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Anti-Ulcerogenic Potential of Phyllanthus emblica Seed Extract: A Preclinical Study in the Context of Formulation Science

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ABSTRACT

Several factors can contribute to the development of ulcers in humans, including stress, chronic use of anti-inflammatory drugs, and other unidentified causes. The underlying mechanism involves an imbalance between aggressive factors and the maintenance of mucosal integrity, which relies on the body's natural defense mechanisms. Traditional healers have long relied on various native plants and their derivatives to treat peptic ulcers. In India, *Phyllanthus emblica,* an evergreen tree, is commonly used by traditional practitioners for gastric ulcer healing. This study aimed to evaluate the in-vitro antiulcer activity of *Phyllanthus emblica* seed aqueous extract (AE). The anti-ulcer activities were assessed using various doses of the aqueous extract (100 mg, 500 mg, 1000 mg, and 1500 mg) through an in-vitro method known as the H+/K+ - ATPase inhibition activity method. The extract exhibited a significant decrease in acid neutralizing capacity (ANC) compared to the standard Aluminum hydroxide + Magnesium hydroxide (500 mg). The antiulcer properties of *Phyllanthus emblica* seed powder have been extensively studied, highlighting the efficacy of its active constituents.

Keywords: *Anti-ulcer, Anti-inflammatory drugs, acid neutralizing capacity, peptic ulcers, Phyllanthus emblica.*

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1. INTRODUCTION

"Peptic ulcers are a disease of the gastrointestinal system caused by an imbalance between aggressive forces (acid, pepsin, and Helicobacter pylori) and defensive factors (bicarbonate secretion, prostaglandins, gastric mucus, and inherent resistance of mucosal cells) [1]. Peptic ulcers arise when harmful stimuli outweigh protective mechanisms [2]. Infection with Helicobacter pylori, acid-pepsin hypersecretion, NSAIDs, tobacco use, psychological stress, rapid gastric emptying, and the syndrome of Zollinger-Ellison," characterized by excessive and uncontrollable acid production, can all disrupt this

