

Review Article

***Phyllanthus amarus*: A medicinally essential herb**

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ABSTRACT

In India, there are about 17000-18000 species of the flowering plants out of which 7000 are mainly used in ayurveda, homeopathy, unani and siddha system. *P. amarus* is an essential annual herb belongs to the family *Phyllanthaceae*. The herb is mostly used to treat diseases like jaundice, diarrhoea, scabies, gall stones, wounds, menorrhagia, skin ulcers etc. *P. amarus* is a kharif annual (monsoon) weed widely distributed in both cultivated and waste lands. This herb has an anti-diuretic, anti-viral, anti-spasmodic, anti-fertility, wound healing activity and anti-diabetic activity etc. The plant has been found in tropical and subtropical areas like southern India, China, Cuba, Nigeria and Philippine. The present review article discusses about the chemical constituents, phytochemicals, pharmacological activity present in the plant and traditional uses of *P. amarus*.

1. INTRODUCTION

P. amarus (Bhumyaamalaki) is an annual herb that grows up to 10-60 cms tall, erect, younger parts rough, cataphylls 1.5-1.9 mm long, deltoid acuminate; leaf 3.0-11.0 by 1.5-6.0 mm, elliptic oblong to ovate, obtuse or minutely apiculate at apex, obtuse or slightly inequilateral at base; flowers axillary, proximal 2-3 axils with unisexual 1-3 male flowers and all succeeding axils with bisexual cymules; indigenous to the rainforests of the Amazon and other tropical areas including Bahamas, southern India and China [1]. *Phyllanthus* means “leaf and flower” because the flowers, as well as the fruit, seem to become one with the leaf. *P. nirui* is a common kharif (rainy season) weed found in both cultivated fields and wastelands. Recently it has attracted the attention of researchers, because of its hepatoprotective properties. It is known for its liver healing properties so used in Chinese medicine for treatment of liver diseases [2].

The plant genus *Phyllanthus* (Phyllanthaceae) is widely distributed in most tropical and subtropical countries. It is a very large genus consisting of approximately 550 to 750 species and is subdivided into 10 or 11 subgenera: *Botryanthus*, *Cicca*, *Conani*, *Embllica*, *Ericocus*, *Gomphidium*, *Isocladus*,

Kirganelia, *Phyllanthodendron*, *Phyllanthus*, and *Xylophyll* [3]. It was described to have the properties of Rasa, Guna, Veerya and Vipaaka. The Ayurvedic literature has shown its uses as Kaasahara (antitussive), Shwaasahara (antispasmodic, antidyspnoic), Kaphapittahara (which relieves the Kapha Pitta Dosha), Pipaasaaghna (which relieves Polydipsia), Raktapittahara (hemorrhage disease), Paanduhara (antianemic), Kaamalaahara (which cures jaundice), Kushthaghna (indicated in leprosy), Daahaghna (refrigerant, relieves burning sensation), Kshatakshayaghna (indicated in Trauma) and Mootrarogahara (which cures urinary disorders). The use of *P. amarus* is gaining momentum because of its novel antiviral activity against hepatitis B virus and for several other biological activities given in table 2 such as kidney and gallbladder stones, for cold, flu, tuberculosis and other viral infections; liver diseases and disorders including hepatitis, jaundice and liver cancer [4]. Moreover, a large number of phytochemicals have been found only in the *Phyllanthus* genus. Many of the active constituents present in various parts of the plant are lignans, glycosides, flavonoids, alkaloids, ellagitannins and phenylpropanoids found in the leaf, stem and root of the plant. Common lipids, sterols and flavonols also occur in the plant (Fig.1)[5].

Taxonomy [6]

Kingdom	:	Plantae
Division	:	Tracheophyta
Class	:	Magnoliopsida
Order	:	Malpighiales
Family	:	Phyllanthaceae
Genus	:	Phyllanthus.L
Species	:	<i>P. amarus</i>

Vernacular name

Hindi	:	Jamgliamli, Jaramla
Malayalam	:	Kilarnelli, kilukanelli
Tamil	:	Kilanelli, Kilakkainelli
Sanskrit	:	Bhunyaamalaki
Telugu	:	Nelausirika[7]



Fig. 1. *P. amarus* leaves [8]



Fig. 2 *P. amarus* flower and fruit capsules [8]

2. CHEMICAL CONSTITUENTS

The active phytochemicals, flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannis, coumarins and saponins, have been identified from various parts of *P. amarus*. Extracts of this herb

have been proven to have therapeutics effects in many clinical studies [7]. Three lignans – niranthin, nirtetralin and phyltetralin have been isolated from leaves. Leaves also contain phyllanthin and hypophyllanthin. Estradiol has been detected in bark and roots. Root also contains Kaempferol-4'-rhamnopyranoside, eriodictyol-7-rhamnopyranoside and lup-20(20)-en-3 β -ol and its acetate [9, 10].

