



**PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF PHYLLANTHUS
NIRURI: A REVIEW**

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ABSTRACT

Phyllanthus niruri Linn. belongs to the Euphorbiaceae family and it is a small herb having a wide range of medicinal properties, and it is used widely across the world. In Indian ayurvedic system, it is used for treatment of jaundice, ulcers, skin diseases, diabetes, chest pain and urinary complications. Its taste is bitter and acts as an astringent and shows a laxative effect. This review covers information about ethno medicinal uses of Phyllanthus niruri in different countries with various pharmacological profiles of the plant. The phytochemical studies were characterized and the presence of various compounds such as lignans, phyllanthin, hypophyllanthin, flavonoids, glycosinoids and tannins were reported. The extracts of Phyllanthus niruri have a wide range of pharmacological activities like antimicrobial, antiviral, hepatoprotective, antioxidant, anticancer, anti-inflammatory, antiplasmodial and diuretic.

KEYWORDS: Phyllanthus niruri, Ethnobotany, Phytochemistry, Activity, Disease, Active constituents.

INTRODUCTION

Phyllanthus niruri Linn. belongs to the Euphorbiaceae family and is spread throughout the tropical and subtropical countries of the world. This is an annual herb and widely spread in coastal areas of India. It is used in the indian ayurvedic systems from the ancient times (more than 2000 years) and is having very short life. P. niruri is a field weed and its genus Phyllanthus comprises of 600-700 species with minor distinguishing features among them. In indian ayurvedic system, Phyllanthus niruri plant extract is used as a medicine and is recommended for treatment of various diseases such as bronchitis, anaemia, leprosy, asthma, urinary disorders. In the Chakra Samhita book, P. niruri is used in effective treatment of asthma, stimulating the liver, improving digestion, increasing appetite and producing laxative effects. Maharshi Charaka has categorized it as Kasahara: alleviates cough, Swasahara: relieves asthma, Mootrarogahara: cures urinary disorders, Kapha Pitta Hara: relieves the kapha pitta dosha, Kaamalaahara: cures jaundice, and Bhavaprakasha Nighantu: cures cough and blood disorders. It is bitter in taste but sweet in the post digestive effect (vipaka) and it is also used as astringent.^[1] Phyllanthus niruri is having various properties like anti-inflammatory^[2], anti-fungal, anti-viral, anti-bacterial^[3], anti-oxidant, hepatoprotective, hypoglycaemic, hypotensive, analgesic, inhibitory effect on renal stone formation.^[4] P. niruri is been used as an

ingredient of almost 175 ayurvedic formulations and the fruits of this plant are commonly used in the treatment of haemorrhages, diarrhoeas, dysentery, jaundice, cough and anaemia. It is also used in the preparation of various health care and personal products like chyawanprash, hair oil dye, face cream, tooth powder.^[5]

The aqueous infusions of the whole plant are employed as antispasmodic, laxative, diuretic, carminative, against constipation, fever including malaria, hepatitis, tuberculosis, cough, diarrhea, and vaginitis.^[6,7] The fresh root P. niruri is believed to be an excellent remedy for jaundice, dropsy and genitor urinary infections and also promotes stone elimination in patients with kidney stones.^[8] The fruits are used in treatment of tubercular ulcers, wounds, sores, scabies and ring worms infection.^[9] Phyllanthus niruri has several bioactive molecules such as lignans, phyllanthin, hypophyllanthin, flavonoids, glycosides, tannins, alkaloids, ellagitannins, triterpenes, phenylpropanoids, steroids, ricinoleic acid, niruriside and phyltetralin.^[10-13] The alkaloids have the antispasmodic activity leading to smooth muscle relaxation.^[14] P. niruri has enormous pharmacological activities such as antiviral activities against hepatitis B, antimicrobial, hepatoprotective, anticancer and also has hypocalcemic activity. Methanolic extract of P. niruri exhibited immunomodulatory activity and anti HIV activity. Phyllanthin and hypophyllanthin shows

antitumor activities. In this review we tried to assess the potential activities of *P. niruri*, its relation with the traditional and bioscientific research to establish several biochemical and pharmacological studies. This review contains several issues of ethnopharmacology, phytochemistry and pharmacology of *Phyllanthus niruri*.

