may be detected in the breath if H. pylori is present and breaks down the solution.[85]
5. **Stool Antigen Test**: This test is another non-invasive option for identifying H. pylori infection. Testing for H. pylori antigens, which are indicators of bacterial infection, in a stool sample.[86]
6. **Blood Tests:**Antibodies against H. pylori may be detected in a blood test, together with other indicators of infection and inflammation. However, blood tests alone cannot determine the presence of an ulcer and are often used in conjunction with other diagnostic methods.[87]

CHAPTER-3

AIM & OBJECTIVE

3.1 Aim and objective

To examine the effects of ethanolic extract of Holoptelea integrifolia (Roxb.) leaves on rat gastric ulcers in comparison to the standard treatment of ranitidine in wistar albino rats.

3.2Procedure:

Selection of plant
↓
Authentication of plant
↓
Collection of leaves
↓
Preparation of ethanolic Extract of leaf
↓
Selection the wistar albino rats
↓
Divided into five group
↓
Result
↓
Conclusion

3.3 Plan of work

1. Collection of Literature Review
2. Collection and authentication of plant materials (Holoptelea Integrifolia)
3. Selection of suitable material on the basis of traditional use
4. Preparation of crude extracts

- Soxhlet Extraction will be used for extraction of plant materials

5. Phytochemical evaluation of extracts of crude drugs (Holoptelea Integrifolia)
6. Physicochemical evaluation

- Determination of abroad organic matter
- Measurement of Relative Moisture
- The Extraction Value of Solvents
- Ash content testing

7. Preparation and evaluation of herbal formulation (Holoptelea Integrifolia)
8. Peptic ulcer study
9. Animal study
10. Computation of data
11. Summary & Conclusions
12. Publication
13. Thesis writing

CHAPTER-4

MATERIAL & METHOD

4.1 Plant Profile

The Indian elm, also known as the jungle cork tree or Holoptelea integrifolia, is a species of tree in the Ulmaceae family and a near related of the genuine elms (Ulmus). Its original borders include most of the Indian subcontinent, as well as Indo-China and Myanmar. Typically reaching a height of 20-25 metres, the Indian elm is a massive deciduous tree with a large crown and many ascending branches (occasionally above 30 metres). In shape, they are elliptic-ovate, measuring 8-13 cm in length and 3-6.5 cm in width. The base of a leaf may be spherical or heart-shaped. [90]

Figure 4.1 Holoptelea integrifolia plant and leaves

Table 4.3 Scientific classification
Scientific classification

Kingdom	Plantae
Clade	Angiosperms
Order	Rosales
Family	Ulmaceae
Genus	Holoptelea
Species	H. integrifolia

4.2 Origin and Distribution

The Pacific Islands were the birthplace of the plant species. It inhabits both tropical and temperate zones in the northern hemisphere. India, Nepal, Sri Lanka, Indo-China, Cambodia, Laos, Myanmar, Vietnam, Burma, and China are all protected because of their tropical locations. From Jammu in the west to Assam and Burma in the east, at altitudes of up to 2,000 feet, and farther south from Bengal through Central, Western, and Southern India to the dry region of Ceylon, you may find the outer Himalayas. .[88]

4.2.1Phytochemistry

Holoptelea integrifolia, a versatile medicinal plant, is the sole known source of a large and diverse family of compounds. The plant species include a wide variety of phytochemicals, such as terpenoids, sterols, saponins, tannins, proteins, carbohydrates, and alkaloids. In addition to flavonoids, phenols, and coumarins, H. integrifolia also contains quinines, cardiac glycosides, phenols, and phenols. .[89]

4.2.2Pharmacology

It is well known that H. integrifolia has therapeutic significance in traditional systems and exhibits a variety of pharmacological activities.

- **Antifungal Activity-**H. integrifolia has a wide range of antifungal potential. Alcoholic leaf and stem extracts of H. integrifolia were tested for antifungal activity using the agar well diffusion method. .[90]
- **Antibacterial Activity**-Holoptelea integrifolia leaf extracts in hexane, diethyl ether, acetone, and water were all effective against a lactam-resistant Staphylococcus aureus strain. .[91]
- **Anti-Inflammatory Activity**-The percent suppression of paw edoema after administration of 250 and 500 mg/kg of H. integrifolia aqueous extract was comparable to that seen following administration of indomethacin (10 mg/kg) as a reference medication. .[92]
- **Antiulcer activity-** When the lining of the stomach, the first portion of the small intestine, or even the lower Antidiabetic activity oesophagus, is damaged and bleeds, this is called peptic ulcer disease (PUD). An oral dosage of 500 mg/kg of H. integrifolia leaf methanolic extract considerably decreased the ulcer in rats, it has been reported. .[93]

4.3 Collection, Identification and Authentication of Plant Specimens

The process of collecting, identifying, and authenticating plant specimens requires expertise and adherence to ethical guidelines, including obtaining necessary permits and permissions, respecting local regulations, and promoting sustainable collection practices. .[94]

Holoptelea integrifolia leaves has been washed, cleaned and dried six days. The plant material was mixed into a coarse powder after the drying and kept for further investigations at room temperature. .[95]

4.4Preparation of crude Extracts

After being washed and air dried at a temperature of no more than 50 degrees Celsius, the newly harvested plant materials were dried in a hot air oven.

The plant's dried aerial parts were ground into a powder and then successively extracted in a soxlet device using ethanol. The extraction was continued for 72 hours for each solvent at 40-45 0 C. The extraction was started with hexane then petroleum ether and continued with chloroform and then lastly with ethanol. The solvent was evaporated after the extraction was complete, and the resulting residue was dried and placed in a desiccator for further testing.

