

Phytoconstituents and Ethnopharmacology of *Phyllanthus niruri*: A Review

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ABSTRACT

India boasts a long history of healthy, diversified, and ancient living circumstances. Many of these cultural practices involve the utilization of medicinal herbs in health systems, including Ayurveda, Homeopathy, Siddha, Unani, and Yoga. The current review was based on the phytoconstituents and ethno pharmacology of Phyllanthus niruri for which an extensive literature survey was done through Scopus, PubMed, and Springer etc. The genus Phyllanthus comprises shrubs, plants, and trees. Phyllanthus species are distributed throughout the planet, with populations concentrated in Africa, America, Asia, and Australia. Phyllanthus niruri is a herb that reaches a height of 30 to 60 cm. It is labours, and the stem frequently branches at the base. The leaves are elliptic, oblong, obtuse, sessile, distichous, and many. Numerous P. nature exudates have demonstrated diverse phytoconstituents i.e., flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarin, and saponins. The entire plant, its aerial parts (leaf and stem), and its roots are used to treat a variety of conditions, including bronchitis, eye conditions, gastrointestinal distress, diabetes, liver and kidney issues, irregular menstruation etc. It removes excess uric acid and is used as laxative, astringent, carminative, digestive, diuretic, tonic, and vermifuge. It concluded that it found effective in treating kidney and gallbladder stones, liver cancer and jaundice, anti-inflammatory, anti-tumour, anti-nociceptive, and antioxidant qualities. Major corporations have been selling P. nature, and it may be investigated further in the near future as a potential source of practical herbal formulations.

Keywords: *Phyllanthus niruri*, phytoconstituents, ethnopharmacology, pharmacological properties, traditional uses.

INTRODUCTION

India boasts a long history of healthy, diversified, and ancient living circumstances. Many of these cultural practices involve the utilization of medicinal herbs in health systems, including Ayurveda, Homeopathy, Siddha/Unani, and Yoga. Due to significant advancements in the biosynthesis of natural chemicals, conventional medications have become increasingly popular in recent years (Vivien, et al; 2022). The rules governing herbal medicines are still in their infancy, despite significant advancements in the field. Herbal medicines contain pharmacologically active chemicals that may cause unwanted or harmful effects, contradicting the general belief that they are safe and "natural" (Izzo, et al; 2016).

The genus *Phyllanthus* comprises shrubs, plants, and trees. *Phyllanthus* species are distributed throughout the planet, with populations concentrated in Africa, America, Asia, and Australia. *Phyllanthus* plants are rich in bioactive chemicals, making them valuable from a pharmaceutical standpoint. The little annual herb *P. niruri* grows in both the tropical and subtropical regions of the world. It is a field weed that grows quickly in Asia, America, and China. The entire plant is used in traditional medicine to cure a variety of ailments due to their well-known medicinal qualities. It is well-known for having hepatoprotective, anti-obesity, hypoglycaemic, anti-fungal, and other qualities in Ayurvedic and Unani medicine (Vyas, et al; 2011). India is home to *Phyllanthus niruri*, an indigenous plant that often appears as a weed in the middle of June and begins to bear fruit in July/August. After the first monsoon showers, it grows in Jharkhand, Bihar & Chhattisgarh. By end of the monsoon season, it can be found in the wild where it can survive until the mid of winter (Sharma, et al; 2011).

Phyllanthus niruri

Description

Phyllanthus niruri is a herb that reaches a height of 30 to 60 cm. It is glabrous, and the stem frequently branches at the base. The leaves are elliptic, oblong, obtuse, sessile, distichous, and many. There are many tiny, green, subsessile leaves that are obtuse, elliptic, ablong, and have a short petiole. The leaves are arranged alternately on both sides of the stem. The flowers are axillary, tiny, yellowish, and abundant. These flowers are monoecious and unisexual; the male blooms have one to three sessile stamens, whereas the female flowers are usually solitary. Fruit is a capsule, with a diameter of 2-3 mm, that is smooth and depressed globose in shape. Its horizontal branches have a height of 30 to 60 cm and a width of 1 to 2.5 mm. It is big and fairly branched (Purohit, et al; 2003).