3. ADULTERANTS AND SUBSTITUTES

Many times *P. niruri* is adulterated with *Phyllanthus amarus* and vice versa. Market samples of *P. niruri* (Linn.) are often adulterated with *P. amarus* Linn. Two plants are the sources of two different Ayurvedic drugs *P. niruri* and *P. amarus* possibly with similar therapeutic effects [11].

4. PHARMACOGNOSTIC CHARACTERISTIC

Various species of *Phyllanthus* are being sold in India under the trade name 'Bhunyaamalaki'. During market surveillance of herbal drug, it was observed that almost all the commercial samples, either comprise of *P. amarus* Schum. & Thonn. Or *P. maderas-patensis* Linn. or mixture of *P. amarus*, *P. fraternus* Webster and *P. maderaspatensis* Linn. The species admixtures have been assessed in raw drug trade of *Phyllanthus* in southern India using morphotaxonomical Characters and molecular analysis. The morphological analysis of these samples revealed six different species of *Phyllanthus*. Seventy-six percent of the market samples contained *P. amarus* as the predominant species (>95%) and thus were devoid of admixtures. The remaining 24% of the shops had five different species namely *P. debilis*, *P. fraternus*, *P. urinaria*, *P. maderaspatensis*, and *P. kozhikodianus*. The trade sample identities were validated and confirmed by these species specific DNA barcodes [12].

Macromorphology, micromorphology, histochemical and physical pharmacognostic studies of *P. amarus* revealed certain diagnostic uncommon characters: basal sub-marginal venation formed by curving of almost unbranched lateral veins, 4–6 angled cortical fibres (TS), 1–2 seriate xylem rays, crystals concentrated along the veins (mostly rosette), combination of paracytic and anomocytic stomata, sinuous epidermal cell walls, vessel members tailed on two ends; high frequency of crystals in leaf (87.5 mm⁻²), stomatal index, palisade ratio, etc. Additionally, distribution of alkaloidal reaction and protein in the secondary xylem, extractive values, ash values, UV fluorescence were also distinctive characteristics [13].

5. PHYTOCHEMICAL STUDIES

P. amarus is a rich source of Phytochemicals many which have been found only in phyllanthus genus. A number of active constituents of the plant are related to biologically active lignans, glycosides, flavonoids, alkaloids, ellagitannins, and phenylpropanoids, found in the leaf, stem, and root of the plant along with common lipids, sterols, and flavonols [6].

Table 1. Phytochemicals in *Phyllanthus amarus*

S. No	Photochemical	Active constituents
	Tannins	Geraniin, corilagin, 1,6 digalloylglucopyranoside rutin , quercetin- 3-O-glucopyranoside ,Amarulone, Phyllanthusiin D & Amariin [14, 15].
	Lignans	Niranthin, Nirtetralin, Phyltetralin, Hypophyllanthin, Phyllanthin, demethylenedioxy-niranthin, 5-demethoxy-niranthin, Isolintetralin [16, 17, 18, 19].
	Ellagitannins	Amariin, 1-galloyl-2,3-dehydrohexahydroxydiphenyl (DHHDP)- glucose, Repandusinic acid, Geraniin, Corilagin, Phyllanthusiin D, and flavonoids namely rutin, and quercetin 3-O-glucoside, 1-Ogalloyl-2,4dehydrohexahydroxydiphenoyl-glucopyranose elaeocarpusin, repandusinic acid A and geraniinic acid [20,21].
	Volatile oil	Linalool and Phytol [22].
	Triterpene	(2Z, 6Z, 10Z, 14E 18E, 22E-farnesil farnesol) [19].