At the beginning of this process, the leaves s and leaves are removed off of the tree and then dried and afterwards homogenised into fine powder. The measurement of powder was determined in contrast with natural solvents in a conical carafe. For 24 hours, it was shaken at 190-220 revolutions per minute in a rotary shaker. The fabric from the mushrooms was then collected by centrifugation. Dissolvable refinery equipment was used to retrieve the remaining one-fourth of the original volume. For later use, it is kept at 40 degrees Celsius in close-air bottles. .[96]

Figure 4.2 Extraction Process

4.5 Phytochemical screening of extract

Alkaloids, carbohydrates, fixed oils, flavonoids, glycosides, phytosterol/terpenoids, saponins, and tannins/phenols were analysed qualitatively in accordance with established techniques for preliminary phytochemical screening. Here are the several diagnostic procedures:

4.5.1Test for Glycosides

i) On a watch glass, the extract was combined with a little amount of anthrone. Conc. H_2SO_4 was added to make a paste, and the mixture was slowly warmed over a water bath. The presence of glycosides is denoted by a dark green tint.

ii) Warm 5 millilitres of diluted H_2SO_4 in a water bath in order to extract 200 milligrammes of medication. After filtering, a 5% NaOH solution was added to neutralise the acid extract. To make it alkaline, heat it in a water bath for 2 minutes after adding 0.1 ml of Fehling's solutions A and B. Take note of the amount of red precipitate that forms and compare it to test B's results.

iii) Warm 5 ml of water, not H_2SO_4, and use it to extract 200 mg of the medication in a water bath. After the water has boiled, add the same quantity that the NaOH test above guaranteed would be effective. Add 0.1 ml of Fehling's solutions A and B until the mixture is alkaline. And 2 minutes in a water bath to heat it up. Take note of how much red precipitate there is. Examine how much precipitate was produced in Test B compared to Test A. If test A yields a larger precipitate than test B, then glycosides are detected. .[96]

4.5.2 Test for flavonoids

i) Shinoda’s test

5 ml of 90% alcohol, 0.5 grammes of magnesium turnings, and a concentration of HCl were added to the extract and heated for a few minutes. When flavonoids are present, they cause a material to become pink or red.

ii) Alkaline test

Alcohol and either a 10% NaOH solution or ammonia were added to the extract. The presence of flavonoids is denoted by a dark yellow colour.

iii) Zinc Hydrochloric Acid test

Add a mixture of Zn dust and highly concentrated HCl to this test solution. The presence of flavonoids is shown by the formation of a red colour after a few minutes. .[97]

4.5.3 Test for Alkaloids

i) Dragendorff’s test

A small amount of acetic acid and Dragendroff's reagent were added to the extract, and the mixture was stirred well. The presence of alkaloids is indicated by an orange-red precipitate.

ii) Mayer’s test

Mayer's reagent and diluted hydrochloric acid were added to the extract. Alkaloids are present whenever there is a white precipitate.

iii) Wagner’s test

A few ml of filtrate had Wagner's reagent dropped into it along the test tube's walls. The presence of a reddish-brown precipitate indicates a test launch.

iv) Hager’s test

One or two millilitres of Hager's reagent was added to a few ml of filtrate. Notable yellow precipitate suggests a positive result. .[98]

Figure 4.3 Phyto chemical screening

4.6 Antiulcer activity

Five groups of 150-200 gm albino wistar rats, ranging in age from 4-6 months, were created. Each group contained six wistar albino rats.

- Group I- Control group-treated with vehicle (normal saline) alone, p.o.
- Negative II-control group-treated with Water.
- Group III- Standard drug Ranitidine (50 mg/kg), i.p.
- Group IV- 200mg/kg low dose .
- Group V- 400mg/kg high dose

Wistar albino rats ranging between 150 and 200 grammas were fasted for two and a half days before even being divided into five groups of six.

1. Animal Selection: Wistar rodents weighing between 150-200 were utilized for the study.
2. Fasting: The rodents were subjected to a 24-hour fasting period before administration of the test compound.
3. Test Compound Administration: The test compound was administered orally to the rodents.
4. Restricted Confinement: The rodents were placed in restricted areas at a temperature of 22°C for 7 day.
5. Water Immersion Stress: Following the confinement, the rodents were immersed in water.
6. Evan's Blue Administration: Ten minutes after water immersion, the rodents received intravenous administration of Evan's blue at a dosage of 50 mg/kg.
7. Stomach Collection: The stomachs were collected and tied at both ends, then stored in normal saline.
8. Lesion Examination: The ulcerative lesions were seen the next day after the stomachs were opened along the larger curvature.
9. Gastric Acidity Measurement: Gastric acidity was not assessed using a pH meter.
10. Stomach Juice Collection: Stomach juices were collected by centrifugation at 500 rpm for five minutes, and the volume was measured using a graduated cylinder

4.7 Acute toxicity study

Acute toxicity study was conducted to determine the safe dose by pair of stairs method. The overnight fasted rats were orally administered with holoptelea leaf suspended in 0.5% lukewarm water at limit test dose of 2000 mg/kg body weight. They were later on observed closely for 1 hr, frequently for the next 4 hrs, periodically once in 4 hrs and then on a daily basis, i.e. once 24 hrs. Animals surviving the first 24 hrs were observed for the next 7 day.

CHAPTER-5

RESULT & DISCUSSION

The earliest scientifically characterized treatments for peptic ulcers and the illness they produce date back to the early 1800s. As a result, experts have been debating this disease's causes and remedies for more than two centuries. In 1823, Prout and William employed animal models to show that HCl is responsible for stomach acidity. The acid's corrosive properties were shown to be damaging the gastrointestinal mucosa in the early stages of investigation. For the treatment of peptic ulcers, soda, magnesium, and chalk were regularly prescribed antacids along with dietary advice and rest.

An extremely small percentage of patients who use NSAIDs experience significant morbidity and weakness. Stomach or duodenal ulcers are more likely to develop in people who have a history of using NSAIDs in large doses or who have a major underlying medical condition. Gastric and duodenal mucosal disease is caused by a variety of factors.

