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Phytochemical and Pharmacological Properties of *Phyllanthus niruri* L: A Comprehensive Review

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ABSTRACT: *Phyllanthus niruri* L., also known as "Bhumi Amla" or "Stonebreaker," is a small herb from the Phyllanthaceae family found in tropical and subtropical regions. It has long been used in traditional medicine systems like Ayurveda for treating various conditions such as jaundice, kidney stones, liver problems, and viral infections. The plant is rich in phytochemicals like alkaloids, flavonoids, terpenoids, and saponins and has a high carbohydrate and fiber content. Recent research has validated many traditional uses of Phyllanthus niruri, showing its effectiveness in protecting the liver, fighting viruses, microbes, and inflammation, as well as lowering uric acid and cholesterol levels. It also shows potential for reducing oxidative stress, boosting immune function, and managing metabolic disorders. However, further research is needed to standardize dosages, improve extraction methods, and gather more safety data for clinical applications. Despite these limitations, Phyllanthus niruri holds promise as a cost-effective and beneficial treatment option with numerous health benefits.

Keywords: *Phyllanthus niruri*, Phytochemicals, Pharmacological properties, Hepatoprotective, Antiviral therapy.

INTRODUCTION

In the traditional system of medicine, a number of plants have been widely used for the treatment of various disorders since ancient times. The knowledge pertaining to these medicinal plants was handed down from generation to generation either orally or through documents and effective plants have been selected by trial- and error-based experiments (Wansi *et al.*, 2019). In fact, plants have various applications, especially in the health, agriculture, food, and cosmetic industries (Mohammad Hosseini *et al.*, 2019). In Ayurveda system of medicine, Phyllanthus niruri Linn (Tamalaki in Sanskrit) is one of the herbs mentioned in all the relevant ancient Ayurvedic texts. This plant belongs to the family Euphorbiaceae and is an annual herb that is widely spread throughout the tropical and subtropical countries of the world including Sri Lanka and India and commonly found as weed in both cultivated and wasteland areas particularly in the rainy season.

A number of research studies have confirmed that Phyllanthus niruri is rich in phytochemicals, such as alkaloids, flavonoids, ellagitannins (including corilagin and geraniin), and lignans (like phyllanthin and hypophyllanthin). These compounds contribute to its various pharmacological benefits, which encompass hepatoprotective, nephroprotective, antioxidant, anti-inflammatory, antidiabetic, and antiviral properties. Notably, Phyllanthus niruri has gained recognition as a plant with significant therapeutic value, particularly for its effectiveness in inhibiting the formation of kidney stones and combating the Hepatitis B Virus (HBV) (Dhawan & Olweny 2020).

Description: Phyllanthus niruri is a small herb that typically grows between 30 to 60 cm in height. The stem is smooth and often branches out at the base. The leaves are numerous, small, green, and arranged alternately along the stem. They are elliptic or oblong with short petioles. The tiny yellowish flowers are plentiful and monoecious, with male blooms featuring one to three stamens and female flowers usually solitary. The fruit is a smooth, depressed globose capsule measuring 2-3 mm in diameter. The plant has horizontal branches reaching heights of 30 to 60 cm and widths of 1 to 2.5 mm, with a dense branching pattern.

Botanical Classification:

Kingdom – Plantae; Division – Magnoliophyta; Class – Magnoliopsida; Order – Euphorbiales; Family – Euphorbiaceae; Genus – Phyllanthus; Species – Niruri

Table 1: Major phytoconstituents of *Phyllanthus niruri* and their reported pharmacological activities.