balance and lead to ulcer formation [3-5]. Side effects are common while using synthetic medications for ulcer treatment, including antacids, anticholinergics, antacids, cytoprotectants, demulcents, prostaglandin analogues, and proton pump inhibitors. Therefore, herbal treatments are seen as alternatives [6] that are superior for treating peptic ulcers. Nausea, stomach discomfort, constipation, and diarrhea have been linked to proton pump inhibitors (omeprazole, lansoprazole), whereas gynecomastia and decreased libido have been linked to H_2 receptor antagonists (cimetidine). Research into medical plants is widespread because of the promise for novel treatments with fewer or no bad effects, which is a response to the problems associated with synthetic pharmaceuticals. Because of their low toxicity, cheap cost, and minimal risk of side effects, herbal drugs are often regarded as a secure option for ulcer therapy [7-8]. Herbal medicine, also called botanical medicine or herbalism, utilizes plants for healing purposes, treating ailments, and enhancing well-being. Herbalists, naturopaths, Ayurvedic doctors, homeopaths, and practitioners of traditional medicine are all involved. Natural plant chemicals are thought to have beneficial effects on health. [11]. Plant-based medicine operates on the idea that some plant compounds have therapeutic effects. Seeds, leaves, stems, bark, roots, flowers, and extracts have long been used in herbal medicine. These remedies were administered in various forms: raw, as teas or tinctures, topically, in liquid preparations, or as pills and capsules. Initially, plants were consumed raw or brewed into soups and teas. Over time, they were dried and crushed for different applications. Their usage was often based on superstitions or visual cues, but as scientific understanding advanced, herbal remedies became more refined. Today, herbs and plants serve as the foundation for many modern medicinal drugs. [12]. The purpose of this research was to determine whether *Phyllanthus emblica* seed extracts contain any of the components that have been shown to inhibit lipid peroxidation, reduce superoxide dismutase, H+K+ ATPase, and boost catalyse activity, all of which protect against oxidative damage to the gastric mucosa. The stomach parietal cells secrete H+ through the dimeric enzyme H+K+ ATPase. The stem component acts specifically to inhibit H+K+ ATPase. E. officinalis or Phyllanthus emblica (Syn: Amla, Indian Gooseberry) is an evergreen tree which is highly prized in Tropical Asia. The genus is natural to tropical Southeast Asia, particularly in Central and South India. It is commonly cultivated in gardens throughout India and grown commercially as a medicinal fruit [13]. It is among the most important medicinal plants in the Ayurvedic Materia Medica and widely used in Indian medicines for the treatment of various diseases [14]In folk medicine, all parts of the plant, including fruit, seed, leaf, root, bark and flowers are used in various Ayurveda /Unani herbal preparations [15]. It is known as amalaka in Sanskrit, amla in Hindi, olay in Punjabi, amla in Gujarati, nellikkai in Tamil. It has antiviral, antibacterial 2, antiproliferative, anti-platelet 3-5 anti -HIV-1, hypolipidamic properties. It is used as antioxidant, aphrodisiac, as chelating agent, in constipitation, dental problems, diabetes , diarrhoea, diuretic fever gonorrhea, hair growth, headache [7], inflammation mouth ulcers, respiratory problems, skin whitening etc. The plant leave have the antineutrophilic activity. It reduces blood cholesterol, blood glucose as well as triglyceride levels8-9. E. officinalis which is rich in vitamin C, gallic acid, flavonoids, and tannins, protects against hepatoxicity-induced liver injury. E. To encourage a disease free healthy life Mother Nature has gifted mankind medicinal plants. Numerous medicinal plants are present in a collection of herbal preparations of the Indian traditional health care system (Ayurveda) named Rasayana, recommended for their interesting antioxidant activities. Phyllanthus emblica Linn. (syn. Emblica officinalis), commonly known as Indian gooseberry or Amla, family Euphorbiaceae, is a main herbal drug utilized in Unani (Graceo-arab) and ayurvedic systems of medicine. It is used equally as a medicine and as a tonic to build up lost energy and vigor. E. officinalis is extremely nutritious and might be a chief dietary source of vitamin C, amino acids, and minerals.

Phyllanthus emblica – Plant Profile

Scientific name: *Phyllanthus emblica* Linn.
Common names: Indian Gooseberry, Amla
Family: Phyllanthaceae (formerly Euphorbiaceae)
Part used: Fruits (mainly), leaves, bark, seeds, roots
Habitat: Widely distributed in tropical and subtropical regions of India, Sri Lanka, China, and Southeast Asia.

Botanical description:

- A small to medium-sized deciduous tree (8–18 meters tall).
- Leaves: Simple, subsessile, and closely arranged, appearing like pinnate leaves.
- Flowers: Greenish-yellow, small, unisexual.
- Fruits: Globular, light greenish-yellow, smooth, and contain six vertical furrows.

Phytochemical constituents:

- **Tannins:** Emblicanin A & B, chebulagic acid, gallic acid, ellagic acid
- **Flavonoids:** Quercetin, kaempferol
- **Phenolic compounds:** Ascorbic acid (vitamin C), polyphenols
- **Alkaloids, saponins, and carbohydrates** also present

Traditional uses:

- Used in **Ayurveda and Unani** systems of medicine.
- Acts as a **rejuvenator (Rasayana)**.
- Used in treating **indigestion, diabetes, inflammation, ulcers, and liver disorders**.
- It is one of the main ingredients of *Triphala* and *Chyawanprash*.