It's no surprise that humans have relied on natural resources for food, drink, and medicine for thousands of years. Herbal treatments are used across cultures and time periods, yet the principles of disease and therapy are universal.It's public knowledge that some plants used in medicine have curative effects. Many ancient civilizations relied on herbs for their curative properties. The discovery of herbs' healing properties, documented in the Vedas and the Bible, ushered in an era of widespread usage of these substances. The enormous green pharmacy of ancient herbal remedies and folktales left behind by long-vanished civilizations never ceases to astound. Herbal medical expertise had been handed down verbally from one generation to the next before the advent of written records.

Western medicine began to supplant folk and learned medicine that had been acquired and traded between civilizations as far back as the Ancient Egyptians. People are rediscovering the benefits of traditional medicine.The purpose of herbal medication research and development is to find single and multi- component bioactive natural substances. Traditional knowledge-driven drug discovery will help rediscover drug discovery by providing a robust search engine for targeted natural product research. Herbal medications make up a substantial portion of our current pharmaceuticals. Around 25% of current prescription drugs contain at least one plant-derived active component.

Natural products are believed to be beneficial to health, increasing interest in medicinal plants. In many cases, medicinal plants can be used for short or long periods of time depending on the health concern.

Stomach ulcer risk may be reduced by dietary and changes in behavior. Fractures in the stomach mucosal barrier larger than 5 millimeters can penetrate the muscularis mucosa. Understanding that this virus can be treated and prevented is essential.

Different stomach ulcers necessitate different treatments depending on the cause.The stomach mucosa is protected from the acidic gastric lumen by the body's natural defences. This might cause damage to the stomach lining, increasing the risk of ulcers and stomach tissue injury.

5.1 Physico-Chemical Evaluation of Crude extracts

Macroscopic and microscopic evaluation of the dried drugs were performed to determine various parameters such as color, odour, taste, shape, size, texture etc. by visual inspection and by optical microscopy.

5.2 Physical Test of Crude extract(Table 5.1)

Crude drugs	Physical Test			
	Nature	Colour	Odour	Taste
Holoptelea integrifolia leaves extract	Powder	Greenish	Aromatic	Vary from bitter to astringent

5.3 Extractive Values(Table 5.2)

Crude drugs	ethenol %w/w
Holoptelea integrifolia leaves extract	15.35

5.4 Loss on Drying And Foreign Organic Matter (Table 5.3)

Crude drugs	Loss on drying (% w/w)*	Foreign matter (% w/w)*
Holoptelea integrifolia leaves extract	12.22	3.20

5.5 Phytochemical Screening

The purpose of phytochemical screening is to determine whether or not a given plant extract contains a certain category of phytochemicals. These tests help in the preliminary identification of bioactive compounds in plants and provide insights into their potential pharmacological or medicinal properties. Here are some common phytochemical screening tests performed:

“+”Found
“-“ Not Found

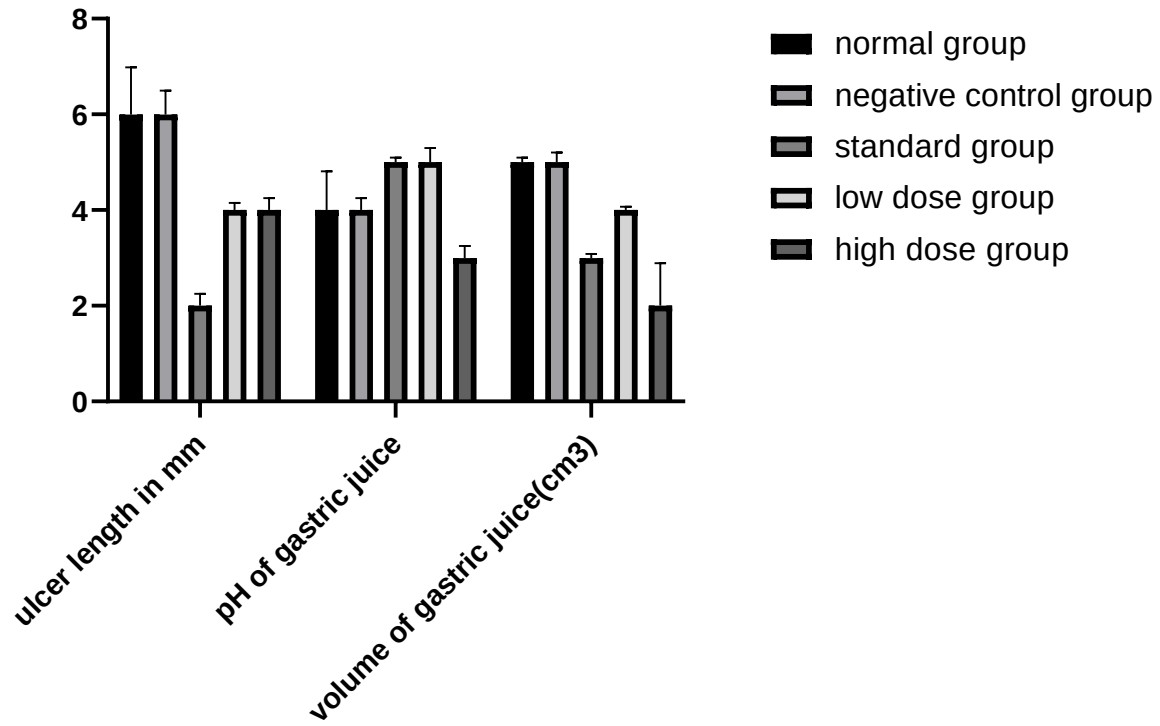
5.7 Ethanol induced ulcer model

In preclinical research, the ethanol-induced ulcer model is often used to examine gastric ulcers in rodents. In order to maximise their vulnerability to ulcer development in the ethanol-induced ulcer model, animals were fasted for a certain amount of time. After the fasting period, the animals are given ethanol, either orally or by injection, in a concentrated form. Ethanol has toxic effects on the gastric mucosa, leading to the development of ulcers. Obtained result are listed below:

