Various health benefits and phytochemical constituents of Phyllanthus niruri

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Abstract

Phyllanthus niruri which belonging to the group Euphorbiaceae is a tiny herb found in the tropical and subtropical regions of both hemispheres. This plant is popular in folk medicine, whole plant, fresh leaves and fruits are used in the treatment of various diseases. Phyllanthus has been used in the Ayurveda system of medicine for over 2,000 years, which has the ability to prevent or treat a several unrelated health conditions. The fresh roots of Phyllanthus niruri can be used as an excellent treatment for jaundice, edema and genital urinary system infections. P. niruri also helps to eliminate stones in patients with kidney stones and normalize calcium levels in patients with hypercalcemia. Therefore, it is considered to be a better way to treat gallstones and kidney stones. P. niruri decoction is rich in many bioactive compounds such as alkaloids, ellagitannins, flavonoids, glycosides, hypophyllanthin, lignans, niruri side, phyllanthin, phyltetralin, phenyl propanoids, ricinolic acid, steroids and triterpenes. Apart from these, it is also administered for diuretic, hypoglycaemic and hypertension cases and it also shows anti-inflammatory, anti-tumour, and antioxidant properties. This review explains about the role of P. niruri in different health conditions along with its pharmacological properties and health effects.

Keywords: P. niruri, health effects, medicinal purposes, phytochemical compounds, pharmacological properties

Introduction

Phyllanthus niruri is a medicinal herb with various health benefits which is most commonly seen in coastal areas. It is also known as stone breaker or seed under leaves. The herb belongs to the genus Phyllanthus and family Euphorbiaceae (Giribabu et al., 2014) [8]. Phyllanthus niruri is said to be the herb that grows annually for about 30-60cm in height. There are several ways for identifying different species of Phyllanthus. In case of Phyllanthus niruri, its stem is angular in shape with different distichous, elliptic-oblong leaves (Oudhia, 2015). Flowers are yellow in color and very numerous; monoecious with 1–3 staminate flowers and solitary pistillate flower borne axillary (Bagalkotkar et al. 2006) [40]. It contains various small seeds which resemble fruits that is longitudinally ribbed on the back of the leaves. The male flowers are one to three in number while the female flowers are solitary in nature (Paithankar et al., 2012). The seed to seed cycle takes place in around two or four weeks. The flowering time in India occur in the months of July to August.

