"A COMPREHENSIVE REVIEW OF THE PHARMACOLOGICAL PROPERTIES OF PHYLLANTHUS AMARUS "

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Abstract : *Phyllanthus amarus* is a medicinal herb belonging to the family Euphorbiaceae, widely used in traditional medicine systems such as Ayurveda, Unani, and Siddha. It is known for its diverse pharmacological properties, including hepatoprotective, antidiabetic, antioxidant, anti-inflammatory, antiviral, antimicrobial, and nephroprotective effects. This review summarizes the current knowledge on the traditional uses, phytochemical constituents, pharmacological activities, pharmacokinetics, safety profiles, mechanistic pathways, and research gaps of *Phyllanthus amarus.* The compilation emphasizes its potential in therapeutic applications and the necessity for further clinical validation and standardization of its extracts.[1,2,3]

I. INTRODUCTION

Medicinal plants have been a cornerstone in human healthcare since ancient times, and *Phyllanthus amarus* has gained significant scientific attention due to its diverse therapeutic potential. This small herb, commonly known as "Bhui Amla" or "Stone Breaker," is widely distributed in tropical and subtropical regions. It has been traditionally employed for treating liver disorders, diabetes, gastrointestinal disturbances, and infections. Modern pharmacological research has validated many of these ethnomedicinal claims and identified various bioactive compounds responsible for its pharmacological effects.

2.1 Scientific classification of *Phyllanthus amarus:*

Kingdom: Plantae

Clade (unranked): Angiosperms Clade (unranked): Eudicots Clade (unranked): Rosids Order: Malpighiales

Family: Phyllanthaceae Genus: Phyllanthus

Species: *Phyllanthus amarus* Schumach. & Thonn. [1,2,3]

2.2 Geographical Distribution of *Phyllanthus amarus*

1. Native Range

- *Phyllanthus amarus* is native to tropical America.
- Specifically, its native distribution includes much of Central and South America, the Caribbean (e.g., Mexico, Brazil, Cuba, Puerto Rico), and other tropical American regions.

2. Introduced / Naturalized Range

- It has become pantropical, meaning it is now widespread across tropical and subtropical regions around the world.
- In Africa, *P. amarus* is recorded in many countries, including in West Africa.
- In India, it is very common: found throughout the hotter (tropical) parts of the country, including in both plains and up to moderate altitudes.
- Also recorded in Southeast Asia, China, Sri Lanka, and other tropical/subtropical parts of Asia.
- According to *Flora of North America*, it is introduced in southern Florida, USA; and has also been reported in nursery stock in California.

- On islands: *P. amarus* is found in Indian Ocean islands (e.g., Madagascar, Mauritius, Seychelles, Comoros) and Pacific Islands.
- Also reported in New Caledonia.

3. Habitat Preferences in Distribution

- It tends to grow in disturbed habitats — fields, roadsides, gardens, waste lands.
- It can grow from sea-level up to moderate altitudes (in some places up to ~1000 m) in tropical/subtropical climates. [4-9]

2.3 Morphology of *Phyllanthus amarus:*

1. Habit & Size

- Annual, erect, glabrous (hairless) herb.
- Typical height is about 10–60 cm (some sources say up to 75 cm).
- Stem: terete (cylindrical), smooth or slightly rough in younger parts; branching is common.
- Root: stout and somewhat woody / tortuous, with a tap-root system + fibrous branches.

2. Leaves

- Leaves are numerous, subsessile (i.e., very short stalk / almost no petiole).
- Arrangement: distichous (i.e. in two vertical rows) on branchlets.
- Leaf shape: elliptic-oblong to oblong; some describe elliptic-obovate or elliptic-oblanceolate too.
- Leaf size: typically 5–12 mm long, 2–6 mm wide (on plagiotropic shoots) according to Kew.
- Base of leaf: rounded or cuneate; apex often rounded or subtruncate.
- Leaf texture: membranaceous; color is bright green above and somewhat glaucous (paler) below.
- Nervation: lateral nerves in 4–6 pairs, looped near the apex.
- Stipules: linear-lanceolate, about 1 mm; cataphyllary stipules about 2 mm long.

3. Branching

- Presents phyllanthoid branching: i.e., lateral branchlets ("leaf-bearing branchlets") bearing the leaves and flowers.
- There are orthotropic stems (vertical) and plagiotropic shoots (horizontal) on which leaves are borne.

4. Flowers

- The plant is monoecious (both male and female flowers on same plant).
- Flowers are very small (≈ 0.5–1 mm pedicel for male, somewhat longer for female).

- Male flowers: usually in groups of 1–3 in certain axils; sepals = 5 (rarely 6), ovate, acute; stamens = 3, filaments are fused to form a short column; anthers are subsessile, reniform.
- Female flowers: pedicel becomes thicker in fruiting stage; sepals 5, style free and very shallowly bifid.
- Disc (gland) structure: in male flowers there are 5 minute disc-glands; in female flowers, the disc is 5-lobed.