Ethnobotany

Phyllanthus niruri has extensive medicinal properties and has a long history in the health care system of tropical countries. The plant is known in traditional health care systems. *P. niruri* is commonly known as “Chanca piedra” (or) “stone breaker”. However there is a lot of confusion about this species identification. *Phyllanthus niruri* is used as a folk medicine for treating kidney stones, gallbladder stones, liver related diseases such as liver cancer and jaundice. Apart from these, it is also administered for diuretic, hypoglycemic and hypertension cases and also shows anti-inflammatory, anti-tumor, antinociceptive and antioxidant properties.^[15]

Botanical description^[16]

Phyllanthus niruri is an erect annual herb, growing 40-70 cm height having ascending herbaceous branching. It is quite glabrous and branching at the base. The genus *Phyllanthus* means “leaf and flower” because the flower and fruit can be associated with the leaf. It is a plumose leaf that carries flower and fruit. **Leaves** are numerous, small, green, sub sessile, closely arranged, elliptic oblong shaped, obtuse, having short petiole and stipules present, they are arranged alternatively on each side of the stem.



Figure 1: *Phyllanthus niruri* L. plant.

The flowers are yellowish, small, numerous, axillary. These are unisexual, monoecious flowers, male flowers having 1-3 sessile stamens and female flowers were solitary in nature. Fruit is a capsule, very small, depressed globose and more over capsule is smooth, 2-3 mm in diameter. **Stem** has horizontal branches and height upto 30-60 cm, 1-2.5 mm width. **Root** is branched and large.

Botanical classification

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Euphorbiales

Family: Euphorbiaceae

Genus: *Phyllanthus*

Species: *Niruri*

Vernacular Names in India^[17]

Assamese: Holpholi; Poram-lokhi

Bengali: Noar

Hindi: Chalmeri, Harfarauri, Bhuiaonla.

Kannada: Kirunelli, Nela Nelli,

Konkani: Bhuin-avalae

Telugu: Ratsavusirike, Nela Usiri,

Tamil: Arunelli, Keela Nelli,

Malayalam: Arinelli, Kizhanelli, Nellipuli

Marathi: Rayavali, Bhuiavli,

Oriya: Narakoli

Sanskrit: Amala, Bhumyamlaki, Sukshmadala, Vitunika,

Bhoodatri



Phytochemistry^[18]

Phyllanthus niruri contains bioactive phytochemical constituents such as alkaloids, glycosides, essential oils, flavonoids, tannins, terpenoids, saponins, phenolic compounds and many more. The different phytochemical constituents along with the active compounds are represented in Table 1. The different test procedures carried out for confirming the presence of phytoconstituents are enlisted in Table 2. The chemical structures of active chemical constituents of *Phyllanthus niruri* are represented in Table 3.

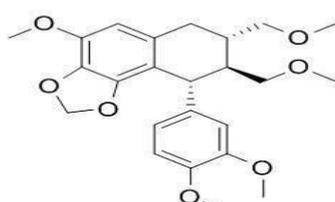
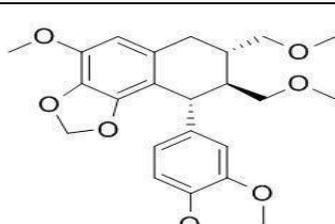
Table 1: Active phytochemical constituents of *Phyllanthus niruri*.