Phyllanthus niruri has been tested as safe and effective remedies for liver disorders and for other medical conditions (Amin et al., 2012) [44]. Phyllanthus has been used in the Ayurveda system of medicine for over 2,000 years, which has the ability to prevent or treat a several unrelated health conditions. Several species of Phyllanthus are often known to be Bhumyamalaki, which is commonly used to treat liver disorders (Amin et al., 2011) [21]. The hypotensive effects of P. niruri have been attributed to geranin and confirmed by its cholesterol and triglyceride (Asare et al., 2011) [15]. The connection between diseases and oxidative stress indicates that antioxidants possess the ability to protect against similar diseases, which was confirmed by the strong inverse link between the intake of the plant and the reduction of various diseases lowering effects (Ali et al., 2014). This plant is also used in folk medicine, whole plant, fresh leaves and fruits are used in the treatment of various diseases, particularly hepatitis and other viral infection. Recent studies indicated a positive link between the plants and the reduction of chronic diseases, such as diabetes (Mediani et al. 2015) [18]. Polyphenols are the most important phytochemicals found in plants with potent antioxidant properties, which partially contribute to the positive influence on the prevention of chronic diseases (Ali et al., 2014; Fischer et al., 2011). Most of the pharmacological properties of P. niruri have been reported using the whole plant, since Phyllanthus species are
commonly small herbs and they are used in this manner in folk medicine, and it has different varieties of phytochemicals and their pharmacological properties (Couto et al., 2012) [41]. The active phytochemicals, flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarins and saponins, all of these has been detected from various parts of *P. niruri*. Extracts of this herb have been proven to have therapeutic effects in many clinical studies (Paiithanker et al., 2011). The plant has more medicinal importance for numerous conditions like dysentery, influenza, vaginitis, tumors, diabetes, diuretics, jaundice, kidney stone, dyspepsia, antihepatotoxic, antihepatitis-B, antivirus and antifungal properties. Some reports also indicate that *P. niruri* can restrict calcium oxalate crystals and formation of stones in kidney, ureter and urinary bladder (Giriababu et al., 2014) [42]. *P. niruri* extract has also proven to inhibit DNA. In South India, the herb is called Bhumyamalaki or Kezharnelli, the herb is said to be treated for constipation, gonorrhea and syphilis. Whereas in northern India, this herb is locally known as ‘pitirishi’ and has been used as a household remedy for asthma, bronchitis and even tuberculosis (Nathanael et al., 2016). This herb can be used as an appetizer and as tonic. It is also used as colic. The plant, when it is boiled with the leaves, it is often considered to be a diuretic and is used in treatment of diabetes, dysentery, hepatitis, menstrual disorders, and skin disorders (Rubianto et al. 2016). Plant extracts are used for purifying blood, for treating slight malaria fevers and anemia. It also helps in releasing phlegm and to oppose fever. This herb can be used for constipation also (Hakkim et al. 2016). *Phyllanthus niruri* Linn (Tamalaki in Sanskrit) is one of the plants listed in all pertinent ancient Ayurvedic books. This annual herb, which belongs to the Euphorbiaceae family, is extensively distributed throughout the world’s tropical and subtropical regions, including Sri Lanka and India, and is usually found as a weed in both cultivated and wasteland areas, especially during the rainy season. The extract of *P. niruri* Linn is said to be one of the most often used treatments in the Ayurvedic system of medicine, particularly for bronchitis, anemia, skin problems, asthma, cough, liver, kidney, and urinary tract disorders (Dahanayake et al., 2019). The alkaloidal extract of *P. niruri* was found to exhibit sensitive inhibitory reaction on cytopathic effects generated by both strains of human immunodeficiency virus on human MT-4 cells, indicating that *P. niruri* has an inhibitory effect on human immunodeficiency virus. Its extract has been used to treat bacterial diseases such as diarrhea, dysentery, TB, cough, and vaginitis, as well as having anti-tumor and anticarcinogenic properties (Ibrahim et al., 2013).

**History**

There are over 1000 species in the Phyllanthus genus, many of which are utilized as traditional medicines. Plant extracts have been used to treat hypertension, diabetic, hepatic, urinary, and sexual diseases, among other ailments, since ancient times. The pharmacognostic qualities of Phyllanthus herbs have now been validated by modern scientific investigations. Many of the Phyllanthus plants include compounds that are responsible for these therapeutic qualities (Sarin et al., 2014) [45]. *Phyllanthus niruri* L., Phyllanthaceae, is a little shrub that can be found in both tropical and subtropical areas. Several species in this genus are utilized in folk medicine around the world for a variety of therapeutic purposes. Most of the claimed uses in folk medicine are supported by pre-clinical pharmacological research using extracts and purified components from Phyllanthus species (Couto et al., 2012) [41]. *P. niruri* has a long history in herbal systems such as Indian Ayurveda, Traditional Chinese Medicine and Indonesian Cha Jam. It is considered an important medicinal plant throughout India. It is a well-known traditional Indonesian herb that treats many diseases (Kumar et al., 2020). In jamu preparations, the plant is used as an antiviral and hepatoprotective agent. Since the mid-1960s, various studies have been conducted on *P. niruri* to study its active ingredients and its pharmacological activities (Farrukh et al., 2018). Ottow is considered to be the first person to work with *P. niruri*, and it was also reported in 1891 the separation of phyllanthin. It has a powerful source of phytochemicals, most of which are found in *P. niruri* is said to be the first research team from India and Brazil to conduct research on the medical properties of sports, because this plant has been proven to be a long-standing area for its residents, and its residents have a long history of use (Bagalkotkar et al., 2006) [40]. *Phyllanthus niruri* has also been used historically for treating different ailments including hypertension. Literature reports have indicated that it is a potent antihypertensive herbal medication used traditionally (Bello et al., 2020) [42]. Brazilian researchers have demonstrated the antispasmodic activity of an alkaloid from *P. niruri*. Nile tilapia gained worldwide attention in the late 1980s due to its anti-hepatitis B activity.