Class	Compound(s)	Reported Pharmacological Properties	References
Alkaloids	4-methoxy-nor-securinine, Nirurine, Ent-norsecurinine	CNS stimulant, antimicrobial, antimalarial-like activity	(Calixto *et al.*, 1998; Srivastava & Shukla, 2010)
Benzenoids	Gallic acid	Potent antioxidant, hepatoprotective, anti-inflammatory	(Kumar *et al.*, 2014; Lim *et al.*, 2016)
Coumarins	Ellagic acid, Ethyl brevifolin carboxylate, Methyl brevifolin carboxylate	Antiviral (HBV, HCV), anticancer, antiurolithiatic, anti-inflammatory	(Notka *et al.*, 2004; Lin *et al.*, 2013)
Flavonoids	Quercetin, Rutin, Astragalin, Quercitrin, Isoquercitrin, Kaempferol glycosides, Nirurin, Gallocatechin, Niruriflavone, Quercetol	Antioxidant, hepatoprotective, antihyperlipidaemic, antidiabetic, cardioprotective	(Bagalkotkar *et al.*, 2006; Akinmoladun *et al.*, 2018)
Lignans	Phyllanthin, Hypophyllanthin, Niranthin, Nirtetralin, Phyltetralin, Hinokinin, Lintetralin, Isolintetralin, Linnanthin, Nirphyllin, Phyllnirurin, Demethylenedioxyniranthin	Potent hepatoprotective (anti-HBV), immunomodulatory, antioxidant, anti-inflammatory, anticancer	(Venkateswaran *et al.*, 1987; Lee *et al.*, 2016)
Tannins	Geraniin, Repandusinic acid, Corilagin	Strong antiviral (anti-HBV, anti-HIV), hepatoprotective, nephroprotective, antioxidant	(Yang *et al.*, 2007; Notka *et al.*, 2004)
Triterpenes	Limonene, p-Cymene, Lupeol acetate, Lupeol, Phyllanthenol, Phyllanthenone, Phyllantheol, Hexamethyl-tetracoshenen-1-ol	Anti-inflammatory, hepatoprotective, anticancer, antimicrobial	(Ghosh *et al.*, 2014; Calixto *et al.*, 1998)
Sterols	β-sitosterol, Estradiol, Isopropyl-24-cholesterol	Anti-inflammatory, hypocholesterolemic, anticancer, immunomodulatory	(Awad *et al.*, 2000; Patel *et al.*, 2011)
Phytallates	Phyllester	Hepatoprotective, antioxidant	(Bagalkotkar *et al.*, 2006; Tewari *et al.*, 2017)
Lipids	Ricinoleic acid	Anti-inflammatory, analgesic, skin protective	(Vieira *et al.*, 2001; Calixto *et al.*, 1998)
Saponins	Diosgenin	Anticancer, anti-inflammatory, antidiabetic, cholesterol-lowering	(Jesus *et al.*, 2016; Lim *et al.*, 2016)
Miscellaneous	β-glucogallin, 1-O-galloyl-6-O-luteoyl-α-D-glucose, Niruriside, Triacontanal, Tricontanol	Antioxidant, hepatoprotective, growth-promoting, antimicrobial	(Patel *et al.*, 2011; Srinivasan *et al.*, 2014)

(Adapted and expanded from Calixto *et al.*, 1998; Bagalkotkar *et al*., 2006; Patel *et al*., 2011; Lim *et al*., 2016, with additional references)

Pharmacological Properties. P. niruri's antidiabetic effects are attributed to its ability to regulate glucose metabolism, enhance insulin sensitivity, and protect against oxidative stress through various mechanisms. These include boosting insulin secretion from pancreatic β-cells, improving insulin sensitivity in peripheral tissues, inhibiting carbohydrate-digesting enzymes like α-amylase and α-glucosidase to lower postprandial hyperglycemia, nurturing pancreatic islet regeneration and restoring islet cell structures, as well as reducing oxidative stress for better β-cell function and decreased insulin resistance (Prasad *et al.*, 2011).

Nephroprotective. Elevated blood sugar levels can lead to the production of reactive oxygen species (ROS), causing cell damage through oxidative stress. This process is a key factor in the development of diabetic nephropathy, ultimately leading to end-stage kidney failure. Research has shown that the aqueous leaf extract of P. niruri can protect the kidneys in male Wistar rats with diabetes. The study revealed that essential kidney enzymes - SOD, CAT, and glutathione peroxidase - were preserved, while lipid peroxidation was reduced. The extract effectively prevented oxidative damage by maintaining enzyme functionality (Giribabu *et al*., 2014).

Hepatoprotective Activity. *Phyllanthus niruri* L. is renowned for its hepatoprotective properties, particularly in guarding against liver damage caused by chemical exposure and viral hepatitis. With a history rooted in traditional medicine practices such as Ayurveda, this plant has been utilized as a remedy for jaundice and chronic liver ailments. Various studies have demonstrated that extracts of P. niruri, including aqueous, ethanolic, and methanolic versions, offer substantial defense against hepatotoxins such as carbon tetrachloride (CCl_4), paracetamol, and ethanol. These extracts have been shown to significantly reduce levels of liver enzyme markers like AST, ALT, ALP, and bilirubin in the bloodstream, while also restoring the healthy structure of hepatic tissues (Sharma *et al.*, 2011; Venkateswaran *et al.*, 1987). The hepatoprotective effects of this substance are mainly attributed to its bioactive components, including flavonoids, lignans (such as phyllanthin and hypophyllanthin), and tannins. These compounds play a vital role in enhancing antioxidant defense mechanisms. These phytochemicals function by scavenging free radicals, diminishing lipid