Fig. 1 *Phyllanthus emblica*

2. MATERIALS AND METHODS

Selection of Medicinal Plant

The purpose of this study is to evaluate natural herbal plant (*Phyllanthus emblica*) for theirin-vitro antiulcer activity. This thesis deals with the investigation in the lab on the scientific validation with the herbal plant as a potential in vitro anti-ulcer activity. There have been several reports of research on the involvement of free radicals in gastrointestinal ulcers. These herbs were chosen for their traditional medicinal usage, and their antioxidant and anti-ulcer properties were investigated using in vitro and in vivo models of acute and chronic peptic ulcers.

Fig. 6- Black Herbal Dry Amla Seed

3. EXPERIMENTAL WORK

Preparation and Evaluation of Novel Extract

The plant was sanitized by rinsing it three times in running water and then spraying it with 70% alcohol. Drying the plant in the shade at normal temperature allows for frequent inspections for fungal infestation. Pestle and motor are used to ground the dried plant into a fine powder. The Soxhlet extraction technique is used to remove the crude medication from

the fine powder using an aqueous solvent.

Chemicals used: The chemicals used were of an analytical standard [5]. These included aluminum hydroxide, sodium hydroxide, hydrochloric acid, sodium CMC, Tween80, sodium benzoate, orange oil, and magnesium hydroxide.

Extraction by Soxhlet Apparatus: This method of crude drug extraction has been used for quite some time. The extracted plant components' composition will determine the extraction method. The aqueous solvent is often used to get the crude extract from the Soxhlet device. The setup includes a condenser, a primary jar containing the material from which the compounds must be extracted, and a round-bottom flask for holding the solvent. The 100 g of plant material powder is transferred to the main Soxhlet container. Under low pressure, with the controlled heating mantle adjusted to bring the solvent to a boil between 60 and 80 degrees Celsius, the extract condensation is performed in a round-bottom flask.

The solvent vapor from the driving tubes is drawn into the condenser through the main jar, where it is cooled by the constant flow of water [6].

As the solvent condenses, it drips back over the packed material in the main jar and eventually collects in a separate jar. The material is being collected and extracted at the same time in the main jar, as seen by the changing color of the solvent as a compound of material dissolves in it. The extraction of plant material has therefore been completed; typically, this takes between 7-8 hours. After the solvent was removed, a brown extract was obtained, which was then placed in the fridge for further use in research.

The ingredients in a 100 ml solution of *Phyllanthus emblica* powder are shown in Table 2. By pulverizing the medication in solvents that are different added substances, such as Tween-80, sodium carboxy methyl cellulose (CMC), as an improving specialist, an enhancing specialist like orange oil, and a settling specialist like sodium benzoate, the medications are properly blended into fine particles of size 60 nm during the period of practical application of the plan. After in vitro Evaluation of Fluid Concentrate from *Phyllanthus emblica*. Seed for Antiulcer Activity [8], more research is needed to define antiulcer suspensions in vitro.

Table No.-1 : Chemical Tests of Sample

Detection	Observation and Result
Test for Alkaloids (Dragendorff's test)	Dragendorff's reagent (a potassium bismuth iodide solution) should be added to the 1 ml of extract.The presence of alkaloids may be seen as an orange-red precipitate.
Test for Saponins	To a graduated cylinder containing 20 ml of distilled water, add 5 milliliters of both the alcoholic and aqueous extracts and mix for 15 minutes. In the presence of saponins.
Test for Glycosides (Legal's test)	To an alkaline solution of sodium nitroprusside, the extract is dissolved in pyridine. The presence of glycosides
Test for Carbohydrates (Fehling's test)	A brick red precipitate appears in the presence of sugars when 1 ml of the extract is combined with 2 ml of Fehlings solutions A and B.
Test for Tannins	To conduct the test, combine a small sample of the solution to be tested with a basic lead acetate solution. If white precipitates form, tannins are present.
Test for Phenol (Bromine Water)	To a bottle of distilled water, add 5 milliliters of bromine and shake well. The transparent liquid may be decanted.
Test for Proteins (Biuret test)	To get a blue hue, combine 1 milliliter of the extract with 0.4 milliliters of a 40% sodium hydroxide solution and 0.2 milliliters of a 1% $CuSO_4$ solution. When a pinkish or purple-violet tint forms, proteins are present.
Test for Flavonoids	When sodium hydroxide is applied to the extract, a yellow color develops, revealing the presence of flavones.