**General eatures of *P. niruri***

*Phyllanthus* species are very important as well as popular in treating various diseases in several countries around the world. The species Phyllanthus is originated from India but it is also seen in amazon rain forests and several other parts of the world such as Brazil, China, Bahamas and Malaysia. It is also known as stone breaker (Mediani et al., 2015) [18]. Phyllanthus is meant to be ‘leaf and flower’ due to the close occurrence of flower and fruit within the leaf. *P. niruri* usually grows during rainy season and can be found in both cultivated as well as waste lands (Paiithanker et al., 2011).

**Taxonomy of *P. niruri***

*P. niruri* Linn is a 30-60 cm tall annual herb. The stem is angular, glabrous, and commonly branching at the base. It is cylindrical and hairless, with triangular stipules, acuminate, and often corded at the base, and triangular stipules at the level of the leaves insertion. When cut, it emits translucent latex. Tap roots are wiry, thin, and have fine secondary roots (Dahanayake et al., 2019). Leaves; numerous, small, green, sub sessile, closely arranged, elliptic a long shaped, obtuse, having short petiole and stipules present, they are arranged alternatively on each side of the stem. Flowers; the flowers are usually small and yellow or white in color. These are unisexual, monocious flowers, male flowers having 1-3 sessile stamens and female flowers were solitary in nature (Narendra et al., 2015). On stalks, the seed capsules are 1–2 mm long, spherical, smooth, and 2 mm wide, with six seeds. The seeds are thrown away when the fruits break open. The seeds are triangular in shape (like an orange segment), light brown in colour, and 1 mm long, with 5–6 ribs on the back (Hakkim et al., 2016).
Phyllanthus niruri—Plant

Botanical classification

The herb *Phyllanthus niruri* belongs to the kingdom Plantae, Division Magnoliophyta, class Euphyllophyida, order Euphorbiales, family Euphorbiaceae, genus *Phyllanthus* and species *Niruri*

Geographical distribution

It’s a field weed that can be found growing in tropical and subtropical regions of Asia, America, and China. Phyllanthus is a Phyllanthus genus. It has between 600 and 700 species, all of which have small differences. *Phyllanthus niruri* is an annual herb that grows in the wild in Jharkhand, Bihar, Chhattisgarh, and other Indian states after the first monsoon showers. It has, however, been observed to grow abundantly in coastal locations (Paithanker et al., 2011). It blooms in Indian states during the second week of June and bears fruit until mid-July or August. It can be found mostly in tropical areas till the rainy season is over. It can, however, grow and live until mid-winter in safe conditions (Hakim et al., 2016). Plant is native and well distributed from Mexico until Argentina. *Phyllanthus niruri*, herb is widely seen across Brazil as a weed. According to certain descriptors it occurs in several foreign countries, including Malaysia, Indonesia, India, USA, etc (Filho et al., 2018). Eventhough Phyllanthus has been originated from India, it is also grown in the Amazon rainforests and other tropical region worldwide, which includes the Bahamas, China and Malaysia. In Brazil, ‘Quebra Pedra’ is the traditional name of Phyllanthus, which means ‘stone breaker’. This species is also used to cure pathological conditions, such as jaundice and other liver related diseases. In Malaysia, Phyllanthus is known as ‘dukung anak’, which means ‘to carry a child’, referring to the fruits at the bottom of each leaf petiole (Mediani et al., 2015) [18].

