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STUDY AND EVALUATION OF AEGLE MARMELOS AS ANTI-ULCER AGENTS

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ABSTRACT

Peptic ulcers are a broad term that includes ulcers of digestive tract in the stomach or the duodenum. The formation of peptic ulcers depends on the presence of acid and peptic activity in gastric juice plus a breakdown in mucosal defenses. There are two major factors that can disrupt the mucosal resistance to injury: non-steroidal anti-inflammatory drugs (NSAIDs) example, aspirin and Helicobacter pylori infection. Numerous natural products have been evaluated as therapeutics for the treatment of a variety of diseases, including peptic ulcer. There has been considerable pharmacological investigation into the antiulcer activity of some compounds. In this work, we shall review the literature on different medicinal plant and alkaloids with antiulcer activity. This article reviews the antiacid/anti- peptic, gastroprotective and/or antiulcer properties of the most commonly employed herbal medicines and their identified active constituents. The experimental parameters used for antiulcer activity were cold restraint stress-induced ulcer model, Diclofenac- induced ulcer model in rats, (HCl–ethanol)-induced ulcer in mice and water immersion stress-induced ulcer in rats. The ideal aims of treatment of peptic ulcer disease are to relieve pain, heal the ulcer and delay ulcer recurrence. About 70% of patients with peptic ulcer disease are infected by Helicobacter pylori and eradication of this microorganism seems to be curative for this disease. This article reviews drugs derived from medicinal plant more commonly used in the world for peptic ulcer and, if reported, the antiulcer activity. This article will be concerned only with the antiulcer and gastro- protective effects.

INTRODUCTION TO AEGLE MARMELOS-

Aegle Mamelos, commonly known as bael, is a sacred medicinal plant belonging to the family Rutaceae. Native to India and Southeast Asia, it has been valued in traditional systems of medicine such as Ayurveda, Siddha, and Unani for its broad spectrum of therapeutic benefits. Various parts of the plant — including its leaves, fruit, bark, and roots possess medicinal properties.

Among its many uses, Aegle marmelos has gained significant attention for its anti-ulcer activity. Scientific studies have demonstrated that extracts from its leaves and unripe fruit provide gastroprotective effects by reducing gastric acidity, increasing mucosal defense, and promoting ulcer healing.

Because of its wide-ranging medicinal applications, Aegle marmelos is often referred to as a "miraculous medicinal tree". The plant also exhibits antimicrobial, anti-diabetic, anti-inflammatory, and antioxidant properties.

An ulcer is basically an inflamed break in the skin or the mucus membrane lining the alimentary tract. Ulceration occurs when there is a disturbance of the normal equilibrium caused by either enhanced aggression or diminished mucosal resistance. About 19 out of 20 peptic ulcers are duodenal. Gastric ulcers, found in the stomach wall, are less common. The gastric mucosa is continuously exposed to potentially injurious agents such as acid, pepsin, bile acids, food ingredients, bacterial products (Helicobacter pylori) and drugs.

These agents have been implicated in the pathogenesis of gastric ulcer, including enhanced gastric acid and pepsin secretion, inhibition of prostaglandin synthesis and cell proliferation growth, diminished gastric blood flow and gastric motility.

1. Drug treatment of peptic ulcers is targeted at either counteracting aggressive factors or stimulating the mucosal defenses;
2. The goals of treating peptic ulcer disease are to relieve pain, heal the ulcer and prevent ulcer recurrence.

A large number of spices and herbs have been evaluated by various researchers for their antiulcer effects to achieve a favorable outcome. Large numbers of medicinal plants and dietary nutrients have been shown to possess gastro-protective activities such as Aloe, Terminalia Cebula, Vetiveria, Ziziinoides, Ginseng, Capsicum etc.

Nature has provided a complete storehouse of remedies to cure ailment of mankind. About 80% of the world's population depends wholly or partially on traditional medicine for its primary health care needs. According to a survey (1993) of World Health Organization, the practitioners of traditional system of medicine treat about 80% of patients in India, 85% in Burma and 90% in Bangladesh. Herbal medicines, as the major remedy in traditional medical systems, have been used in medical practice for thousands of years and have made a great contribution to maintain human health. The medicinal plants are rich in secondary metabolites (which are potential sources of drugs) and essential oils of therapeutic importance. The important advantages claimed for therapeutic uses of medicinal plants in various ailments are their safety besides being economical, effective and their easy availability.