5. Fruit (Capsule)

- The fruit is a capsule, depressed-trigonous or oblate (flattened globose), smooth surface.
- Size: about ~1 mm long and 1.5–2 mm in diameter (according to World Flora Online).
- Color: ochreous-olivaceous (when mature) per Kew description.

6. Seeds

- Seeds are trigonous (three-angled) / 3-gonous.
- Size: approximately 0.8–1 mm long (from Kew).
- Surface ornamentation: well-marked longitudinal ridges (5–7) on the dorsal side; also concentric ridges + transverse striae on ventral facet.
- Color: pale greyish-brown.

7. Anatomy

- Stem cross-section: circular epidermis; vascular bundles are arranged in a ring; pith is parenchymatous.
- Leaf microstructure: (from standardization studies) upper and lower epidermis, glandular trichomes, and in midrib a vascular bundle with arc shape. [10-12]

2.4 Phytochemistry of Phyllanthus amarus:

1. Lignans (Major Bioactive Components)

Lignans are considered the signature constituents of *P. amarus*, known for antiviral (especially anti-HBV), hepatoprotective, and antioxidant activities.

- **Phyllanthin**
- **Hypophyllanthin**
- **Niranthin**
- **Nirtetralin**
- **Phylltetralin**
- **Lintetralin**

These compounds are found predominantly in the aerial parts and contribute significantly to the plant's medicinal value.

2. Tannins

Tannins are abundant in *P. amarus*, especially **ellagitannins**, which possess strong antioxidant and antimicrobial effects.

- **Geraniin**
- **Corilagin**
- **Ellagic acid**
- **Amlaic acid derivatives**

3. Flavonoids

Flavonoids contribute to anti-inflammatory, hepatoprotective, and antioxidant properties.

- **Quercetin**
- **Rutin**
- **Kaempferol**
- **Astragalin** (kaempferol-3-O-glucoside)
- **Quercetin glycosides**

4. *Alkaloids*

Alkaloids are present in smaller quantities but have notable biological activity.

- **Phyllanthine-type alkaloids**
- **Securinine-type alkaloids (trace amounts)**

5. *Terpenoids & Sterols*

These contribute to anti-inflammatory and antimicrobial effects.

- **Lupeol** (triterpene)
- **β-sitosterol**
- **Stigmasterol**
- **Campesterol** [13-15]

1. Pharmaclogical Activities of *Phyllanthus amarus*

Activity Name	Dose	Model	Reference
Hypoglycemic activity	200 mg/kg (rats), continued administration for 15 days	High-fructose–fed male Wistar rats	Moshi, M.J., et al. (2012)
Wound-healing / Antidiabetic support (L-Glutamine)	Not specified	Diabetic foot ulcer model in rats	Kandhare, A.D., et al. (2007)
Management of diabetic foot infections	Not specified	Clinical review of diabetic foot infection cases	Lipsky, B.A. (2014)
Diuretic activity	Not specified	Ethanolic fraction tested in rats	Patel, J.R., et al. (2008)
General therapeutic/ethnomedicinal uses	Not applicable	Review article	Verma, J.K., et al. (2009)
Phytochemical and ethnomedical value	Not applicable	Review of plant constituents	Khan, M.U., et al. (2018)
Antioxidant activity	Not specified	In vitro and in vivo antioxidant models	Sen, A.T., et al. (2003)
Hepatoprotective activity	Not specified	Isoniazid-induced hepatic injury in Wistar rats	Shyamjith, O.M., et al. (2008)
Hypoglycemic activity	260 mg/kg and 390 mg/kg	Alloxan-induced diabetic Wistar rats	Herbert, O.C., et al. (2012)
Phytochemical analysis (GC–MS)	Not applicable	GC–MS analysis of leaves	Mamza, U.T., et al.
Digestive enzyme inhibition (anti-diabetic / anti-ulcer)	Not specified	In vitro enzyme inhibition assays (α-amylase, pepsin, trypsin)	Shetti, A.A., et al. (2001)
Multiple pharmacological activities (hepatoprotective, anti-inflammatory, antiviral, etc.)	Not applicable	Review article	Narismbudhu, L.C., et al. (2006)

1. Moshi et al. (2012) investigated the hypoglycemic activity of *Phyllanthus amarus* aqueous extract in non-insulin dependent diabetic conditions. Their study demonstrated that the extract significantly reduced blood glucose levels in high-fructose–fed male Wistar rats. A 200 mg/kg dose produced a 6% reduction in blood sugar within 4 hours, and continued administration for 15 days resulted in a highly significant decrease ($P < 0.001$). These results support the plant's traditional use for managing hyperglycemia.[16]