Preparation of herbal suspension dosage form

The ingredients in a 100 ml solution of *Phyllanthus emblica* powder are shown in Table 2. By pulverizing the medication in solvents that are different added substances, such as Tween-80, sodium carboxymethyl cellulose (CMC), as an improving agent, an enhancing specialist like orange oil, and a settling specialist like sodium benzoate, the medications are properly blended into fine particles of size 60 net during the period of practical application of the plan. After in vitro Evaluation of

Fluid Concentrate from *Phyllanthus emblica* seed for Antiulcer Activity [8], more research is needed to define antiulcer suspensions in vitro.

Table No. 2: Composition of aq. extract of the seed of *Phyllanthus Emblica* herbal suspension

S.No	Ingredients list	Quantities in suspensionF1	Quantities in suspensionF2	Quantities in suspensionF3	Quantities in suspensionF4
1.	P.E. Extract	0.1 gm	0.5 gm	1 gm	1.5 gm
2.	Sodium CMC	0.6%	0.6%	0.6%	0.6%
3.	Tween 80	0.1 w/v	0.1 w/v	0.1 w/v	0.1 w/v
4.	Sodium benzoate	1.5 gm	1.5 gm	1.5 gm	1.5 gm
5.	Orange oil	1 ml	1 ml	1 ml	1 ml
6.	Purified water q.s	100 ml	100 ml	100 ml	100 ml

In-vitro Evaluation of Antiulcer Activity

Acid Neutralizing Capacity (ANC):

Each suspension was produced fresh in a 250 ml beaker and heated to 37oC. The liquid in suspension was aerated. Constant rotation at 30 revolutions per minute of a magnetic stirrer was used to simulate the stomach. To determine the optimal pH for testing, 90ml of newly produced solution was combined with 3 drops of phenolphthalein and titrated with fake gastric juice. The amount of gastric juice replacement that was actually ingested was calculated to be V.

The total consumed H+ (mmol) which is also termed as ANC was measured as 0.063096 (mmol/ml) × V (ml).

The reference points are aluminum hydroxide (500 mg) and magnesium hydroxide (500 mg).

"H+/K+ -ATPase Inhibition Activity: Preparation of H+/K+ - ATPase Enzyme: A fresh goat stomach was acquired from the local butcher, the gastric mucosa of the fundus was cut off and opened, and the inner layer of the stomach was scraped out for the parietal cell in order to create an H+/K+ - ATPase enzyme sample. To block H+/K+- ATPase, stomach parietal cells were homogenized in 16 mM Tris buffer at pH 7.4 with 10% Triton X-100, centrifuged at 6000 rpm for 10 minutes, and the supernatant solution was employed. Bradford's technique, using BSA as the standard, was used to calculate the protein content."

4. RESULTS AND DISCUSSION

Acid Neutralizing Capacity: The neutralizing effect of the extract was studied for four concentration (F1, F2, F3 and F4) and standard Aluminum Hydroxide + Magnesium Hydroxide [$Al(OH)_3$+$Mg(OH)_2$](500mg). The results obtained envisaged that the extract at concentration F1, F2, F3 and F4 showed a significant reduction in acid-neutralizing capacity (ANC), *i.e.*, 0.7762, 0.5993, 0.5332 and 0.5246, respectively, as compared to standard Al(OH)3+Mg(OH)2 (500 mg) which is 0.9157. The extract at a concentration of 1500 mg in F4 formulation has been found to neutralize acid less significantly as compared to standard. The results have been tabulated in **Table 3**.