Taxonomy

Kingdom	- Plantae
Division	- Magnoliophyta
Class	- Magnoliopsida
Order	- Euphorbiales
Family	- Euphorbiaceae
Genus	- <i>Phyllanthus</i>
Species	- <i>niruri</i>



a. Leaves



b. Fruits

Fig 1. Different parts of *P. niruri*

P. niruri has different names in different area and languages (Taylor, 2003)(Krishnamurthy, 2014).

Assamese: *Holpholi*

Bengali: *Noar*

Hindi: *Chalmeri, Bhuiaonla.*

Kannada: *Kirunelli,*

Konkani: *Bhuin-avalae*

Telugu: *Ratsavusirike*

Tamil: *Arunelli*

Malayalam: *Nellipuli*

Marathi: *Bhuiavli*

Oriya: *Narakoli*

Sanskrit: *Amala, Sukshmadala, Bhoodatri*

Phytoconstituents

Numerous *P. niruri* sections have confirmed for phytoconstituents i.e., flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarin, and saponins. Numerous clinical trials have demonstrated the beneficial effects of this herb's extract. (Satya, et al; 2012)-

Category	Phytoconstituents
Alkaloid	Nirurin, 4-Methoxy-nor-securinine, entnorsecurin
Benzenoid	Gallic acid, Corilagin
Coumarin	Ellagic acid, ethyl-brevifolin carboxylate
Flavonoid	Quercetin, rutin, astragalin, quercitrin, isoquercitrin, kaempferol-4-rhamnopyranoside, eridictyol-7- rhamnopyranoside, fisetin-4-O-glucoside, nirurin
Lignin	Phyllanthin, hypophyllanthin, niranthin, nirtetralin, phyltetralin, hinokinin, isolintetralin
Phytallate	Phyllester
Lipid	Ricinoleic acid
Tannin	Geranin
Triterpene	upeol acetate, lupeol, phyllanthanol, phyllanthenone, phyllantheol.
Sterol	Estradiol, β -sitosterol, isopropyl-24-cholesterol

Traditional uses (Onkar, et al; 2015)(Fariab, et al; 2013)(Suresh, et al; 2011)

- The entire plant, its aerial parts and its roots are used to treat numerous illnesses, including bronchitis, eye conditions, gastrointestinal distress, diabetes, liver and kidney issues, irregular menstruation, burns and cuts on the skin, respiratory illnesses, and vaginal discharge.
- It removes excess uric acid.
- It is used as an astringent, carminative, digestive, diuretic, laxative, tonic, and vermifuge.
- It is purgative and abortive at large dosages.
- Ink and dyes are made from a mixture of dark-colored plants and stems in several regions of India.
- Seeds are effective in ulcer, wounds, scabies and ringworms.

Pharmacological Properties

Nephroprotective

Cell damage is caused by ROS, which are produced when blood sugar levels are elevated. As a result, oxidative stress is crucial to cellular damage (Tiwari, et al; 2013). It is a typical pathogenetic factor that causes diabetic nephropathy, which in turn causes end-stage kidney failure. It has been found that *P. niruri* aqueous leaf extract protects the kidneys in adult male Wistar rats with diabetes.

The results indicated that the enzymes required for normal kidney function, SOD, CAT, and glutathione peroxidase, were maintained along with a decreased lipid peroxidation product. Extract reduced oxidative damage by avoiding enzyme malfunction (Kumar, et al; 2014).