Aegle marmelos (L.) Correa (*A. marmelos*), commonly known as Bael belonging to the family Rutaceae, has been widely used in indigenous systems of Indian medicine due to its various medicinal properties. *A. marmelos* is native to Northern India, but widely found throughout the Indian Peninsula and in Ceylon, Burma, Bangladesh, Thailand and Indo-China. It is a medium to large sized deciduous glabrous, armed tree with the axillary and 2.5 cm long alternate trifoliate leaves, short flower and globular fruits.

Fig no. 1- Aegle Maemrlos plant.

Table 1-TAXONOMICAL CLASSIFICATION OF AEGLE MARMELOS:-

Kingdom	**Tracheobionta**
Super division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Order	Sapindales
Family	Rutaceae
Subfamily	Aurantioideae
Genus	Aegle
Species	Aegle marmelos
Common name	Bacl patra,bael

1.2.1 PARTS OF A. MARMELOS:-

Bark:- The bark of A. marmelos is brownish or greyish in color and it consist straight long spinal column. It comprises clear and transparent gum which frequently releases from the injured tranches and become solidify Bark is rich in a variety of chemical constituents, **including polysaccharides, phenolic polymers like lignin and tannins, and lipids like suberin.**

Uses:

Traditional Medicine:

Bark extracts are used for their anti-microbial, antioxidant, anti-inflammatory, and wound-healing properties.

Industrial Applications:

Bark can be used to create bio-adhesive resins, foams, coatings, surfactants, and pigments.

Fig no. 2-Bark of Aegle Marmelos.

Leaves:- The leaf of A. marmelos is trifoliate, alternate, ovate with pointed tip and rounded boe. Each leaf has 4 to 12 pairs of side veins at the margin. Young leaves are pale green in color with finely hairy appearance while mature leaves are dark green and completely smooth.

Leaves contain a variety of chemical constituents**, alkaloids, coumarins, and flavonoids**

Uses:

- **Anti-diabetic:**

Some constituents, particularly flavonoids and phenolic compounds, have shown potential for regulating blood sugar levels.

- **Anti-inflammatory:**

Bael leaves have been shown to possess anti-inflammatory properties, which may help in treating conditions like asthma and arthritis.

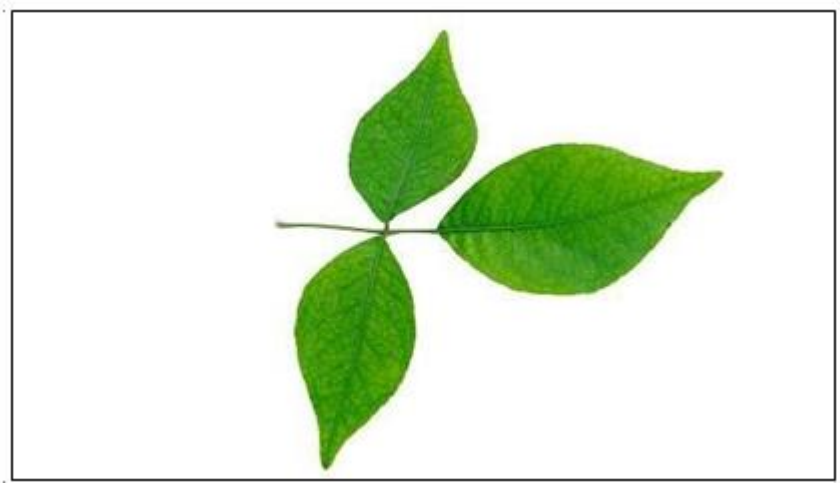

Fig no. 3-Leaves of Aegle Marmelos.

Flowers:- The flowers of A. marmelos are pale green or yellowish in color and usually visible young leaves The calyx is flat with 4 or 5 small teeth and the four or five petals of 6-8 mom overlap in the bud. Stamens have light brown, short filaments and short style anthers.

The Aegle marmelos flower, like other parts of the plant, contains various chemical constituents with potential medicinal properties. These include **alkaloids, coumarins, terpenoids, and essential oils.**

Use:

- **Astringent and Antiseptic:** Used for its ability to constrict tissues and prevent infection.