Table .5.5: Effect of ethanol induced stress ulcer model

Groups	Ulcer length in (mm)	pH of gastric juice	Volume of gastric juice (cm^3)
Control group	**6.98**	**4.81**	**5.10**
negative group	**6.50**	**4.25**	**5.20**
standard group	**2.25**	**7.10**	**3.08**
Low dose group	**4.15**	**4.30**	**4.07**
High doge group	**4.25**	**5.25**	**2.89**

Figure 5.1



Effect of ethanol induced stress ulcer model

Effect of holoptelea (200, 400 mg/kg) and ranitidine (50 mg/kg) on (a) ulcer length in mm, (b) pH of gastric juice and (c) volume of gastric juice (cm3) in the acidified ethanol-induced gastric ulcer. Data has been presented as mean±SEM. The ulcer length in mm effect ±2.5 standard & holoptelea leaf extract respectively using One-way ANOVA followed by Dunnett's multiple comparison test, comparing with the negative control group.

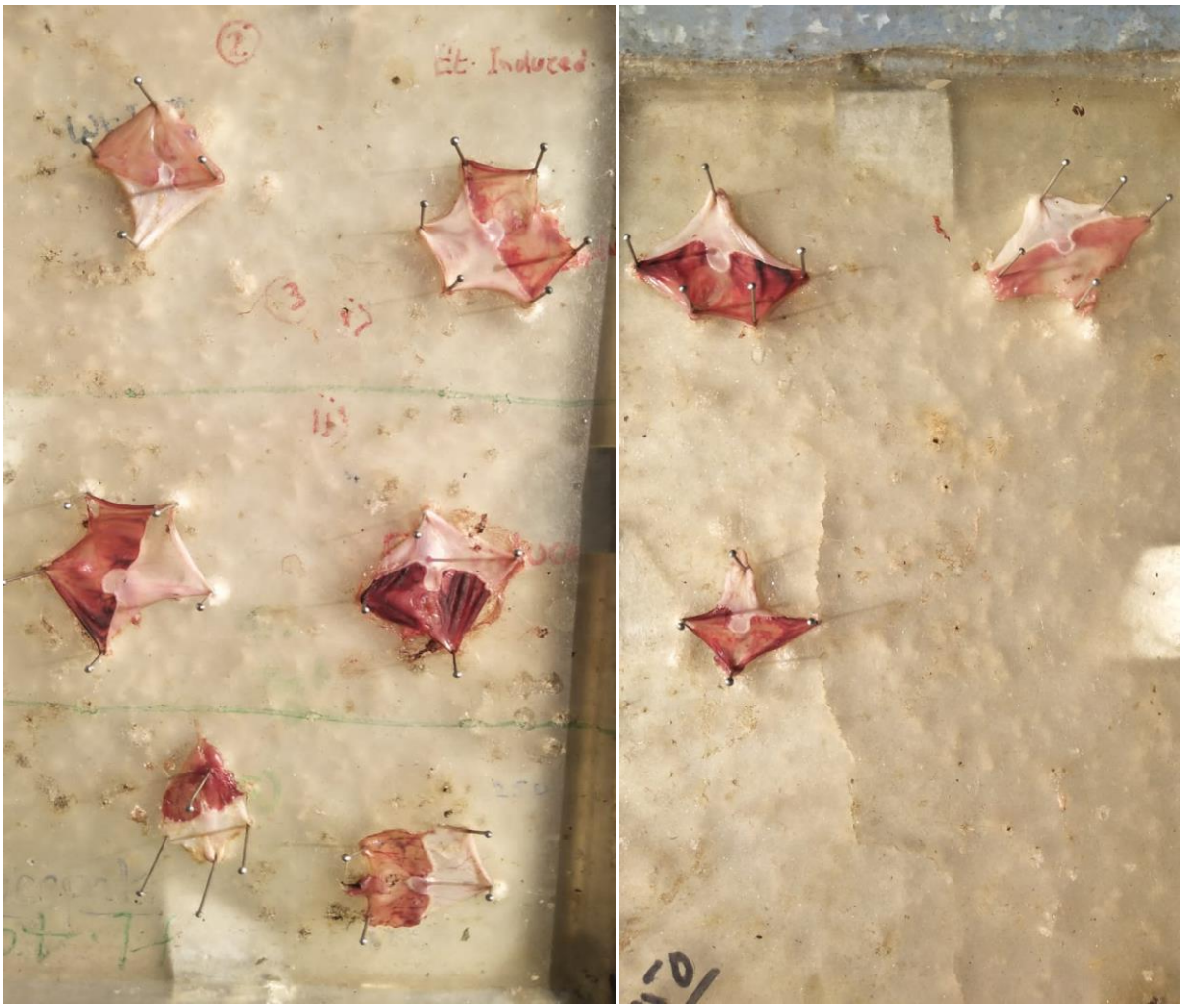


Figure 5.2 Stomach of Animals

5.8 Discussion

Considering *Holoptelea integrifolia* historical use for treating a range of illnesses, there are no records of a scientific evolution of its anti-ulcer activity. A Holoptelea integrifolia leaf ethanolic extract was found to include saponins, alkaloids, flavonoids, phenolic compounds, proteins. The anti-ulcer effects of an ethanolic extract derived from the Holoptelea integrifolia leafs on albino rat were demonstrated in the current study using Pylorus Ligation Induced Ulcer in Rats model. rat were used as the experimental model for the development of anti-ulcer activity because they exhibit clear ulcer lesion. These are clearly useful for evaluating the effects of anti-ulcer activity substances.

The results indicated that treatment of Rat with an ethanolic extract of a plant at doses of 200 mg/kg and 400 mg/kg greatly improved the amount of time spent and the number of entry into open arms.