Anti-ulcer

P. niruri's anti-ulcer efficacy was assessed using stress-induced ulcer model (ethanol acid and indomethacin model). The extract dramatically reduced the incidence of ulcers, and its anti-ulcer properties were linked to cytoprotection, most likely as a result of increased prostaglandin synthesis (Akah, et al; 2009). The anti-ulcer efficacy of leaf extract of *P. niruri* was investigated against ethanolinduced gastrointestinal mucosal damage in rats. Leukocyte infiltration of the submucosa, inhibition, and reduction of oedema were observed at 1000mg/kg concentration drop in ulcer regions. The prevention of stomach ulcer was attributable to the presence of tannin (Abdulla, et al; 2010).

Analgesic and anti-inflammatory

Investigations into the hydro-alcoholic and dried extract of *P. niruri* in vivo anti-nociceptive properties revealed that the extract exhibited strong and sustained anti-inflammatory and analgesic activity in a number of pain models as well as in animal model (hemorrhagic cystitis) caused by cyclophosphamide. Both the hydroalcoholic and dried extracts of *P. niruri* are abundant in phenolic compounds, i.e., flavonoids, gallic acid, rutin, quercetin demonstrated a range of therapeutic activities i.e., cytotoxic, anti-inflammatory, and anti-nociceptive effects (Porto, et al; 2012).

Antimicrobial

Research was done on the antibacterial role of the ethanolic extract of various *P. niruri* sections, and the findings made it abundantly evident that the extracts have distinct modes of action. Leaf extracted reduced the growth of *Micromonospora purpurea* and the outcome was equivalent with common antibiotic ampicillin. The extract from seeds and leaves showed increased sensitivity to *Acinetobacter calcoaceticus*. *Zymomonas mobilis* was significantly inhibited by root extract, whereas *Staphylococcus epidermidis* was grown more slowly by seed extract. Other plant parts were also shown to be equally effective in preventing bacterial growth for as long as 38%. When *P. niruri* leaf and seed extracts were compared to other sections, they showed noticeable inhibitory zones against *Phanerochaete chrysosporium* and *Penicillium chrysogenum* (Sharma, et al; 2013).

Sumathi and Parvathi (2013) investigated the antimicrobial role of extracts of plants i.e., *P. niruri*, against pathogens- *S. paratyphi* A and *Klebsiella pneumonia*. They discovered that *P. niruri*'s dimethyl sulfoxide leaf extracts have a significant and profound effect on *S. typhi* and *S. aureus*, even at the lowest concentration (50µg/ml). Therefore, *P. niruri* might offer a treatment for staphylococcal infections and typhoid fever. This explains why it is utilized in traditional medicine as an intestinal anesthetic and a remedy for typhoid fever. *Vibrio cholera*, *Shigella flexnerii*, and *Staphylococcus aureus* were all successfully combatted by the ethanolic, methanolic, and aqueous *P. niruri* extract (Sumathi,et al; 2013).

Anti-hyperlipidaemia

Triglyceride levels in the blood are elevated in hyperlipidaemia. The two main clinical consequences of hyperlipidemia are atherosclerosis and severe pancreatitis. Patients with high-level hyperlipidemia experience the former. Triglyceride management can stop the occurrence and serious attack of this fatal illness. Khanna et al. (2002) investigated the lipid-lowering activity of *P. niruri* in Triton-induced and cholesterol-fed hyperlipidaemic Charles foster rats. For 30 days, animals given *P. niruri* (100mg/kg) and cholesterol (25mg/kg) concurrently saw a decrease in their lipid and LDL apoprotein levels as well as a reduction in lipid levels. (Khana, et al; 2002).

Bashir et al. (2015) examined the cytosolic glutathione S-transferase (GST) activity of a methanolic extract of *P. niruri* both ex vivo and in vitro in young female Sprague Dawley rats that were diabetic due to streptozotocin. In vitro, it was found that the extract had no discernible impact on the activity of the GST enzyme in young female diabetic rats. However, induction effects on GST activity were permitted at 500 mg/kg in ex vivo investigations. Consequently, an increase in antioxidant potential against free radicals and hazardous chemicals was seen as a result of an increase in GST activity (Bashir, et al; 2015).