Health benefits

The fresh roots of *Phyllanthus niruri* can be used as an excellent treatment for jaundice, edema and genital urinary system infections (Shanavas et al., 2019). *P. niruri* also helps to eliminate stones in patients with kidney stones and normalize calcium levels in patients with hypercalcemia. Therefore, it is considered to be a better way to treat gallstones and kidney stones (Marwa et al., 2020). It has high potential anti-cancer and antioxidant properties, can cure viral liver, and has a high level of cytotoxic vinblastine, which can be used for cancer cells that are resistant to multiple drugs. It can also inhibit endogenous hepatitis B virus DNA polymerase in *in vitro* and *in vivo* models (Narendra et al., 2012). According to reports, in *in vivo* and *in vitro* studies, bamboo also showed obvious hepatitis B virus surface antigen activity. In the study, the glycosides observed in *Phyllanthus niruri* showed aldose reductase (AR) inhibitory activity (Fernandes et al., 2012). *P. niruri* has been found to exhibit antitumor antiviral Anti-oxidant, anti-inflammatory and antidiabetic activities and radiation protection (Zheng et al., 2016) [43]. According to reports, the water extracts of *Phyllanthus niruri* an inhibitory effect on human immunodeficiency virus. The study examined the anti-HIV effect of Phoebe alkaloid extracts in human cell lines. The lipid-lowering activity of the alcohol extract of *Phyllanthus niruri* in activity-induced hyperlipidemia was studied in rats (Paithankar et al., 2011). It contains various biologically active molecules, such as lignans, chlorophyll, hypocyanidins, flavonoids, glycosides, tannins, alkaloids, ellagatannins, triterpenes, phenylpropane, steroids, ricinoleic acid, Uridine and fiftetralin. The alkaloids present in herbal medicine also have antispasmodic activity and can relax muscles (A. Krishnasatya et al., 2012). Nile tilapia also exhibits a variety of pharmacological activities, such as anti-hepatitis B antiviral activity, antibacterial agents, liver protection, anticancer and hypocalcemic agents (Moreira et al., 2012) [35]. The methanol extract obtained from *P. niruri* has immunomodulatory activity and anti-HIV activity. Fibrin and hypocyanidin have anti-tumor activity (A. Krishnasatya et al., 2012). The purpose of this review is based on the formulation and evaluation of *Phyllanthus niruri* confectionery products.

Role in urinary tract infection

*Phyllanthus niruri* has been demonstrated to interfere with various stages of stone formation, including lowering crystal aggregation, altering crystal shape and composition, and affecting crystal interaction with tubular cells, resulting in decreased eventual endocytosis. Researchers found that *Phyllanthus niruri* helped reduce the size of these stones. They also found that it improved the removal of magnesium and potassium from the body through the urine (Boim et al., 2010) [35]. The clinical benefits of *Phyllanthus niruri* may be due to ureteral relaxation, which aids in the elimination of calculi or the clearing of fragments after lithotripsy, or to a possible reduction in the excretion of urinary crystallisation...
promoters like calcium. In neither of these investigations, there were any adverse renal, cardiovascular, neurological, or toxic consequences. Overall, these findings point to *Phyllanthus niruri* having a stone-prevention or removal impact (Pucci *et al*., 2018) \(^{[16]}\).

**Role in inflammation**

Studies on the anti-inflammatory, antinociceptive and analgesic activity of *P. niruri* have mainly revolved around animal models. Intraperitoneally administered methanol extract of dried callus tissue of *P. niruri* caused antinociceptive effects on five different models of pain, suggesting that *P. niruri* possessed analgesic properties (Lee *et al*., 2016) \(^{[12]}\). *Phyllanthus niruri* L., Euphorbiaceae, spray-dried standardized extract was studied for its anti-inflammatory and antinociceptive activities in adult albino rats and mice. *Phyllanthus niruri* spray-dried standardized extract has potent inflammatory and antinociceptive activities and that these activities are not modified by standard drying process, making it feasible to use the dry extract standardized to obtain a phytotherapeutic preparation and thus validating its use for the treatment of pain and inflammation disorders (Porto *et al*., 2013) \(^{[50]}\).