- **Conjunctivitis:** "Marmala water" (distilled from the flower) is used to treat conjunctivitis.

Fig no. 4 Flowers of Aegle Marmelos.

Fruit:-The frabs of A. marmelos have a diameter around 5-10cm. It has hard outer shell with y petr shape. It is green in color in unripe condition while it turns into yellowish in color in by zipe condition. The fruits take zround 11 months to achieve fully ripe condition. Inside the della flled with aromatie orange pulp.

The fruits of Aegle marmelos are rich in **flavonoids, terpenoids, carotenoids and coumarins.**

Use:

- **Antidiabetic Activity:** Some compounds in bael, like aegelin, have been shown to have antihyperglycemic effects.
- **Antioxidant Activity:** The phenolic compounds and flavonoids in bael possess antioxidant properties, helping to protect against oxidative stress.

Fig no. 5-Fruit of Aegle Marmelos.

Seeds:- The seeds of A. marmelos are small, hard and flattened-oblong and bearing woolly heirs The seeds are around 1 cm in length. Each seeds are enclosed in sac of adhesive and vasparent mucilage.

The seeds of Aegle marmelos (Bael) contain various chemical constituents and have been traditionally used for medicinal purposes. The seeds are rich in **fatty acids like ricinoleic acid and also contain alkaloids, coumarins, and essential oils.**

Use:

- **Digestive Issues:**

Bael seeds have been used to treat constipation, diarrhea, and other digestive problems.

- **Fertility Control:**

Some studies suggest that bael extracts, including those from seeds, may have antifertility effects, potentially impacting sperm motility and reducing male fertility.

Fig no. 6-Seeds of Aegle Marmelos.