peroxidation, and boosting antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), which helps alleviate oxidative stress in hepatic cells (Syamasundar *et al.*, 1985; Harish & Shivanandappa 2006). Additionally, P. niruri demonstrates antiviral hepatoprotective effects, especially against the hepatitis B virus (HBV).Research conducted both in vitro and in vivo has demonstrated that plant extracts reduce HBV surface antigen expression and inhibit the activity of viral DNA polymerase, leading to a decrease in viral replication (Lee *et al.*, 1996). These findings have been bolstered by clinical trials demonstrating that oral administration of P. niruri extract in patients infected with HBV results in significant reductions in viral DNA levels and improvements in liver function markers, thereby validating its use in traditional medicine for managing viral hepatitis (Thyagarajan *et al.*, 1988; Wang *et al.*, 2014). Taken together, these results underscore P. niruri as a potential hepatoprotective agent that connects traditional medical wisdom with contemporary pharmacological evidence.

Antiviral Activity. Research findings indicate that extracts derived from Phyllanthus niruri possess notable antiviral properties, particularly in combating the hepatitis B virus (HBV). Studies have shown that the bioactive lignans present in this plant extract have the ability to inhibit HBV DNA polymerase and reduce the expression of viral surface antigens, effectively suppressing viral replication (Lee *et al.*, 1996). Its effectiveness in blocking HBV and other viral pathogens is further validated by in vitro and in vivo models (Venkateswaran *et al.*, 1987). Clinical trials showed that patients infected with HBV who were treated with P. niruri extracts experienced significant reductions in HBV DNA and improvements in liver function (Thyagarajan *et al.*, 1988). The results confirm its conventional use as an antiviral agent and endorse its therapeutic potential in contemporary medicine.

Antioxidant Activity. New research has demonstrated that Phyllanthus niruri is a potent antioxidant, with both aqueous and ethanolic extracts displaying substantial free radical scavenging capabilities in DPPH and ABTS tests. Additionally, these extracts exhibit impressive ferric-reducing antioxidant power (FRAP) in laboratory conditions (Radha & Saranya 2020). A study utilizing P. niruri extracts to aid in the production of silver nanoparticles showed notable DPPH radical-scavenging capabilities similar to those of ascorbic acid. This highlights its role in promoting redox balance improvement (Preeja *et al.*, 2020). Standardized methanol-water extracts exhibited a high total phenolic and flavonoid content, with IC_{50} values in DPPH and ABTS assays that are remarkably low, indicating a strong antioxidant potential (Anonymous, 2017). *Phyllanthus niruri* L Whole-plant extracts have recently demonstrated a significant ability to scavenge ABTS and DPPH, along with effectively inhibiting superoxide and nitric oxide, highlighting their in vitro antioxidant effectiveness. These results underscore the substantial antioxidant potential of P. niruri, supporting its value both as a traditional remedy and a promising pharmacological option.

Antidiabetic Activity. Recent in vivo studies demonstrate that leaf extracts of Phyllanthus niruri significantly lower elevated serum glucose levels in alloxan-induced diabetic mice, confirming a notable hypoglycemic effect. In rats that were obese and diabetic due to streptozotocin induction, hyperglycemia was significantly alleviated and lipid profiles improved with oral administration of the extract (500 mg/kg), demonstrating effective metabolic modulation (Metabolomics study, 2016). Aqueous and ethanolic extracts were found to inhibit α-glucosidase in vitro, with IC_{50} values of approximately 3.7 and 6.3 µg/mL, respectively. Corilagin and repandusinic acid A were recognized as strong inhibitors, with IC_{50} values of approximately 0.9 and 1.9 µM. According to Santwana Rani and Baidyanath Kumar (2015) the extracts promote glucose uptake in muscle cells and encourage adipogenesis in adipocytes, both of which indicate enhanced glucose utilization. Together, these results emphasize P. niruri's diverse potential as an antidiabetic agent, corroborating its traditional applications and contemporary pharmacological prospects.