Hepatoprotective

Without influencing the other blood enzymes, pretreatment of rats with *P. niruri* extracts significantly decreased CCl₄-induced alterations in the liver injury markers (enzymes) (Harish, et al; 2006). When given orally to male albino rats, the Ayurvedic herbal preparation HPN-12 (1ml/100g) which contains *P. niruri*, was found to be effective in curing liver damage. A 35-kDa antioxidant protein molecule was isolated and described from *P. niruri*. It was then tested against thioacetamide-induced cytotoxicity. Because protein has the ability to scavenge free radicals, it has been discovered to be an excellent hepatoprotector, both preventing and treating oxidative stress and liver damage. Additionally, the protein shielded hepatocytes from apoptosis and shown cytoprotective action against tert-butyl hydroperoxide (Sarkar, 2010). Amin and colleagues (2013) assessed *P. niruri*'s hepatoprotective effects in male Sprague Dawley rats with thioacetamide-induced liver cirrhosis. The ethanol solution extract effectively inhibited increased extracellular matrix production and decreased the expression of metalloproteinase 2, collagen α 1, and transforming growth factor β . The bioactive components 4-O-caffeoylquinic acid and quercetin-3-Orhamnoside, which were extracted from an active fraction of *P. niruri*, were credited with the hepatoprotective function (Amin, et al; 2013).

Antimalarial

The antiplasmodial activity of *P. niruri* against chloroquine resistant and chloroquine sensitive strains of *Pl. falciparum* was reported to be good by Mustofa and Wahyuono (2007). The IC₅₀ values of these extracts ranged from 2.3-3.9, 132.6-200.4, and 2.9-4.1 μ g/mL, respectively. After a 24-hour incubation, the mean cytotoxicity index of the methanolic extract was lower than aqueous (Subeki, et al; 2005).

Anti-cancer

Diverse 4 species of *Phyllanthus* have been shown to have anti-proliferative effects on 4 distinct cancer cell lines without having any cytotoxic effects on their corresponding normal cells. Furthermore, because these plants' MEs showed their effects at a relatively low dose, they were superior than aqueous extracts in their ability to inhibit the proliferation of cancer cells. Plants that are known to restrict growth exhibited a specific effect on cancer cells by modifying the cell cycle and triggering apoptosis by activating caspases. Therefore, *P. niruri* can be utilized to create a powerful anticancer drug that induces apoptosis (Tang, et al; 2010).

P. niruri's cytoprotective action on normal cells and cytotoxic effect on pre-neoplastic/neoplastic cells combined to produce this activity. The considerable decrease in the prevalence and no. of skin papillomas was attributable to potent phytochemicals, that is, quercetin and rutin. They utilized 1000 mg/kg b. wt of a hydroalcoholic *P. niruri* extract (Sharma, et al; 2008).

Anti-diabetic

Diabetes management has been a global issue up to this point, and a viable cure has not yet been found (Malviya et al., 2010). In eastern Nigeria, *P. niruri* has long been used to treat diabetes. To test the plant's potential to prevent diabetes, male albino rats with normal and alloxan-diabetic conditions were given methanol extract (ME) of *P. niruri*'s aerial parts. The extract's hypoglycemic effect was demonstrated by the normal rats' reduced fasting blood glucose levels after just one oral dose. The blood glucose level in normal glycaemic rats receiving ME likewise decreased in a dose-dependent manner, as did the blood glucose level after a high-glucose diet. When the effect of long-term extract administration to ME-treated rats was evaluated, it was found that the white blood cell count of the ME-treated diabetic rats increased steadily while hemoglobin levels and red and white blood cell counts decreased significantly and then gradually increased. Studies on the histology of pancreatic extracted from diabetic rats receiving ME treatment showed that, in contrast to control groups where necrosis was clearly visible, the extract healed and restored the integrity and function of the injured pancreas in these animals (Okoli, et al; 2010).