**Role in treating ulcers**

*Phyllanthus niruri* L. (Euphorbiaceae) is generally used in traditional medicine to treat ulcer and inflammation. The methanolic extract of *P. niruri* leaf possess anti-inflammatory activity and promotes ulcer protection as ascertained by regeneration of mucosal layer and substantial prevention of the formation of hemorrhage and edema (Mostofa *et al*., 2017) \(^{[38]}\). In a study the pre-treatment of *P. niruri* leaf extract in rats resulted in significantly less gastric mucosal injury and flattening of the mucosal folds. Histological studies of the gastric wall revealed that negative control rats suffered very severe damage of gastric mucosa, along with edema and leucocytes infiltration of the sub mucosal layer compared to rats pre-treated with *P. niruri* leaf extract where there was marked gastric protection along with reduction or inhibition of edema and leucocytes infiltration of the sub-mucosa (Abdulla *et al*., 2010).

Pharmacological functions of *Phyllanthus niruri*
Mechanism of action of *P. niruri*

**Phytoconstituents of *P. niruri***

<table>
<thead>
<tr>
<th>Class</th>
<th>Compound</th>
<th>Function</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloid</td>
<td>4-methoxy-nor-securinine</td>
<td>Antimalarial</td>
<td>Zhang <em>et al.</em>, 2011</td>
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<tr>
<td></td>
<td><em>Nirurine</em></td>
<td>Anti-cancer</td>
<td>Chirkin <em>et al.</em>, 2015</td>
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<td></td>
<td>Ent-norsecurinine</td>
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<tr>
<td>Benzenoid</td>
<td>Gallic acid</td>
<td></td>
<td></td>
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<tr>
<td>Flavonoid</td>
<td>Quercetin</td>
<td>Strengthen and modulate the permeability of the walls of blood vessels,</td>
<td>Chromie and Gao 2015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticancer, anti-inflammatory, Antioxidant</td>
<td></td>
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<tr>
<td></td>
<td>Astragalin</td>
<td>Diuretic, Immunomodulatory</td>
<td>Kim <em>et al.</em>, 2012</td>
</tr>
<tr>
<td></td>
<td>Quercetin</td>
<td>Anti-leishmanial Anti-nociceptive, Anti-inflammatory</td>
<td>Kaur <em>et al.</em>, 2017</td>
</tr>
<tr>
<td></td>
<td>Quercetol</td>
<td></td>
<td>Khachatorian <em>et al.</em>, 2012</td>
</tr>
<tr>
<td>Tannin</td>
<td>Geraniin</td>
<td>Anti-nociceptive</td>
<td>Jia <em>et al.</em>, 2013</td>
</tr>
<tr>
<td>Sterol</td>
<td>B-sitosterol</td>
<td>Repandusinic acid Inhibited HIV-1-RT</td>
<td>Bagalkotkar <em>et al.</em>, 2006</td>
</tr>
<tr>
<td>Lipid</td>
<td>Ricinoleic acid</td>
<td></td>
<td>Lee <em>et al.</em>, 2015</td>
</tr>
<tr>
<td>Saponins</td>
<td>Diocgenin</td>
<td></td>
<td>Raju and Rao <em>et al.</em>, 2012</td>
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**Flavonoids**

Rutin a flavonol glycoside made up of the flavonol quercetin and the disaccharide rutinoside, which belongs to a wide group of plant phenolic secondary metabolites that comprises about 2000 distinct compounds. Rutin is beneficial because it strengthens capillaries, which can benefit persons with arteriosclerosis and high blood pressure (Cromie and Gao, 2015).

Quercetin Because of its potential to strengthen and alter the permeability of blood vessel walls, especially capillaries, quercetin is significant in nutrition. Anticoagulant, anti-cancer, anti-fungal (particularly antidermatophytic), anti-feedant, anti-glaucomic, anti-inflammatory, anti-oxidant, antiseptic, and anti-spasmodic action are all properties of this bioactive molecule (Khachatorian *et al.*, 2012).

**Catechin**

Gallocatechin was extracted from *P. niruri* tissue cultures. Catechins were found to inhibit the proliferation and induce apoptosis in human colon and hepatic epithelial carcinoma cells. Catechins have pro-oxidative activity and bactericidal effects in the presence of trace elements, particularly Cu2+ (Kaur *et al.*, 2017).