Anti-inflammatory Activity of Phyllanthus niruri extracts have been found to demonstrate significant anti-inflammatory properties by blocking inflammatory markers such as TNF-α, IL-1β, and IL-6 in laboratory experiments as well as in living organisms. (Rajeshkumar *et al.*, 2020). The plant plays an immunomodulatory role by inhibiting the production of nitric oxide (NO) and the expression of cyclooxygenase (COX-2) in LPS-stimulated macrophages (Rani & Sharma 2021). Leaf extracts high in lignans (phyllanthin, hypophyllanthin) decrease NF-κB activation and lessen inflammation mediated by reactive oxygen species (Chowdhury *et al.*, 2022). Animal models demonstrated a reduction in carrageenan-induced paw edema and an improvement in antioxidant status after treatment with P. niruri extract.

Anticancer Activity. The leaf and aerial parts of Phyllanthus niruri show anti-proliferative properties and improve the responsiveness of resistant breast cancer cells to doxorubicin. Particularly, a CH_2Cl_2 fraction notably reduced the effectiveness of DOX in MCF-7^{ADR} cells while maintaining a moderate level of independent cytotoxicity (Rajeshkumar *et al.*, 2021; Lee *et al.*, 2022). Isolated lignans, such as phyllanthin and hypophyllanthin, complemented the effects of doxorubicin by enhancing apoptosis and blocking autophagy evasion. This highlights the significance of utilizing bioactive compounds derived from leaves as adjuncts in treatment (Yang *et al.*, 2020; Tan *et al.*, 2021). George *et al*. (2020) found that a standardized dry extract triggered caspase-3-dependent apoptosis in hepatocellular carcinoma cells (HepG2, Huh-7) without affecting normal hepatocytes, highlighting its specific anti-cancer properties. Phenolics and lignans such as phyllanthin, hypophyllanthin, and nirtetralin obtained from leaves have been shown to effectively induce cell-cycle arrest and apoptosis in various cancer models

including lung, prostate, and breast cancer (Rizvi *et al.,* 2021). Recent nano formulations incorporating P. niruri leaf extract (such as ZIF-8 nanocarriers) improve delivery and therapeutic efficacy, providing modern pharmacological translation strategies.

Immunomodulatory Activity. Phyllanthus niruri has demonstrated considerable immunomodulatory potential by influencing both innate and adaptive immune responses (Gupta *et al.,* 2020). Its extracts enhance the phagocytic activity of macrophages, the function of natural killer (NK) cells, and cytokine production, thereby strengthening host defense (Meena *et al.,* 2021). Plant-derived bioactive lignans and flavonoids help adjust the Th1/Th2 balance, leading to improved immune regulation during infections and inflammation (Das *et al.,* 2022). Research carried out in controlled environments has shown that while there is an increase in IL-10, excessive pro-inflammatory cytokines (TNF-α, IL-6) are reduced. This suggests a dual function in maintaining immune balance. This has led to P. niruri being viewed as a promising phytomedicine for treating immunological disorders and bolstering immune resilience.

Antimalarial Activity. In tropical and subtropical regions, including many African countries, Phyllanthus has been utilized by people as an antimalarial remedy. Research conducted in laboratory settings has revealed that both aqueous and ethanol extracts of P. niruri effectively impede the growth of Plasmodium falciparum, showcasing notable IC50 values. Additionally, experiments on animal models infected with Plasmodium have indicated a decrease in parasitemia levels and an improvement in survival rates upon administration of P. niruri extracts. Consequently, there is evidence to suggest that P. niruri may complement the effectiveness of traditional antimalarial medications such as chloroquine or artemisinin, potentially enable the use of lower dosages and minimize adverse effects (Maia *et al.,* 2020).

CONCLUSIONS

The diverse pharmacological benefits of Phyllanthus niruri, including its anti-cancer, anti-inflammatory, anti-urolithiatic, and immunomodulatory properties, can be largely attributed to its robust phytochemical composition containing lignans, flavonoids, alkaloids, and phenolic compounds. The plant's ability to regulate crucial cellular processes like apoptosis, reduce oxidative stress, modulate cytokines, and dissolve crystals is supported by evidence from both lab experiments and clinical research, validating its extensive use in traditional medicine. Additionally, advancements in drug delivery methods such as nano formulations are enhancing its efficacy and potential for practical application. In summary, P. niruri presents itself as a promising herbal remedy that bridges traditional wisdom with contemporary pharmacology, underscoring the significance of further clinical trials and molecular investigations to ascertain its standardized, safe, and efficient usage in modern healthcare practices.

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