Stone dissolution

Khare et al. (2014) investigated the in vitro anti-lymphatic efficacy of *P. niruri* leaves against common medications, Neeri and Cystone as a control, using several solvents i.e., petroleum ether, ethyl acetate, methanol, & water. Of all the extracts, water extract demonstrated the greatest inhibition in the turbidity test and calcium oxalate crystal aggregation (53.09% and 56.8%), and when compared to the medicines employed, water extract and Cystone demonstrated equal potential (Khare, et al; 2014).

Antioxidant

In the current work, three distinct extracts—aqueous, methanol, and chloroform—were used to determine the reducing property of *P. niruri* leaf extract in order to screen its free radical scavenging activity against a battery of free radicals, including DPPH, ABTS, H₂O₂, and hydroxyl radicals, in vitro. The scavenging activity of DPPH and ABTS indicated that the aqueous extract had the strongest activity among all the extracts, but the scavenging activity of methanol and chloroform extract was modest.

The competition b/w deoxyribose and the extract for hydroxyl radicals produced by the Fe^{3+} /Ascorbate/EDTA / H_2O_2 in both the presence and absence of the leaf extracts was used to quantify the hydroxyl radical scavenging. The aqueous extract of the leaves significantly decreased the amount of TBARS production with deoxyribose, whereas the other two extracts shown only moderate efficacy. The aqueous extracts of the leaves demonstrated superior H_2O_2 scavenging than the other two extracts, according to their ability to efficiently scavenge the non-radical oxidant H_2O_2 . The *P. niruri* leaf extracts' metal-reducing activities revealed that the aqueous extract had the highest level of activity. The aqueous extract outperformed the methanol and chloroform extracts as the most potent scavengers among the three extracts. The plot of inhibition (%) against extract concentration was used to determine the extract concentration that provided 50% inhibition (IC_{50}). A standard of ascorbic acid was employed for comparison. Accordingly, the findings demonstrated that *P. niruri* leaf extracts have the ability to scavenge radicals and function as antioxidants in vitro (Radha, et al; 2020).

Anti-fertility

The effects of *P. niruri* aqueous extract on fructose, testosterone, and epididymal sperm parameters were studied. When compared to the control, the fructose content of the seminal fluid, motility/count, and viability of sperm the treated groups showed a significant drop ($p < .05$) after the extract was treated for 14 days. These reductions varied in dosage. Although not substantially different, the treated animals' testosterone levels were lower than those of the control group. These results imply that *Phyllanthus niruri*'s aqueous crude extract possesses antifertility properties. However, a factor that was not included in this study may be the cause of the group's overall observations of increasing weakness and decreased agility (Valentine, et al; 2011).

Anti-viral

Researchers examined the anti-tumor efficaciousness of a hydroalcoholic *P. niruri* in male Swiss albino rats aged 7-9 weeks. The data showed that the early phase of papillomagenesis significantly reduced tumor incidence, tumor yield, tumor burden, and cumulative number of papillomas as compared to carcinogens fed group (Krishna, et al; 2012).

Immunomodulation

Using peritoneal mouse macrophages, an arabinogalactan (AG) derived from *P. niruri* tea preparations was discovered to have immunological characteristics. Using human stomach juices and aqueous solutions, the glycoside exhibited the same action in both acidic and neutral gastrointestinal environments (Mellinger, et al; 2008).

CONCLUSION

The little herbaceous medicinal plant *Phyllanthus niruri* Linn. is used all over the world to cure a variety of conditions, including jaundice, leprosy, asthma, bronchitis, kidney and gall bladder stones, anemia, and liver cancer. Numerous bioactive substances i.e., alkaloids, ellagitannins, flavonoids, glycosides, hypophyllanthin, lignans, niruriside, phyllanthin, ricinolic acid, steroids and triterpenes are abundant in *P. niruri* decoction.

It concluded that it found effective in treating kidney and gallbladder stones, liver cancer and jaundice, anti-inflammatory, anti-tumor, anti-nociceptive, and antioxidant qualities. Major corporations have been selling *P. niruri*, and it may be investigated further as a potential source of practical herbal preparations.

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