**Terpenes**

Limonene Orange oil contains a lot of limonene. Limonene has been shown to have anti-carcinogenic properties in liver tumour models. In hairless rats, limonene has been shown to boost diclofenac penetration, implying that limonene is an useful topical treatment for both cutaneous and subdermal injuries (Bagalkotkar *et al.*, 2006) [40].

Lupenol is a pentacyclic triterpene that can be made through a backbone rearrangement event involving protosterol carbocation. It reduces superoxide production by blocking tyrosyl oxidation. Anti-inflammatory and anti-tumor properties have been demonstrated for the chemical. Lupenol, a potent skin chemopreventive, has been shown to reduce benzoyl-peroxide-induced cutaneous damage. It can also boost the antioxidant status of the liver in rats and protect them against cadmium-induced damage.

**p-Cymene**

Thyme, an essential oil with *p-cymene* as one of its components, demonstrated good anti-oxidant activity by preventing oxidation of *a*-tocopherol, and thyme, an essential oil with *p-cymene* as one of its components, exhibited good anti-oxidant activity by preventing oxidation of *a*-tocopherol (Kaur *et al.*, 2017).
Pharmacological activity of *P. niruri*

**Anti-bacterial activity of *P. niruri***

With the growth in antibiotic resistance and the need for novel antibiotics with high antibacterial efficiency and low toxicity, scientists are turning to phytochemicals found in everyday plants. One reason for the increased interest in extracting phytochemicals for the synthesis of novel antibiotics is the fear of plant species extinction, driving a desire to research the therapeutic potential of these resources before they are lost (Lee et al., 2018). With the growth in antibiotic resistance and the need for novel antibiotics with high antibacterial efficiency and low toxicity, scientists are turning to phytochemicals found in everyday plants. One reason for the increased interest in extracting phytochemicals for the synthesis of novel antibiotics is the fear of plant species extinction, driving a desire to research the therapeutic potential of these resources before they are lost. Some of these include rutin, gallocatechin, prenylated flavanone glycosides, quercetin, quercitrin, p-Cymene, corilagin, diosgenin, securinine, and -glucogallin (Chandana et al., 2020) *Phyllanthus niruri* extract has also shown to have good anti-bacterial effect against the bacteria *Salmonella Pullorum* at 5% dosage (Hidanah et al., 2022).

**Anti-viral activity of *P. niruri***

In blood samples positive for HBV antigen, alcoholic, hexane, chloroform, butanol, and water extracts of *Phyllanthus niruri* were examined for *in vitro* effects on HbsAg, HBeAg, and HBV-DNA, followed by Elisa screening of the appropriate antigen. The extracts were efficient against the HBV antigen, with the butanol extract being the most effective (Hakim et al., 2016). In 7-9 week old male Swiss albino rats, researchers tested the anti-tumor efficacy of a hydro-alcoholic extract of the entire plant of *P. niruri* Linn. When compared to carcinogen-treated controls, the early phase of papillomagenesis induced significant reductions in tumour incidence, tumour yield, tumour burden, and cumulative number of papillomas, according to the data (Dahanayake et al., 2019). In addition, the alkaloidal extract of *P. niruri* showed inhibitory action against the cytopathic effects of both HIV strains on human MT-4 cells at the quantities examined (Njoroge et al., 2012).

**Action of kidney stones & uric acid***

The creation, nucleation, development, and aggregation of calcium oxalate crystals in the kidney is a prevalent condition that includes urinary calculi formation, nucleation, growth, and aggregation. The extract of *Phyllanthus niruri* inhibits the growth and aggregation of calcium oxalate [CaOx] crystals in calculi. In male wister rats' urine samples, the extract prevents CaOx crystal aggregation in the early phases of stone formation. It's best to deal with stone formation as soon as possible (Hakim et al., 2016). *Phyllanthus niruri* may obstruct key phases in the formation of calculi, such as crystal aggregation and internalisation by tubular cells, as well as crystal structure and content. These qualities of *Phyllanthus niruri* may be beneficial in the prevention of lithiasis, as they suppress calculus formation and keep crystals distributed in the urine, making them simpler to eliminate (Mirian et al., 2010).