However, when compared to ranitidine , a traditional medication that reflects plants and anti-ulcer qualities, they decreased the time spent and the frequency of entry in close arms depending on dose.

The results showed that 200 mg/kg and 400 mg/kg doses of an ethanolic extract of a plant's roots significantly increased the amount of time spent.

CHAPTER-6

SUMMARY & CONCLUSION

We summarized these points from study:

- The physical characteristics of the crude extract from Holoptelea integrifolia leaves are as follows: It is in powder form, exhibiting a greenish color. The extract has an aromatic odour and its taste can range from bitter to astringent.
- The extractive value of the Holoptelea integrifolia leaves extract using methanol as the solvent is 15.35% w/w.
- The Holoptelea integrifolia leaves extract has a loss on drying of 12.22% w/w, indicating the percentage of moisture or volatile components present in the extract. The foreign organic matter content in the extract is 3.20% w/w, which refers to the presence of extraneous or undesired organic material in the sample.
- The Holoptelea integrifolia bark extract has a total ash value of 5.20% w/w, indicating the total inorganic residue left after complete incineration of the extract. The water-soluble ash value is 4.15% w/w, representing the percentage of inorganic residue that is soluble in water. The acid-insoluble ash value is 3.25% w/w, indicating the percentage of inorganic residue that remains insoluble in acid after the water-soluble fraction is removed.
- The chemical tests conducted on Holoptelea integrifolia leaves extract indicate the presence or absence of various compounds. Saponins, alkaloids, tannins and phenolic chemicals, flavonoids, and proteins were all identified in the extract. Despite extensive testing, the extract showed no signs of containing steroids, triterpenoids, glycosides, or carbohydrates.
- In order to compare the results of the various groups on ulcer length, gastric juice ph, and gastric juice volume, a cold-water immersion stress ulcer model was utilised. The gastric juice volume, acidity, and ulcer length were all worse in the control group. Gastric juice volume was reduced, acidity was greatest, and ulcer duration was shortened the most in the control group. The low dosage group and the high dose group both had moderate impacts on these parameters, although the high dose group had a somewhat greater decrease in ulcer length and ph of gastric juice than the low dose group.
- Comparisons were made between groups with respect to ulcer length, gastric juice ph, and gastric juice volume using an indomethacin-induced stress ulcer model. Gastric juice volume was greater, gastric juice acidity was lower, and ulcer duration was greater in the control group. When compared to the control group, the standard group significantly improved in terms of ulcer duration, gastric juice ph, and gastric juice volume. There were no drastic changes seen in either the low dose or high dosage groups, however the high dose group did have a shorter ulcer duration and greater gastric juice ph than the low dose group. Both the low-dose and high-dose groups' gastric juice volumes were reduced in comparison to the placebo group.

CHAPTER-7

REFERENCES

1. Tortora, G. J., & Derrickson, B. H. (2017). Principles of Anatomy and Physiology. Wiley.
2. Moore, K. L., Dalley, A. F., & Agur, A. M. R. (2018). Clinically Oriented Anatomy. Lippincott Williams & Wilkins.
3. Vander, A., Sherman, J. H., & Luciano, D. S. (2014). Human Physiology: The Mechanisms of Body Function. McGraw-Hill Education.
4. Guyton, A. C., & Hall, J. E. (2015). Textbook of Medical Physiology. Elsevier.
5. Johnson, L. R. (Ed.). (2012). Physiology of the Gastrointestinal Tract (5th ed.). Academic Press
6. Yamada, T., Alpers, D. H., & Kalloo, A. N. (Eds.). (2015). Textbook of Gastroenterology (6th ed.). Wiley
7. Tortora, G. J., & Derrickson, B. H. (2017). Principles of Anatomy and Physiology. Wiley.
8. Johnson, L. R. (Ed.). (2012). Physiology of the Gastrointestinal Tract (5th ed.). Academic Press.
9. Katz, P. O., Gerson, L. B., & Vela, M. F. (2013). Guidelines for the diagnosis and management of gastroesophageal reflux disease. American Journal of Gastroenterology, 108(3), 308-328.
10. Hershcovici, T., & Fass, R. (2013). Nonerosive reflux disease (NERD): an update. Journal of Neurogastroenterology and Motility, 19(2), 125-133.
11. Baumgart, D. C., & Sandborn, W. J. (2012). Crohn's disease. The Lancet, 380(9853), 1590-1605.
12. Torres, J., Mehandru, S., Colombel, J. F., & Peyrin-Biroulet, L. (2017). Crohn's disease. The Lancet, 389(10080), 1741-1755.
13. Danese, S., Fiocchi, C., & Ulcerative Colitis. (2011). New England Journal of Medicine, 365(18), 1713-1725.
14. Podolsky, D. K. (2002). Inflammatory bowel disease. New England Journal of Medicine, 347(6), 417-429.
15. Baumgart, D. C., & Carding, S. R. (2007). Inflammatory bowel disease: cause and immunobiology. The Lancet, 369(9573), 1627-1640.
16. Talley, N. J., & O'Connor, S. (Eds.). (2017). Clinical Gastrointestinal Endoscopy. Elsevier.
17. Feldman, M., & Friedman, L. S. (Eds.). (2020). Gastrointestinal and Liver Pathology (2nd ed.). Elsevier.
18. Hensel, W., & Kindermann, A. (Eds.). (2018). Gastrointestinal Imaging: A Core Review. Lippincott Williams & Wilkins.
19. Greenberger, N. J., Blumberg, R. S., Burakoff, R., & Peppercorn, M. A. (Eds.). (2020). Current Diagnosis & Treatment: Gastroenterology, Hepatology, & Endoscopy (3rd ed.). McGraw-Hill Education.
20. Malfertheiner, P., Chan, F. K., McColl, K. E., Peptic Ulcer Disease. (2019). The Lancet, 392(10142), 144-154.
21. Feldman, M., Friedman, L. S., & Brandt, L. J. (Eds.). (2020). Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management. Elsevier.