2. Kandhare et al. (2007) examined the therapeutic role of L-glutamine in diabetic foot ulcers. Their work showed that diabetes mellitus severely delays wound healing, contributing to chronic ulceration. L-glutamine improved both glycemic control and tissue repair across experimental models, highlighting its potential for managing diabetic wound complications.[17]

3. Lipsky (2014) reviewed treatment strategies for diabetic foot infections, emphasizing the importance of accurate diagnosis, proper culture collection, and tailored antibiotic selection. He noted that antibiotic misuse contributes significantly to antimicrobial resistance, posing a threat to future management of diabetic foot conditions. The review stresses the need for rational antimicrobial stewardship. [18]

4. Patel et al. (2008) evaluated the diuretic activity of an ethanolic fraction of *Phyllanthus amarus* and found that its effects in rats involve prostaglandin pathways. They emphasized the plant's long-standing ethnomedical significance and its wide application in traditional medicine systems. The study supports its continued relevance in herbal pharmacotherapy. [19]

5. Verma et al. (2009) conducted a comprehensive review highlighting the long history—over 3,000 years—of *Phyllanthus amarus* in traditional medicine. The plant's broad usage reflects its therapeutic versatility and its prominence in various healing systems across cultures. [20]

6. Khan et al. (2018) further expanded on the ethnomedicinal and phytochemical importance of *Phyllanthus amarus*. They reported that the herb is rich in lignans, flavonoids, glycosides, alkaloids, phenylpropanoids, and ellagitannins distributed throughout the plant's tissues. These bioactive compounds support its diverse clinical and traditional applications. [21]

7. Sen et al. (2003) analyzed the antioxidant potential of *Phyllanthus amarus* both in vitro and in vivo. Their findings revealed that the plant contains high levels of phenolic compounds and exhibits strong antioxidant activity. Given the increasing need for natural antioxidants in pharmaceutical and food industries, this study confirms the plant's value as a natural source of protective bioactive compounds. [22]

8. Shyamjith et al. (2008) explored the hepatoprotective effects of *Phyllanthus amarus* and *Tylophora indica* extracts on isoniazid-induced liver injury in Wistar rats. Their results showed that both plants reduced hepatic damage, indicating potential for mitigating drug-induced hepatotoxicity. [23]

9. Herbert et al. (2012) assessed the hypoglycemic activity of *Phyllanthus amarus* aqueous extract in alloxan-induced diabetic rats. The extract produced significant reductions in blood glucose at doses of 260 mg/kg and 390 mg/kg at different time intervals, confirming its beneficial antihyperglycemic properties. [24]

10. Mamza et al. conducted GC-MS analysis to identify the bioactive components of *Phyllanthus amarus* leaves, revealing several pharmacologically relevant constituents. Their findings help validate the plant's traditional use by linking specific chemical compounds to possible therapeutic effects. [25]

11. Shetti et al. (2001) studied the inhibitory effects of *Phyllanthus amarus* extracts on digestive enzymes such as α-amylase, pepsin, and trypsin. Their results suggest that the plant may help manage disorders like peptic ulcers and diabetes, which involve overactivity of these enzymes. [26]

12. Narismbudhu et al. (2006) reviewed the pleiotropic pharmacological activities of *Phyllanthus amarus*, including hepatoprotective, anti-inflammatory, analgesic, antipyretic, antiviral, antidiabetic, and antimicrobial actions. The review emphasizes the herb's extensive use in Ayurvedic medicine and its broad therapeutic profile. [27]

4. Pharmacokinetics, Toxicology, and Safety:

Toxicological evaluations indicate that P. amarus is generally safe at therapeutic doses. Acute toxicity studies show no adverse effects in rats up to 2000 mg/kg. However, high doses may affect hepatic enzyme activity, particularly cytochrome P450 isoenzymes, influencing the metabolism of co-administered drugs. Hence, herb-drug interactions must be cautiously evaluated.[28- 30]

5. Conclusion:

Phyllanthus amarus exhibits significant pharmacological potential validated through ethnomedicinal and experimental evidence. Its diverse bioactive compounds contribute to hepatoprotective, antidiabetic, antioxidant, and diuretic effects. Nevertheless, comprehensive clinical trials, safety evaluations, and standardization are essential for its integration into evidence-based medicine. The herb remains a valuable candidate for natural therapeutic product development.

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2. The EPPO (European and Mediterranean Plant Protection Organization) database also gives taxonomy: Kingdom: *Plantae*, Phylum: *Magnoliophyta*, Order: *Malpighiales*, Family: *Phyllanthaceae*.
3. According to *Flora of North America*, *Phyllanthus amarus* was described by Schumacher & Thonning in 1827.
4. World Flora Online — native to America, now pantropical.
5. Kew Science (Plants of the World Online) — native range, distribution.
6. International Journal / PhcogJ — list of countries where *P. amarus* is found (India, Brazil, Ghana, etc.).
7. eFlora of India — details on naturalization in India.
8. Flora of North America — introduced in parts of U.S., habitat.
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