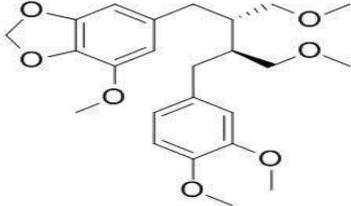
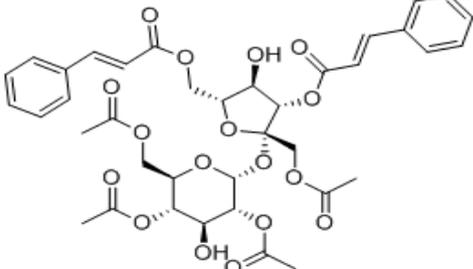
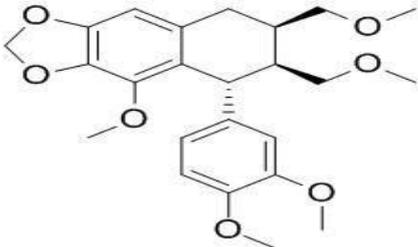
Sr. No.	Class	Active compounds
1	Alkaloids	4-Methoxy-nor-securinine, nirurin, ent-norsecurin
2	Benzenoids	Gallic acid, Corilagin
3	Coumarin	Ellagic acid, ethyl brevifolin carboxylate
4	Flavonoids	Quercetin, rutin, astragalins, quercitrin, isoquercitrin, kaempferol-4-rhamnopyranoside, eridictyol-7-rhamnopyranoside, fisetin-4-O-glucoside, nirurin
5	Lignin	Phyllanthin, hypophyllanthin, niranthin, nirtetralin, phyltetralin, hinokinin, isolintetralin
6	Lipid	Ricinoleic acid
7	Phytallate	Phyllester
8	Sterol	Estradiol, β -sitosterol, isopropyl-24-cholesterol
9	Tannin	Geranin
10	Triterpene	Lupeol acetate, lupeol, 3,7,11,15,19,23-hexamethyl-2Z,6Z,10Z,14E,18E,22E-tetracosane 1-ol, phyllanthanol, phyllanthone, phyllanthol

Table 2: Test procedures for different phytoconstituents.^[19]

Sr. No.	Test	Procedure
1	Alkaloids	2ml. of extract was treated with a few drops of Hager's reagent (picric acid dissolved in benzene). Formation of a yellow precipitate indicated the presence of alkaloids.
2	Flavonoids	1ml. of extract was treated with 10% of 1ml. Pb(OAc) ₄ . Formation of intense yellow colour indicated the presence of Flavonoids
3	Phenols	2ml. of extract was treated with 3 to 4 drops of FeCl ₃ solution. The formation of bluish black colour indicated the presence of Phenols.
4	Saponins	5ml. of extract, a drop of sodium bicarbonate solution was added. The test tube was shaken and allowed to stand for 3 minutes. Formation of honeycomb-like froth indicated the presence of Saponins.
5	Terpenoids	2ml. extract, was treated with 2ml (CH ₃ CO) ₂ O and 2 to 3 drops of conc. H ₂ SO ₄ was added. Appearance of the red colour indicated the presence of Terpenoids.
6	Tannin	1ml of extract was treated with 2 to 3 drops of FeCl ₃ solution. Formation of green precipitate indicated the presence of Tannin.
7	Coumarins	2 ml extract was treated with 3 ml of 10% NaOH solution. Appearance of yellow colouration indicated the presence of Coumarins.
8	Phytosterols	Extract was treated with 2ml. chloroform and then filtered. Filtrate was treated with a few drops of H ₂ SO ₄ , shaken gently and allowed to stand. Appearance of golden colour (reddish brown) indicated the presence of Phytosterols.

Table 3: Chemical structures of active chemical constituents.

Sr. No.	Name of constituent	Chemical structure
1	Phyllanthin	
2	Hypophyllanthin	

3	Niranthin	
4	Niruriside	
5	Nirtetralin	

Pharmacological activities

Plants as a source of new drugs are still poorly explored of all plant species. Only a small percentage has been investigated phytochemically and even a smaller percentage has been properly studied in terms of their pharmacological properties.^[20]

Anti-diabetic activity

Ethanol extract of *Phyllanthus niruri* was found to have significant antidiabetic activity in insulin-dependent diabetes mellitus rats, but showed no effect on non-insulin-dependent diabetes mellitus rats. Additionally, the ethanol extract was found to lower lipid profiles cholesterol, triglycerides, low density lipoprotein cholesterol, very low density lipoprotein cholesterol and atherogenic index. There is increase in high-density lipoprotein cholesterol in both insulin-dependent diabetes mellitus and non-insulin dependent diabetes mellitus animals.^[21] Concordantly, a one week study carried out on non-insulin dependent diabetic patients using aqueous extract of aerial parts of *Phyllanthus amarus* showed that, it is not effective in lowering both fasting blood glucose and postprandial blood glucose level in untreated non-insulin dependent diabetic patients.^[22] Aqueous extract of *Phyllanthus niruri* demonstrated significant hypoglycemic activity in streptozotocin induced diabetic rats.^[23] The methanol extract of the plant has also been found to lower blood sugar level in alloxan-induced diabetic rats.^[24]