22. American College of Gastroenterology. (2017). Guidelines for the Management of Helicobacter pylori Infection. The American Journal of Gastroenterology, 112(2), 212-239.
23. Malfertheiner, P., Chan, F. K., McColl, K. E. (2017). Peptic Ulcer Disease. The Lancet, 389(10080), 41-54.
24. Talley, N. J., & Hunt, R. H. (Eds.). (2015). Peptic Ulcer Disease. Oxford University Press.
25. Feldman, M., Friedman, L. S., & Brandt, L. J. (Eds.). (2020). Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management. Elsevier
26. Feldman, M., Friedman, L. S., & Brandt, L. J. (Eds.). (2020). Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management. Elsevier.
27. Malfertheiner, P., Chan, F. K., McColl, K. E. (2017). Peptic Ulcer Disease. The Lancet, 389(10080), 41-54.
28. American College of Gastroenterology. (2017). Guidelines for the Management of Helicobacter pylori Infection. The American Journal of Gastroenterology, 112(2), 212-239.
29. Talley, N. J., & Hunt, R. H. (Eds.). (2015). Peptic Ulcer Disease. Oxford University Press.
30. Lanas, A., Chan, F. K., & Peptic Ulcer Bleed Management International Working Group. (2017). Management of acute bleeding from a peptic ulcer. New England Journal of Medicine, 376(12), 1174-1175.
31. Dajani, A. I., Abu Hammour, A. M., & Yousef, Z. H. (2012). Smoking and peptic ulcer in 1. Lanas, A., Dumonceau, J. M., Hunt, R. H., Fujishiro, M., Scheiman, J. M., Gralnek, I. M., ... & Kuipers, E. J. (2019). Non-variceal upper gastrointestinal bleeding: guidelines. Endoscopy, 51(8), 775-794.
32. 2. Cheung, K. S., Chan, E. W., Wong, A. Y., Chen, L., Wong, I. C., & Leung, W. K. (2017). Long-term proton pump inhibitors and risk of gastric cancer development after treatment for Helicobacter pylori: a population-based study. Gut, 66(8), 1352-1361.
33. Chan, F. K., Sung, J. J., & Suen, B. Y. (2007). Therapy of Helicobacter pylori infection for prevention of gastric cancer. Journal of Gastroenterology and Hepatology, 22(8), 1084-1091patients infected with Helicobacter pylori. ISRN Gastroenterology, 2012.
34. Laine, L., & Jensen, D. M. (2012). Management of patients with ulcer bleeding. American Journal of Gastroenterology, 107(3), 345-360.
35. Kuipers, E. J. (1997). Review article: exploring the link between Helicobacter pylori and gastric cancer. Alimentary Pharmacology & Therapeutics, 11(Supplement 1), 3-14.
36. Bjorkman, D. J. (2009). Nonsteroidal anti-inflammatory drug gastropathy. Gastroenterology Clinics of North America, 38(2), 263-279.
37. Targownik, L. E., & Nabalamba, A. (2009). Trends in management and outcomes of acute nonvariceal upper gastrointestinal bleeding: 1993–2003. Clinical Gastroenterology and Hepatology, 7(6), 607-616.
38. Lanas, A., & Chan, F. K. (2017). Peptic ulcer disease. The Lancet, 390(10094), 613-624.
39. Farre, R., & van der Merwe, S. (2019). The molecular pathology of NSAID-induced lesions in the gastrointestinal tract. Trends in Molecular Medicine, 25(11), 1011-1023.
40. Aro, P., Storskrubb, T., Ronkainen, J., Bolling-Sternevald, E., Engstrand, L., Vieth, M., ... & Agréus, L. (2006). Peptic ulcer disease in a general adult population: the Kalixanda study: a random population-based study. American Journal of Epidemiology, 163(11), 1025-1034.
41. Barrett, K. E., Barman, S. M., Boitano, S., & Brooks, H. L. (2017). Gastrointestinal Physiology (2nd ed.). Elsevier.