PHYTOCHEMISTRY OF A. MARMELOS:-

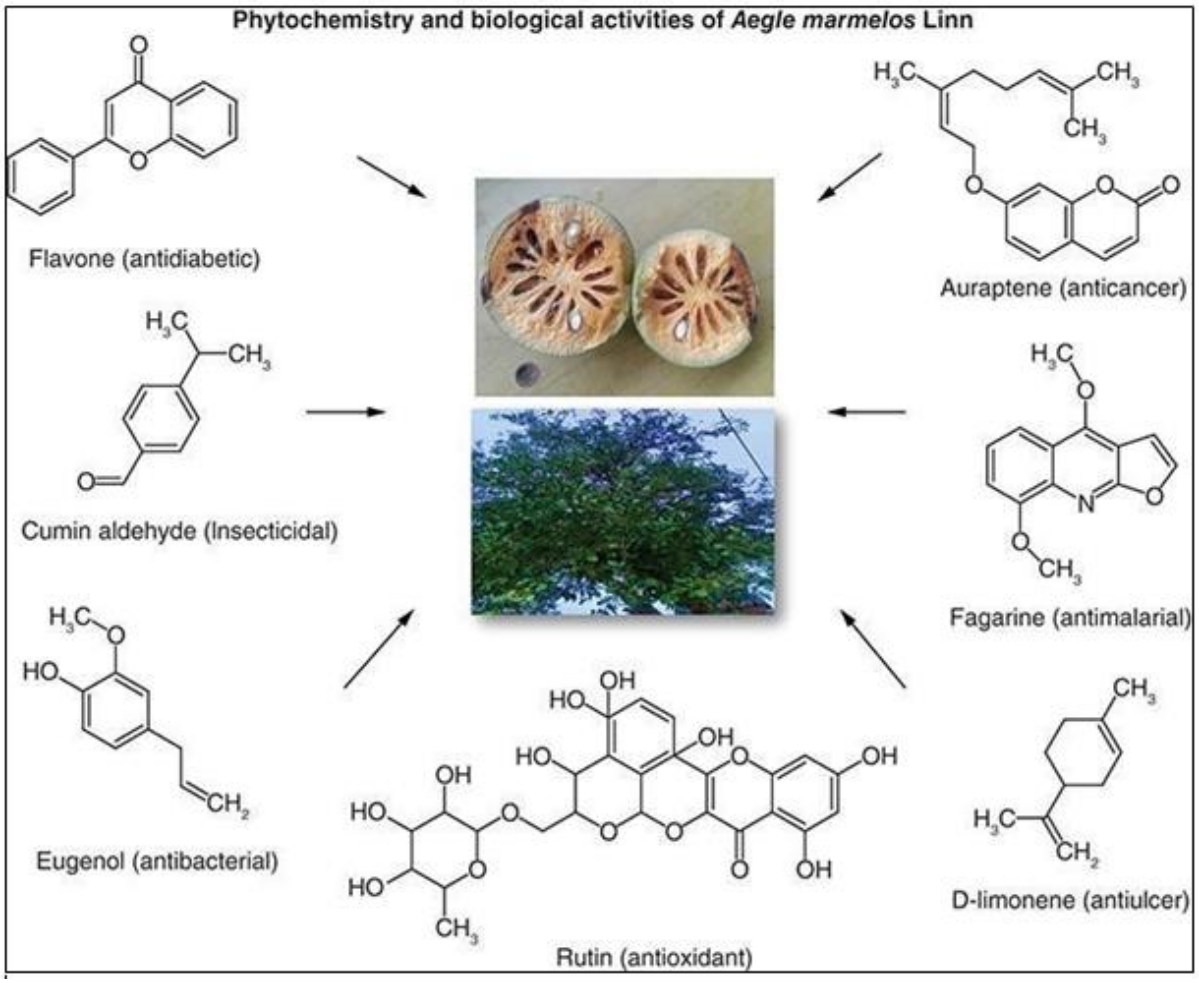

Fig no. 7-Aegle Marmelos Structure.

PEPTIC ULCER:-

Peptic ulcer is one of most common gastrointestinal disease that affects the 10% of the global population. It can develop at any age and duodenal peptic ulcers account for about 19 of every 20 cases. An approximate of 15,000 mortalities is attributed to peptic ulcers every year. Peptic ulcer bleeding and perforation is estimated to occur annually in 19.4–57 and 3.8–14 cases per 100,000 people, respectively. The average long-term repetition of perforation was 12.2%, while the average 7-day repetition of bleeding was 13.9%. Antacids and antiulcer medications both are share 6.2 billion rupees and 4.3% market share of the Indian pharmaceutical market.

Peptic ulcer disease is usually occurs in gastrointestinal tract. Peptic ulcers are open sores that develop on the inside lining of stomach and the upper portion of small intestine. Stomach pain is the most common symptom of peptic ulcer. "Peptic" means it is associated to digestion.

The word "Peptic" is derived from pepsin which is major digestive enzyme that produces by stomach. Stomach acid and pepsin are major active component of stomach juices that helps in food digestion and these juices are highly corrosive in nature. These juices also pass into the upper part of small intestine.

METHOD-

The most effective technique for continuously extracting a solid using a denied solvent, and it bears the name of the German agricultural scientist Franz Riner von Soxhlet. continuous heat extraction or a continuous solid/liquid extraction is involved. The apparatus used to extract glass is called a Soxhlet extractor, It features a condenser on top, an chamber, a siphon tube and a spherical bottom flask. Plant material that has been brief ground and finely powdered is carefully put into a porous bag (thimble) made of sturdy and proper or a clean cloth**.**