Antiplasmodial activity

Ethanol extract of *Phyllanthus niruri* was found to have potential anti plasmodial activity in vitro by inhibition of the developmental stage of trophozoite to schizonts. Similar in vitro study also showed that the callus extract and intact *Phyllanthus niruri* extract inhibited the development of trophozoites to schizonts (developmental stage of *Plasmodium falciparum*) in a dose-dependent manner. The anti plasmodial activity of extract of *Phyllanthus niruri* (whole plant) exhibited a higher anti plasmodial activity than all calli and intact fresh apical stem extracts.^[25] It was reported that the water extraction of *Phyllanthus niruri* gives better results of antiplasmodial activities than ethanolic extraction and only leaves and stems parts of the plant were active in vitro against plasmodium.^[26] 1-O-galloyl-6-O-luteoyl R-D-glucose isolated from the *Phyllanthus niruri* was found to have inhibitory effect against Chloroquine-susceptible *P. falciparum* strain in vitro.^[27] Chloroform/ethanol /extract of *Phyllanthus niruri* showed significant inhibition of *P. falciparum* growth at different concentrations.^[28]

Action on kidney stones and uric acid

Kidney stone is a common problem that accumulates calcium oxalate crystals, and it includes urinary calculi formation, nucleation, growth, and aggregation of crystals. *Phyllanthus niruri* extract interferes in the growth and aggregation of calcium oxalate (CaOx) crystals in the calculi. The extract inhibits CaOx crystal aggregation in the early stages of stone formation in the

urine samples of male wistar rats. It is advisable to treat stone formation in the early stages.^[29] The CaOx metastable limit was decreased by the treatment of *P. niruri* (5% v/v) extract and it can also deprive the CaOx crystals and formation of nucleation. The extract has the ability to prevent the growth of calculi and also change the shape and texture of the calculi. When treated on the preformed calculi it can form a matrix like material on its surface and it can modify the appearance and texture of the calculus.^[30] The extract is also administered in hypercalciuric patients; it can decrease the urinary calcium levels and also reduces the excess uric acid in hyperuricemic people by the lignans with uricosuric action in the extract.^[31]

Antispasmodic, pain relieving and anti-inflammatory activity

The wound healing nature of *Phyllanthus niruri* has been evaluated by the healing of wounds by oral and topical administration. *P. niruri* was proved to have a significant role in wound contraction and epithelialization. When Dexamethasone (suppress the wound healing) suppressed rats were treated with the extract a significant increase in wound contraction was found by both oral and topical administration.^[32]

Antinociceptive activity

The analgesic activity of *P. niruri* is demonstrated against formalin induced nociception in mice. The hydro alcoholic extract of *P. niruri* is given orally (25-200 mg/kg) or intra peritoneally (1-30 mg/kg) which causes dose related inhibition of capsaicin induced pain. The *phyllanthus* genus is having high potential level anti analgesic plants and isolated hydroalcoholic extracts of four new species of *phyllanthus* showed significant inhibition of acetic acid induced abdominal constrictions.^[33-35]

Anti-ulcer activity

The acidic heteroxylyan and another polysaccharide showed anti-ulcer activity. These compounds reduced the gastric lesions induced by 65% and 78% ethanol. *P. niruri* proved to be efficient against peptic ulcers.^[36]

Antimalarial activity

Malaria is one of the most prominent health problems in tropical and subtropical countries. The herbal plants show antagonistic properties against malaria. *P. niruri* and *Mimosa pudica* showed antiplasmodial activity, when feeded with ethanol extracts in albino mice.^[37] *P. niruri* ethanolic extract of one month old in vitro grown callus showed higher antiplasmodial activity than extract prepared from fresh apical stem extract.^[38]