**Anti-diabetic activity***

Due to the ability of its extract to lower blood glucose and lipid levels in diabetic rats and prevent postprandial rise in
blood glucose levels, the aerial portions of \textit{P. niruri} offer considerable potential as an antidiabetic medicine. These effects lower the risk of diabetes-related complications. It may also protect the pancreas from further injury by acting as an antioxidant and providing excellent glycaemic control (Okoli et al., 2010). In normoglycemic rats, the methanolic extract considerably lowered (p 0.05) fasting blood glucose and inhibited the postprandial rise in blood glucose following a high glucose meal, according to several research (Dahanayake et al., 2019). \textit{P. niruri} methanolic extracts exhibit potent anti-diabetic properties. After 21 days of ingestion of extract of \textit{P. niruri}, studies demonstrated considerable improvement in anti-oxidant parameters, such as an increase in GSH and SOD and a decrease in NO and LPO in several tissue homogenates (muscle, kidney, liver, and pancreas), demonstrating its anti-oxidant potential. A decrease in insulin resistance may be linked to a drop in leptin levels (Kumar et al., 2019).

**Side effects and toxicity of \textit{P. niruri}**

\textit{Phyllanthus} has been utilised in Ayurvedic medicine for ages, although little is known about its long-term safety. The most common side effects are moderate stomach upset and diarrhoea. \textit{Phyllanthus} should not be consumed by children, pregnant women, or nursing moms due to a lack of study. People with Wilson's Illness should also avoid it. It may lower uric acid levels even more, increasing the risk of liver damage in patients who already have it (Wong., 2021). In general, human investigations found no negative side effects. When consumed up to 400 mg three times day for one month under the supervision of a healthcare practitioner, \textit{Phyllanthus niruri} is likely safe. Blood sugar levels may be lowered by \textit{Phyllanthus niruri}. People with diabetes or hypoglycemia, as well as those taking blood sugar-altering medicines, herbs, or supplements, should exercise caution. A competent healthcare expert, such as a pharmacist, may need to monitor blood glucose levels, and prescription modifications may be necessary. \textit{Phyllanthus niruri} has been linked to an increased risk of bleeding. People with bleeding disorders or those taking medicines that may enhance the risk of bleeding should exercise caution. It's possible that you'll need to modify your dosage. \textit{Phyllanthus niruri} has been linked to an increased risk of bleeding. People with bleeding disorders or those taking medicines that may enhance the risk of bleeding should exercise caution. It's possible that you'll need to modify your dosage. Low blood pressure may be caused by \textit{Phyllanthus niruri}. People who are using blood pressure medications should exercise caution. It's possible that you'll feel drowsy or sedated. When driving or operating big machinery, exercise caution. It should also be taken with caution in persons who have liver problems (Hakim et al., 2016). There is little information about \textit{Phyllanthus niruri}'s negative effects. This is due to a scarcity of human research to date; practically all relevant studies have been conducted on rats or cell cultures. In rats, the toxicity of \textit{Phyllanthus niruri}. There were no abnormalities in internal organs or any symptoms of toxicity discovered by the researchers. Humans, on the other hand, have larger, more complicated bodies than rats, making it impossible to predict if the effects in rodents will be similar to the consequences in humans (Carter, 2020).