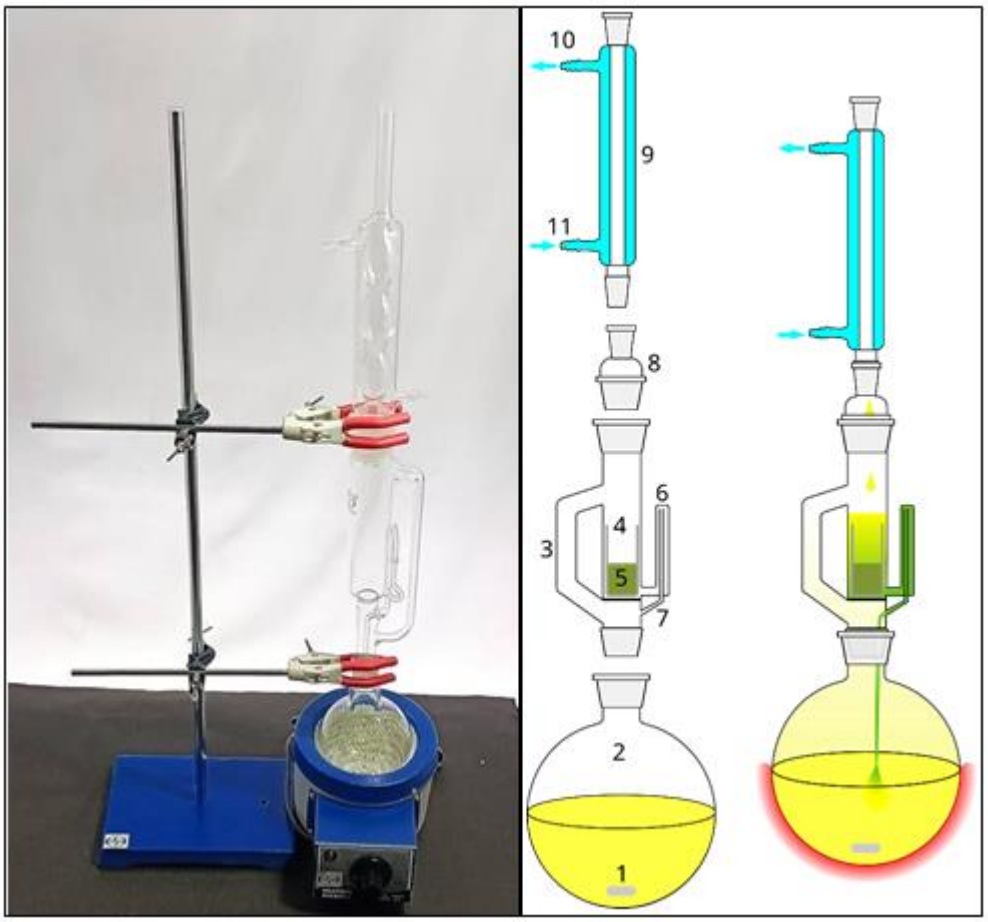

FIG NO. 9- SOXHLATION APPARATUS.

PROCEDURE FOR SOXULATION: -

✓ Ground the brunt course powder and weight 200gm

- ✓ Transfer course powder into Soxhlet apparatus
- ✓ Add the solvent 500 ml (approx.)
- ✓ Hent the solvent at appropriate temperature
- ✓ Continued the process for 72 hrs. successively for each of solvents
- ✓ Collect each extracted material separately.
- ✓ One kilogram of A. marmelos leaves were collected, sun-dried, and then coarsely ground in a mechanical grinder. The Drug Research Laboratory at the Center for Advanced Research of Science (CARS), Dhaka University, developed the aqueous extract. The powdered dried plant terial was steeped for 72 hours at room temperature in distilled water and then filtered. A. marmelos semi-liquid extract was produced by concentrating the filtrate in a vacuum rotator (40-50 C), and it was then stored at 4 C until needed. To achieve the desired centration, the extract was diluted with a predetermined volume of distilled water before Seing used.

DETERMINATION OF ANTI-ULCER ACTIVITY OF AEGLE MARMELOS:-

Preparation of Plant Extract

- **Plant material**: Collect and authenticate *Aegle marmelos* leaves, fruits, or bark.
- **Drying and powdering**: Shade dry the plant parts and grind to a fine powder.
- **Extraction method**: Use aqueous or alcoholic extraction via Soxhlet apparatus or maceration.
- **Concentration**: Evaporate the extract under reduced pressure and store at 4°C.

Assessment Parameters

- **Ulcer index**: Score based on the number and severity of lesions.
- Gastric volume and pH
- **Total acidity and free acidity**
- **Mucus content**: Alcian blue binding method
- **Histopathology**: Stomach tissue examination under microscope

Statistical Analysis

- **Mayer's Test:**

Mayer's reagent is added to the sample. A yellowish or white precipitate confirms the presence of alkaloids.

- *Wagner's Test:*

Wagner's reagent is added to the sample, and a brownish precipitate indicates the presence of alkaloids.

- *HPLC (High-Performance Liquid Chromatography):*

This technique separates and identifies coumarins based on their chemical properties, allowing for precise quantification.