Anticancer and cellular protective actions

P. niruri has high potential to inhibit the growth and initiation of cancerous cells which were introduced into mouse skin cells with 7, 12 dimethylbenz (a) anthracene (100µg/100ml acetone) and croton oil (1%) and there is drastic increase in the catalase, reduced glutathione and

protein levels in the skin. In albino mice the chemopreventive action of *P. niruri* with DMBA induces skin papillomagenesis.^[39, 40]

Nematocidal activity

The two prenylated flavones were isolated from the hexane extract of *P. niruri* which showed nematocidal activity against two nematocides, *Meloidogyne incognita* and *Rotylenchulus reniformis*. The two compounds showed moderate Nematocidal activity against nematodes.^[41]

Antiviral action (Hepatitis B)

The plants of the *Phyllanthus* genus have been used for natural remedies for thousands of years in Asia. *P. niruri* has been used to inhibit the hepadna virus and it is extensively used to treat jaundice and hepatitis B virus. The *phyllanthus* genus plants inhibit duck hepatitis B virus by inhibiting 50% of DNA polymerase.^[42] Hepatitis B is the most prominent disease in emerging era. *Phyllanthus niruri* extract can prevent Hepatitis B by binding to the endogenous DNA polymerase and even it can bind to the hepatitis B surface antigen in vitro. Woodchuck hepatitis virus (WHV) was tested against the extract in wood chucks (*Marmota monax*), it efficiently inhibited the woodchuck hepatitis virus (WHV) and elimination of both surface antigen and DNA polymerase activity was found.^[43]

Lipid lowering activity

The *Phyllanthus niruri* has the capacity to reduce the serum lipid levels. The extract is fed orally (250 mg/kg) in hyper lipidemic rats and results followed by reducing lipid levels. Methanol extract of *P. niruri* was tested against chlorpyrifos (CPF) that evoked erythrocyte fragility and lipo peroxidative changes in wistar rats and observed lipid peroxidative changes and protection from the chlorpyrifos induced erythrocyte fragility.^[44]

Antioxidant activity

Phyllanthus niruri showed significant improvement of body antioxidant activities in both insulin and non-insulin dependent diabetes mellitus animals.^[45] A protein isolated from *Phyllanthus niruri* has also been shown to act as radical scavenger, thereby scavenging the free radicals released by the toxic effect of carbon tetrachloride in hepatocytes. The hepatoprotective effect of *Phyllanthus niruri* may be associated with its action at cellular level by reducing oxidative stress as a radical scavenger and promoting antioxidative defense mechanisms of the cells. In vitro antioxidant assay showed that the plant is an effective radical scavenger.^[46] High phenolic content of *Phyllanthus niruri* showed a strong correlation with its antioxidant activity. *Phyllanthus niruri* has a high antioxidant activity because of its several phenolic constituents and it inhibits chromium (VI) induced oxidative toxicity to MDA MB-435S human breast carcinoma cells. Similarly, it was also reported that *Phyllanthus niruri* has a strong free radical scavenging activity and ferric reducing property;

its strong free radical scavenging activity is associated with its high phenolic content. The methanol extract of dried *Phyllanthus niruri* has lower antioxidant property compared to fresh sample.^[47]

CONCLUSION

Phyllanthus niruri Linn. belongs to the Euphorbiaceae family and is a small herb having a wide range of medicinal properties and used widely across the world. *Phyllanthus niruri* plant extract is used as a medicine and is recommended for bronchitis, anaemia, leprosy, asthma, urinary disorders etc. *Phyllanthus niruri* has several bioactive molecules such as lignans, phyllanthin, hypophyllanthin, flavonoids, glycosides, tannins, alkaloids, ellagitannins, triterpenes, phenylpropanoids, steroids, ricinoleic acid, niruriside & phylltetralin. *Phyllanthus niruri* is used as a folk medicine for treating kidney stones, gallbladder stones, liver related diseases such as liver cancer and jaundice. Apart from these, it is also administered for diuretic, hypoglycemic and hypertension cases and also shows anti-inflammatory, anti tumor, antinociceptive and antioxidant properties. By the above applications, *Phyllanthus niruri* has been marketed by prominent companies. The market product of *Phyllanthus niruri* is recommended in daily used medicines like chyawanprash which were produced by many remarkable companies.

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