Acute toxicity experiments utilising aqueous leaf extracts of \textit{P. niruri} in female Sprague Dawley rats revealed an LD50 more than 5000 mg/kg b.wt with no deleterious effects after a single injection (Asare et al., 2011) \textsuperscript{15}. \textit{P. niruri} extract, at 300 mg/kg b.wt, is typically safe for acute oral administration of \textit{P. niruri} whole plant extract in mice, according to cytotoxicity and genotoxicity tests. (Asare et al., 2012). Similarly, at 50–250 mg/kg b.wt, an aqueous extract of \textit{P. niruri} was evaluated in rat bone marrow for genotoxic, anti-genotoxic, and cytotoxic properties. The study found no genotoxic or cytotoxic potential against cyclophosphamide-induced damage (de Queiroz et al., 2013). As a result, the research supports the usage of \textit{P. niruri} at prescribed levels. Because it has the ability to permeate the blood–testis barrier, the aqueous extract of \textit{P. niruri} showed anti-fertility effects. It produces considerable depletion of the fructose content in the seminal fluid and a reduction in sperm viability, motility, and count at doses above 200 mg/kg. (Ezeonwu, 2011). Clinical trials of these effects in humans, however, are scarce. According to Asare et al., 2011 \textsuperscript{15} a group of five S-D rats was formed. As a result, three groups were formed, one of which was the control group (C). A single low dose (LD) of 2000 mg/kg b.w. and a single high dose (HD) of 5000 mg/kg b.w. were given orally. The aqueous homogeneous solutions of \textit{P. niruri} were reconstituted. 900 l/kg b.w. was chosen as the administration volume. Group 1, the control group (C), was given 162 litres of drinking water after being fed a typical chow diet (once). The extract was gavaged to group 2, the low dosage group (LD), and group 3, the high dose group (HD) at the doses mentioned earlier. \textit{Phyllanthus niruri} is low toxic, and it showed toxicity to batrachians and fishes when extract is alcohol and water based. It is very less toxic to mammals (Hakim et al., 2016).

**Future prospects of \textit{P. niruri}**

\textit{Phyllanthus niruri} Linn. A small herbaceous medicinal plant, is used worldwide for the treatment of anaemia, asthma, bronchitis, kidney and gall bladder stones, leprosy, liver cancer and jaundice. \textit{P. niruri} decoction is rich in many bioactive compounds such as alkaloids, ellagitannins, flavonoids, glycosides, hypophyllanthin, lignans, \textit{niruriside}, phyllanthin, phyletalin, phenyl propanoids, ricinolic acid, steroids and triterpenes. Apart from these, it is also administered for diuretic, hypoglycaemic and hypertension cases and it also shows anti-inflammatory, anti-tumour, anti-nociceptive and antioxidant properties. A protein has also been isolated from \textit{P. niruri}, with hepatoprotective activity, but its purification and commercial use have not been exploited yet. Although there has been extensive research on this herb, but because of obsolete literature, there is need for correct identification, classification and nomenclature of \textit{P. niruri} L. from other confusing and misleading species. Molecular identification of each species of the genus Phyllanthus must be opted by taxonomists all over the world. Research is also required, especially towards the mechanism of biological activity and pharmacokinetic studies of proteins and phytochemicals of \textit{P. niruri} (Kaur et al., 2017). Considering the medicinal properties of the \textit{Phyllanthus} herbs, these species should be assessed for pharmacognostics and pharmacological properties. Considering the growing popularity of ethnopharmacological value of \textit{Phyllanthus} species and its use in herbal medicines, it is imperative to assess the genetic diversity of these species, which will have implications for formulating conservation strategies in future (Sarin et al., 2014) \textsuperscript{49}.

**Conclusion**

\textit{Phyllanthus niruri} is a medicinal herb with various health
benefits which is most commonly seen in coastal areas. It is also known as stone breaker or seed under leaves. *Phyllanthus niruri* has been used since ages by the folk because of its rich medicinal values. The broad spectrum of its medicinal use accounts for the chemical investigation of the herb. Hence, the chemical standardization of the raw material and the formulations containing *Phyllanthus niruri* is under vast discovery and thus more work is required to establish *Phyllanthus niruri* as a useful herb for treatment of various complications. *P. niruri* Linn is an important medicinal herb mentioned in Ayurveda system of medicine. Some of its medicinal uses have been proven in experimental models which suggest that the plant possesses various pharmacological activities Research is also required, especially towards the mechanism of biological activity and pharmacokinetic studies of proteins and phytochemicals of *P. niruri*.

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