Table No. 3: Effect of aqueous extract of seed of *Phyllanthus emblica* on acid neutralizing capacity

S.no.	Formulation / Concentration of extract(mg)	The consumed volume (V) of the artificial gastric juice	ANC was measured as 0.063096 (mmol/ml) × V (ml).
1.	F1	12.30	0.7762
2.	F2	9.50	0.5993
3.	F3	8.45	0.5332
4.	F4	8.30	0.5246
5.	$Al(OH)_3$+$Mg(OH)_2$ 500mg	14.53	0.9157

H+/K+ - ATPase Inhibition Activity: The H+/ K+ - ATPase inhibition activity of aqueous extract at a various concentration (20µg, 40µg, 60µg, 80µg, 100µg) was compared with Omeprazole as standard. The extract significantly showed activity in a dose-dependent manner. Maximum percentage inhibition of 59.56% has been observed for extract at

a concentration of 100µg (F1), and standard Omeprazole showed 66.98%. The results have been tabulated in **Table 4, 5, 6, 7 for F1, F2, F3 and F4.**

Table No. 4: Effect of aqueous extract on In-vitro H+/K+ - ATPase Inhibition Activity For F1

S. No.	Concentration (µg)	Percentage Inhibition (%)	
		Standard	Extract
1.	20	34.56	28.95
2.	40	48.07	30.54
3.	60	50.89	31.47
4.	80	56.36	46.57
5.	100	66.98	59.56

Table No. 5: Effect of aqueous extract on In-vitro H+/K+ - ATPase Inhibition Activity For F2

S. No.	Concentration (µg)	Percentage Inhibition (%)	
		Standard	Extract
1.	20	34.56	25.33
2.	40	48.07	28.24
3.	60	50.89	30.17
4.	80	56.36	45.18
5.	100	66.98	57.26

Table No. 6: Effect of aqueous extract on In-vitro H+/K+ - ATPase Inhibition Activity For F3

S. No.	Concentration (µg)	Percentage Inhibition (%)	
		Standard	Extract
1.	20	34.56	23.15
2.	40	48.07	27.24
3.	60	50.89	29.20
4.	80	56.36	41.27
5.	100	66.98	54.56

Table No. 7: Effect of aqueous extract on In-vitro H+/K+ - ATPase Inhibition Activity For F4

S. No.	Concentration (µg)	Percentage Inhibition (%)	
		Standard	Extract
1.	20	34.56	21.22
2.	40	48.07	25.14
3.	60	50.89	27.20
4.	80	56.36	36.22
5.	100	66.98	51.06

5. CONCLUSION

The acid-neutralizing capacity (ANC) of an antacid is the amount of acid that it can neutralize, and it has been measured by a process known as back titration. In ANC, the aqueous extract at 100µg concentration showed a significant reduction in ANC 0.7762 of aqueous extract of seed of *Phyllanthus emblica.* Additionally, a Maximum percentage inhibition of 59.56% was observed for the extract at a concentration of 100 µg, while the standard Omeprazole showed 66.98% inhibition for H+/K+-ATPase activity. The results indicate that the seed of *Phyllanthus emblica*has the potential to be an effective antiulcer agent.In this study, the ability of aqueous extract to inhibit H^+ -K^+ ATPase in vitro isolated from goat stomach was studied. In vitro studies are considered necessary in order to evaluate the potential of phytochemicals to enter in the cell and additionally to exemplify their interaction with the gastric ATPase. Enzyme H^+ -K^+ ATPase is an important enzyme system located on apical secretory membrane of partial cell. In this study, dose-dependent inhibition of enzyme by omeprazole and extract was observed, suggesting that the aqueous extract of seed of *Phyllanthus emblica* was significantly able to inhibit enzyme H^+ -K^+ ATPase, responsible for the secretion of acid and effect was comparable to omeprazole. Therefore, it can be concluded that the inactivation of H+-K+-ATPase is the major gastroprotective mechanism of action of the seed of Phyllanthus emblica, which indicates its protective role against inhibiting the gastric proton pump and opens the door for the isolation and characterization of active compounds responsible for it.

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