42. Sachs, G., & Prinz, C. (2013). Gastric acid secretion: Activation, regulation, and inhibition. In Physiology of the Gastrointestinal Tract (5th ed., pp. 1091-1122). Elsevier.
43. Martín, M. G., & Wang, J. (2012). Sulfur amino acid metabolism in the small intestine: a tale of two cyst(e)ines. Trends in Endocrinology and Metabolism, 23(2), 81-88.
44. Bongaerts, G. P., Tolboom, J. J., & Naber, T. H. (2000). The role of bicarbonate ions in digestion. Acta Anaesthesiologica Belgica, 51(2), 107-111.
45. Geibel, J. P., & Wagner, C. A. (2005). Carbanion formation and transport in the gastric H+/K+-ATPase. Journal of Experimental Biology, 208(11), 2029-2039.
46. Davenport, H. W. (2002). Physiology of the Digestive Tract: An Introductory Text. Lippincott Williams & Wilkins.
47. Silen, W. (1995). Physiology of the Gastrointestinal Tract (3rd ed.). Raven Press.
48. Allen, A., Flemström, G., & Garner, A. (2005). Gastroduodenal mucus bicarbonate barrier: protection against acid and pepsin. American Journal of Physiology-Gastrointestinal and Liver Physiology, 288(1), G1-G19
49. HWarren, J. R., & Marshall, B. (1983). Unidentified curved bacilli on gastric epithelium in active chronic gastritis. The Lancet, 321(8336), 1273-1275.
50. Peek Jr, R. M., & Blaser, M. J. (2002). Helicobacter pylori and gastrointestinal tract adenocarcinomas. Nature Reviews Cancer, 2(1), 28-37.
51. Correa, P., & Piazuelo, M. B. (2012). Helicobacter pylori infection and gastric adenocarcinoma. US gastroenterology & hepatology review, 8(6), 393-396.
52. Malfertheiner, P., Megraud, F., O'Morain, C. A., Gisbert, J. P., Kuipers, E. J., Axon, A. T., ... & Graham, D. Y. (2017). Management of Helicobacter pylori infection—the Maastricht V/Florence Consensus Report. Gut, 66(1), 6-30.
53. Laine, L., Jensen, D. M., & Management of Patients With Ulcer Bleeding. American Journal of Gastroenterology, 115(8), 1145-1148.
54. Lanza, F. L., & Chan, F. K. (2017). Peptic ulcer disease. New England Journal of Medicine, 376(24), 2367-2376.
55. Chey, W. D., Leontiadis, G. I., Howden, C. W., & Moss, S. F. (2017). ACG clinical guideline: treatment of Helicobacter pylori infection. American Journal of Gastroenterology, 112(2), 212-239.
56. Hunt, R. H., Xiao, S. D., & Megraud, F. (2015). Helicobacter pylori in developing countries. World Gastroenterology Organisation Global Guideline. Journal of Gastrointestinal and Liver Diseases, 24(3), 319-330.
57. Malfertheiner, P., Megraud, F., O'Morain, C. A., Atherton, J., Axon, A. T., Bazzoli, F., ... & Vakil, N. (2017). Management of Helicobacter pylori infection—the Maastricht V/Florence Consensus Report. Gut, 66(1), 6-30.
58. Graham, D. Y., & Fischbach, L. (2010). Helicobacter pylori treatment in the era of increasing antibiotic resistance. Gut, 59(8), 1143-1153.
59. Wakodkar, Seema & Shuddalwar, Aditya & Baheti, Dr. (2021). Herbal Potentials for Treatment of Peptic Ulcers: A Review. International Journal of Pharmaceutical Sciences Review and Research. 68. 10.47583/ijpsrr.2021.v68i02.019.
60. Singh, Anjani & Vl, Ashoka & Azamthulla, Mohammad. (2022). Herbal Remedies Used for the Treatment of Peptic Ulcer. 8. 346-355

61. Abdel-Sater, Khaled. (2011). Herbal Treatment of Peptic Ulcer: Guilty or Innocent. 10.5772/18926.
62. Murthy, Sudarshan. (2011). Strategies for Gastric Ulcer Therapy by using herbal drugs.
63. Kaur, D. & Rana, & Sharma, N. & Kumar, Shikshit. (2012). Herbal drugs with anti ulcer activity. Journal of Applied Pharmaceutical Science. 2. 160-165.
64. Deb Roy, Saumendu & Chakraborty, Jashabir & Shil, Dibyendu & Das, Sumit & Begum, Narzima. (2013). Herbs Used In Peptic Ulcer : A Review. International Journal of Pharmaceutical Research and Allied Science.. 2. 9-23.
65. Ardalani, Hamidreza & Hadipanah, Amin & Sahebkar, Amirhossein. (2020). Medicinal Plants in the Treatment of Peptic Ulcer Disease: A Review. Mini Reviews in Medicinal Chemistry. 20. 662-702. 10.2174/1389557520666191227151939.
66. Kumar, M. & Niyas, K. & Mani, T. & Rahiman, Fasalu & Kumar, B.. (2011). A review on medicinal plants for peptic ulcer. Der Pharmacia Lettre. 3. 414-420.
67. Kuna, Lucija & Jakab, Jelena & Smolic, Robert & Raguz-Lucic, Nikola & Vcev, Aleksandar & Smolic, Martina. (2019). Peptic Ulcer Disease: A Brief Review of Conventional Therapy and Herbal Treatment Options. Journal of Clinical Medicine. 8. 179. 10.3390/jcm8020179.
68. Ansary, Sayed & Y, Jyothi & V, Rajendra. (2020). A Comprehensive Review on Antiulcer properties of Herbal drugs. International Journal of Research in Pharmaceutical Sciences. 11. 3637-3644. 10.26452/ijrps.v11i3.2524.
69. Rambhai, Pahadiya & Sisodia, Siddhraj. (2018). Indian Medicinal Plants For Treatment of Ulcer: Systematic Review. UK Journal of Pharmaceutical Biosciences. 6. 38. 10.20510/ukjpb/6/i6/179237.
70. Vanan, Thillai. (2013). A REVIEW ON ANTI-ULCER HERBS IN SIDDHA MEDICINE. IJPRBS.
71. Vimala, G & Shoba, F. (2014). A Review on Antiulcer Activity of Few Indian Medicinal Plants. International journal of microbiology. 2014. 519590. 10.1155/2014/519590.
72. Bansal, Vijay & Goyal, Sandeep & Goswami, Dhruba & Singla, Shiffali & Rahar, Sandeep & Kumar, Suresh. (2009). Herbal approach to peptic ulcer disease- review. J Biosci Tech. 1. 52.
73. Sadacharam, V & Thillaivanan, S & Kanagavalli, K & Parthiban, P. (2013). A review on anti –ulcer herbs in siddha medicine international journal of pharmaceutical research and bio-science paper-qr code.
74. Radhakrishna, Kollipara. (2014). Potential Use of Herbal Medicines in the Treatment of Diabetic Foot Ulcers. Medical Science Educator. 14. 34-42.
75. Priyanka,. (2015). Some of the medicinal plants with Anti-Ulcer activity- A Review. Journal of Pharmaceutical Sciences and Research. 7. 772-775.
76. Gupta, Mukta & Kapoor, Bhupinder & Gupta, Reena & Singh, Naresh. (2021). Plants and phytochemicals for treatment of peptic ulcer: An overview. South African Journal of Botany. 138. 105-114. 10.1016/j.sajb.2020.11.030.
77. B, Anbarasan & G, Anitha & S, Jayapriya & N, Anbu & Kanakavalli, Kadarkarai. (2017). Anti-ulcer activity of Medicinal Herbs - A Review. International Journal of Current Research in Chemistry and Pharmaceutical Sciences. 4. 37-43. 10.22192/ijcrcps.2017.04.06.007.