6. PHARMACOLOGICAL ACTIVITY

6.1 Antidiabetic activity

Diabetes is a metabolic disorder of carbohydrate, fat and protein and is considered as the world's largest endocrine disease [11]. The methanolic extract of *P. amarus* was found to inhibit lipid peroxidation, and scavenge hydroxyl and superoxide radicals' in vitro and thus showed antidiabetic activity. Moreover, the extract was found to reduce the blood sugar in alloxan-induced diabetic rats. In addition, the continuous administration of the extract for 15 days has been shown to produce significant reduction in blood sugar levels that further confirmed the antidiabetic potential of the plant [13].

6.2 Anticancer activity

The aqueous extract of *P. amarus* demonstrates potent anticancer activity against 20- methylcholanthrene (20-MC) induced sarcoma development. The aqueous extract inhibits DNA topoisomerase II of mutant cell cultures and inhibited cell cycle regulatory enzyme cdc 25 tyrosine phosphatase of *Saccharomyces cerevisiae*. The anticarcinogenic and anti-tumour activity of *P. amarus* proposed to be inhibition of metabolic activation of carcinogen as well as the inhibition of cell cycle regulators responsible for cancerous growth and DNA repair [23].

6.3 Analgesic activity

Methanol extract of dried callus tissue at a concentration of 10mg/kg, administered intraperitoneally to mice was active vs. acetic acid induced within and vs. formalin –induced pedal edema. The

extract, at 50 mg/kg was inactive v/s tail flick response to radiant heat. Ethanol/ water (1:1) extract of dried entire plant at a dose of 50 mg/kg, administered intragastric to male mice was active. The extract also administered intraperitoneally to male mice at a dose of 0.3 mg/kg was active. In both cases antinociceptive effects were demonstrated using 5 different models of nociception [24].

6.4 Antifertility activity

P. amarus possess antifertility activity. This activity was shown in the experimental study where alcoholic extract of *P. amarus* brought changes in 3-beta and 17-beta hydroxyl steroid dehydrogenase (HSDs) levels, thereby effecting hormonal conversions in the female mice that confirmed by observation of no pregnancy in cohabited normal females and male mice [25].

6.5 Wound healing activity

As we know that *P. amarus* has anti-oxidant activity, this character of hear also contributes to wound healing in a person .The herb extract was applied to wounded laboratory rats and effect on wound healing was studied. The extract was found to enhance the wound healing process. It also reduces the size of the scar formed and enhances the recovery of periphery nerves after injury [25, 26]. It's been reported that plant extract inhibits the microbial and fungal growth at the site of injury. It also boosts angiogenesis resulting in formation of fibroblasts and hence leads to improved wound healing time [19].

6.6 Anticonvulsant activity

Epilepsy is a major neurological disorder characterized by the occurrence of recurrent seizures. The two widely proposed mechanisms involve alterations in the voltage-dependent ion channels such as reduction in inhibitory GABA-mediated drive or increase in excitatory glutamate mediated inputs. This chronic progressive CNS disorder affects a large population of the world. In search of herbal treatment, aqueous and ethanolic extract of *P. amarus* were evaluated for anticonvulsant effect using pentylenetetrazole (PTZ) and maximal electroshock-induced seizures (MES) in swiss albino rats. The result showed ethanolic and aqueous extract of leaves and stem of *P. amarus* significantly effective in abolishing hind limb extension induced by MES as well as PTZ induced seizures [28].

6.7 Antiatherosclerotic activity

P. amarus is known to produce cardiovascular effects by acting as hypotensive agents. The extract of herb is known to lower the cholesterol level in body and also enhance lipid metabolism thus preventing the vasculature from blockage resulting due to the accumulation of lipid in lumen [29-31]. The effect of herb extract in lowering blood pressure in rabbit was studied. The drug causes significant decrease in blood pressure and this effect was inhibited by dose of atropine. The hypotensive action of drug was dose dependent [30].

6.8 Antiviral activity

P. amarus possess antifungal and anticancerous properties [32]. Further, evaluation of antiviral activity of *Phyllanthus* species were evident from experiment study where aqueous extract of *P. amarus* along with other species of *Phyllanthus* genus were evaluated against Herpes Simplex Virus type-1 and Herpes Simplex Virus type-2 in vero cells by quantitative polymerase chain reaction. Western blot and 2D-gel electrophoresis were used to study protein expressions of treated and untreated infected vero cells. *P. amarus* along with *P. urinaria* demonstrate the strongest antiviral activity against Herpes Simplex Virus type-1 and Herpes Simplex Virus type-2 which is proposed to its action in the early stage of infection and replication [32].