- **HPTLC (High-Performance Thin-Layer Chromatography):**

Another method for separating and visualizing coumarins, offering a quick and cost- effective way to assess the presence and concentration of different coumarins.

Comparison

- Compare effects of *Aegle marmelos* with standard anti-ulcer drugs like ranitidine or omeprazole.

RESULTS AND DISCUSSION

The present study was undertaken to evaluate the anti-ulcer potential of Aegle marmelos (Bael) leaf extract using various experimentally induced ulcer models in rats. The extract was tested for its efficacy against pylorus ligation-induced ulcers and ethanol-induced gastric mucosal damage.

The results clearly indicate that Aegle marmelos possesses significant anti-ulcer activity. The gastroprotective effects may be attributed to multiple mechanisms including reduction in gastric acid secretion, enhanced mucosal defense, and free radical scavenging activity due to the presence of flavonoids and tannins. The dose-dependent response suggests that higher concentrations of the extract offer greater protection.

Histological observations supported the biochemical findings, showing a relatively intact mucosal layer in treated groups, whereas severe disruption and hemorrhagic lesions were observed in the control group.

These findings are consistent with previous reports on the traditional use of Aegle marmelos in gastrointestinal disorders and provide scientific evidence supporting its efficacy as a natural anti-ulcer agent.

Phytochemical Screening

Preliminary phytochemical analysis of the Aegle marmelos extract revealed the presence of alkaloids, flavonoids, tannins, saponins, and phenolic compounds. These constituents are

known to contribute to gastroprotective and antioxidant properties, which are relevant in anti ulcer activity.

Pylorus Ligation-Induced Ulcer Model

In this model, rats treated with Aegle marmelos extract (200 mg/kg and 400 mg/kg) exhibited a significant decrease in ulcer index compared to the control group. The reduction in gastric volume, free acidity, and total acidity was statistically significant($p<0.05$), indicating the protective effect of the extract against gastric hypersecretion and mucosal erosion.

Ethanol-Induced Ulcer Model:-

In the ethanol-induced ulcer model, pre-treatment with Aegle marmelos significantly protected the gastric mucosa from necrotic lesions. The ulcer index was considerably lower in treated groups compared to the control. Histopathological examination confirmed reduced epithelial damage, edema and hemorrhage in extract-treated groups.

Table 2: Parameter and Observation/Value.

Group	Ulcer index	Gastric Volume(ml)	Free Acidity(mEq/L)	Total Acidity (mEq/L)
Control	12.8 ± 1.2	5.3 ± 0.4	48.2 ± 2.1	72.4 ± 3.5
Standard (Omeprazole)	3.2 ± 0.7	2.1 ± 0.2	18.4 ± 1.3	27.6 ± 1.8
A. marmelos 200 mg/kg	6.8 ± 0.9	3.6 ± 0.3	30.5 ± 1.8	45.2 ± 2.7
A. marmelos 400 mg/kg	4.1 ± 0.8	2.5 ± 0.2	22.8 ± 1.4	31.4 ± 2.0

Table 3: Positive and Negative Effects of Chemicals Used in Aegle Marmelos As Anti Ulcer Agents.

Group	Ulcer Index	Inhibition (%)
Control	14.6 ± 1.3	-
Standard (Ranitidine)	2.1 ± 0.5	85.6%
A. marmelos 200 mg/kg	5.9 ± 0.6	59.6%

A. marmelos 400 mg/kg	3.4 ± 0.4	76.7%

CONCLUSION:-

➢ The present study demonstrates that Aegle marmelos possesses significant anti-ulcer activity in both pylorus ligation and ethanol-induced gastric ulcer models. The extract showed a dose-dependent reduction in ulcer index, gastric acidity, and mucosal damage, which was comparable to standard anti-ulcer drugs.

➢ The anti-ulcer effects of Aegle marmelos may be attributed to its ability to reduce gastric acid secretion, enhance mucosal protection, and exert antioxidant effects due to the presence of bioactive constituents such as flavonoids, tannins, and phenolic compounds.

➢ These findings provide scientific validation for the traditional use of Aegle marmelos in the treatment of peptic ulcers and support its potential as a natural, plant-based anti ulcer remedy. However, further studies including isolation of active compounds, mechanism of action, and clinical evaluations are needed to fully establish its therapeutic efficacy and safety.

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