78. Singh, Amit & Singh, Sandeep & Singh, Prem & Srivastava, Akhileshwar & Pandey, Kapil & Kumar, Ajay & Yadav, Himansu. (2018). Biotechnological aspects of plants metabolites in the treatment of Ulcer: A new prospective. Biotechnology Reports. 18. 10.1016/j.btre.2018.e00256.
79. Anna, Gawron-Gzella & Witkowska-Banaszczak, Ewa & Dudek, Marlena. (2005). [Herbs and herbal preparations applied in the treatment of gastric hyperacidity, gastric and duodenal ulcer in cigarette smokers]. Przegląd lekarski. 62. 1185-7.
80. Gohar, A. A., & Zaki, A. A. (2014). Assessment of some Herbal Drugs for Prophylaxis of Peptic Ulcer. Iranian journal of pharmaceutical research : IJPR, 13(3), 1081–1086.
81. Roy, A. J., Maut, C., Gogoi, H. K., Ahmed, S. I., & Kashyap, A. (2022). A Review on Herbal Drugs Used in the Treatment of Peptic Ulcer. Current drug discovery technologies, 10.2174/1570163820666221212142221. Advance online publication. https://doi.org/10.2174/1570163820666221212142221
82. ME, Lauret & M, Rodriguez-Pelaez & Perez, Ivett & Rodrigo, Luis. (2015). Peptic Ulcer Disease. Journal of Gastroenterology and Hepatobiliary Disorders. 01. 10.19104/jghd.2015.105.
83. Jaiswal, Falguni & Awani, Rai & Wal, Pranay & Wal, Ankita & Singh, Shashi. (2021). Peptic ulcer: a review on etiology, pathogenesis and treatment. Asian Journal of Pharmaceutical Education and Research. 10. 1. 10.38164/AJPER/10.4.2021.1-17.
84. Erceg, D. & Milojeviæ, P.. (2010). Ulcers: Causes, diagnosis, and treatment.
85. Sivakumar, Aran & Stubbs, Benjamin. (2021). Peptic ulcer disease. InnovAiT: Education and inspiration for general practice. 14. 372-378. 10.1177/17557380211005791.
86. Habeeb, Aejaz & Tiwari, Santosh & Avinash, Bardia & Khan, Shaswathi & Vishwakarma, Sandeep & Habeeb, Safwaan & Khan, Dr. Aleem. (2016). Peptic Ulcer Disease: Descriptive Epidemiology, Risk Factors, Management and Prevention.
87. Mouzan, Mohammad & Abdullah, Asaad. (2004). Peptic Ulcer Disease in Children and Adolescents. Journal of tropical pediatrics. 50. 328-30. 10.1093/tropej/50.6.328.
88. Malfertheiner, Peter & Chan, Francis K.L. & Mccoll, Kenneth. (2009). Peptic ulcer disease. Lancet. 374. 1449-61. 10.1016/S0140-6736(09)60938-7.
89. Ganaie, & Yadav, Surender. (2014). Holoptelea integrifolia (Roxb.) Planch: A Review of Its Ethnobotany, Pharmacology, and Phytochemistry. BioMed research international. 2014. 401213. 10.1155/2014/401213.
90. Srivastava, J. & Prasad, S.K. & Dwivedi, K.N. & Pandey, H.P.. (2013). Holoptelea integrifolia Planch: A potential Ayurvedic medicinal plant. International Journal of Pharmaceutical Sciences Review and Research. 21. 281-286.
91. Kumar, Dinesh & Kumar, Karunesh & Gupta, Jyoti & Bishnoi, Navita & Kumar, Sunil. (2012). A mini review on chemistry and biology of Holoptelea integrifolia Roxb. Planch (Ulmaceae). Asian Pacific Journal of Tropical Biomedicine. 2. S1200-S1205. 10.1016/S2221-1691(12)60384-0.
92. More, Dr.D.R & Nalla, manoj kumar. (2021). Studies on phytochemical analysis of the leaves of Holoptelea integrifolia (ROXB.) plant the wonders of a medicinal tree.

93. Kumar, Vijay & Singh, Simranjeet & Bhadouria, Ragini & Singh, Ravindra & Prakash, Om. (2019). Phytochemical, Analytical And Medicinal Studies Of Holoptelea Integrifolia Roxb. Planch - A Review. Current Traditional Medicine. 05. 10.2174/2215083805666190521103308.
94. Sharma, Shrinivas. (2023). Evaluation of antidiarrhoeal potentials of ethanolic extract of leaves of Holoptelea integrifolia in mice model. International Journal of PharmTech Research CODEN(USA): IJPRIF ISSN. 1. 974-4304.
95. Mahmud, Shaukat & Shareef, Huma & Ahmad, Maryam & Gouhar, Shahnaz & Rizwani, Ghazala. (2010). Pharmacognostic studies on fresh mature leaves of Holoptelea integrifolia (ROXB) Planch. Pakistan Journal of Botany. 42.
96. Kumar, Vijay & Singh, Simranjeet & Bhadouria, Ragini & Singh, Ravindra & Prakash, Om. (2019). Phytochemical, Analytical And Medicinal Studies Of Holoptelea Integrifolia Roxb. Planch - A Review. Current Traditional Medicine. 05. 10.2174/2215083805666190521103308.
97. Sharma, Shrinivas. (2023). Evaluation of antidiarrhoeal potentials of ethanolic extract of leaves of Holoptelea integrifolia in mice model. International Journal of PharmTech Research CODEN(USA): IJPRIF ISSN. 1. 974-4304.
98. Mahmud, Shaukat & Shareef, Huma & Ahmad, Maryam & Gouhar, Shahnaz & Rizwani, Ghazala. (2010). Pharmacognostic studies on fresh mature leaves of Holoptelea integrifolia (ROXB) Planch. Pakistan Journal of Botany. 42.