6.9 Immunomodulatory activity

P. amarus produced the strongest oxidative burst of polymorphonuclear leukocytes with luminol-based chemiluminescence [33].

Nephroprotective activity

The aqueous extracts of leaf and seeds of *P. amarus* showed significant protective effects against acetaminophen and gentamicin- induced nephrotoxicity [34].

Table 2. Worldwide Traditional uses of *P. amarus* [35]

S. No	Country	Uses
1.	Amazonia	Gallstones ,Kidney Diseases, kidney stones
2.	Bahamas	Cold, Constipation, Fever, Flu, Laxative, Stomach Ache, Typhoid
3.	Brazil	Joint Ache, Antispasmodic, Bladder Diseases, Cystitis, Diabetes, Diuretic, Fever, Gallbladder Diseases, Gallstone, Hepatitis, kidney Trouble, Kidney Stones, Liver, Prostate and Urinary Diseases
	India	Anemia, Asthma, Bronchitis, Cough, Diuretic, Dysentery, Gonorrhoea, Hepatitis, Jaundice, Thirst, Tuberculosis, Abdomen Tumor
	Java	Cough, Gonorrhoea, Stomachache
	Malaya	Dermatosis, Diarrhoea, Diuretic, Itch, Miscarriage, Pesticide, Renosis, Syphilis, Vertigo
7.	Haiti	Stomach Ache,, Carminative, Colic, Digestive, Diuretic, Fever, Malaria, Stomachic, Tenesmus
8.	Marianas	Dysentery, Itch, Rectitis, Vaginitis
9.	Peru	Diuretic, Hepatitis, Gallstone, Kidney stones
10.	Elsewhere	Blennorrhagia, Diabetes, Diarrhoea, Diuretic, Dropsy, Dysentery, Dyspepsia, Emmenagogue, Fever, Gallstone, Gonorrhoea, Kidney Stones, Malaria, Tonic.

Table 3. Pharmacological effect of major phytochemicals in *P. amarus*.

Species	Class	Phytoconstituent	Pharmacological effect
<i>P. amarus</i>	Lignan	Phyllanthin	Antioxidant, Anti-inflammatory [36]
			Anticancer, Antitumour [37]
			Hepatoprotective[38]
			Antileukemia [40]
			Antiamnestic [41]
		Hypophyllanthin	Antitumor, anticancer [38]
		Niranthin	Anti-inflammatory [37]
			Antitumor [40]
			Antiviral [41]
		Phyltetralin	Anti-inflammatory
	Nirtetralin	Anti-inflammatory	
		Reverses multidrug resistance [41,45]	
	Hinokinin	Anti-viral [42]	
	Flavonoid	Rutin	AntioxidantA [49]
		Quercetin-3-O-glucoside	Antioxidant A [46]
Tannin	Geraniin	Antiviral [43]	
		Radioprotective [46]	
		Heptaoprotective [47]	
	Amariin	Antioxidant	
	Radioprotective [46]		
Repandusinic acid A	Antioxidant A		
		Radioprotective [46]	
	Corilagin	Antioxidant	
		Anti viral [50]	
		Radioprotective [46]	
	Phyllanthusiin A, B, C, D	Antioxidant	
		Radioprotective [46]	
Alkaloid	Norsecurinine	Antifungal [48]	
Volatile oil	Linalool, phytol	Antimicrobial [51]	
Polyphenol		Anticancer [52]	

7 CONCLUSION

Herbs have always formed an integral part of human health and are used in the treatment of several human diseases. *P. amarus* grows anywhere in gardens and road sides. It is a tasteless herb with a soft bitter aftertaste. It is used for the treatment of various diseases like diarrhoea, dysentery, intermittent fevers, menorrhagia, ophthalmopathy, scabies, ulcers, indigestion, skin diseases and wounds. In Jaundice, paste of *P. amarus* made with

buttermilk is recommended. It is widely spread throughout the tropical and subtropical countries of the world including India [53, 54]. This review aims was to collect and study the various traditional uses, pharmacological studies and discussed about the several photochemical present till date on *P. amarus* plant in order to provide sufficient information for future research work.

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