



ISSN (E): 2277-7695
 ISSN (P): 2349-8242
 NAAS Rating: 5.23
 TPI 2022; SP-11(6): 1886-1895
 © 2022 TPI
www.thepharmajournal.com
 Received: 23-03-2022
 Accepted: 29-04-2022

Varsha KP
 Institution, Lovely Professional
 University, Punjab, India

Various health benefits and phyto chemical constituents of *Phyllanthus niruri*

Varsha KP

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, phylltetralin, 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

Corresponding Author
Varsha KP
 Institution, Lovely Professional
 University, Punjab, India

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 (Paithankar *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, antihyperglycemic and also exhibits antiviral and antibacterial properties. Some reports also indicate that *P. niruri* can restrict calcium oxalate crystals and formation of stones in kidney, ureter and urinary bladder (Giribabu *et al.*, 2014) ^[8]. *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, gonorrhoea and syphilis. Whereas in northern India, this herb is locally known as 'pitrishi' 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 anti-carcinogenic 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 only 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) ^[48]. 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 (Paithanker *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, monoecious 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 (Hakim *et al.*, 2016).



Phyllanthus niruri- Plant

Botanical classification

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

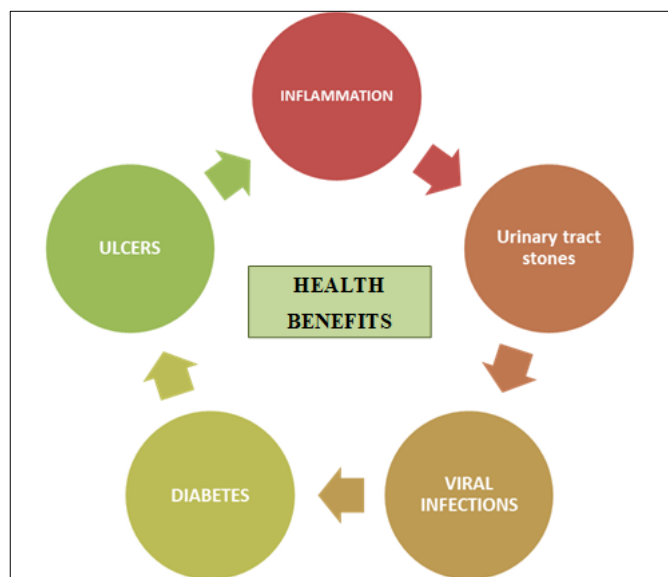
Geographical distribution

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 ha *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, ellagitannins, triterpenes, phenylpropane, steroids, ricinoleic acid, Uridine and fildetralin. 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) [20]. 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].

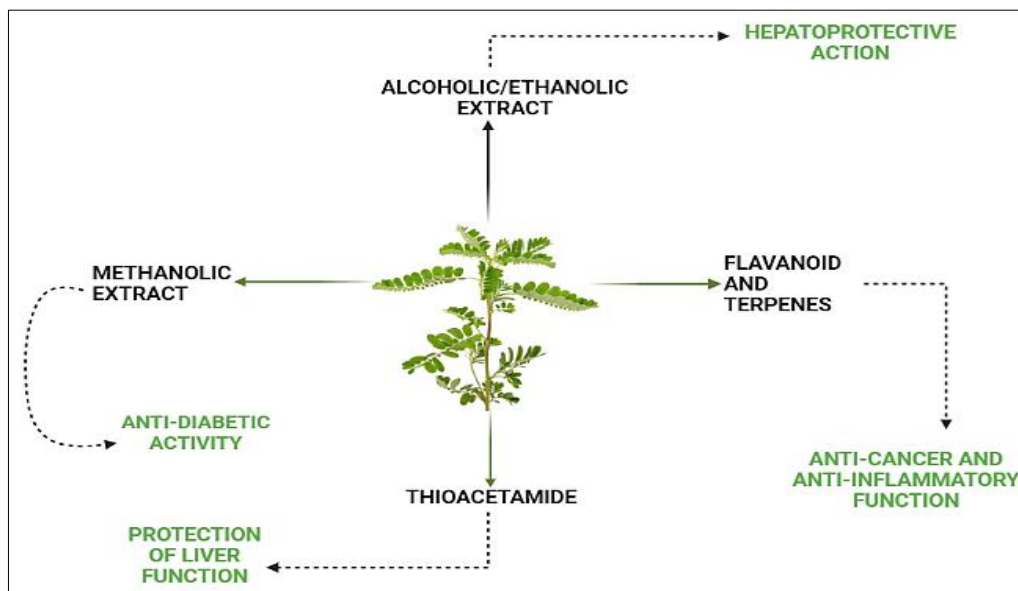
Role in inflammation

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

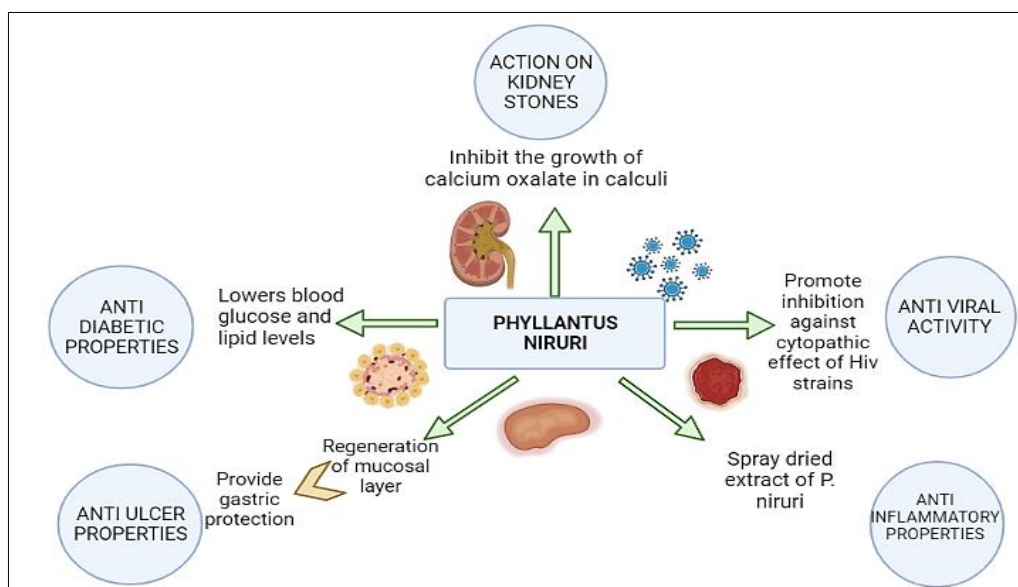
use for the treatment of pain and inflammation disorders (Porto *et al.*, 2013) [50].

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).

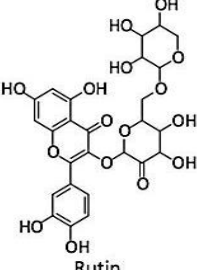
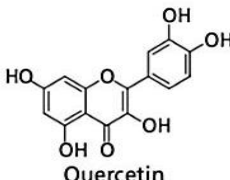
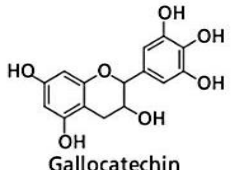
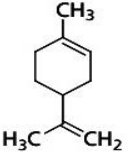
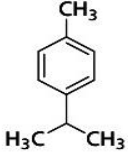
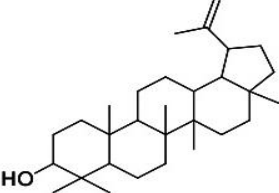


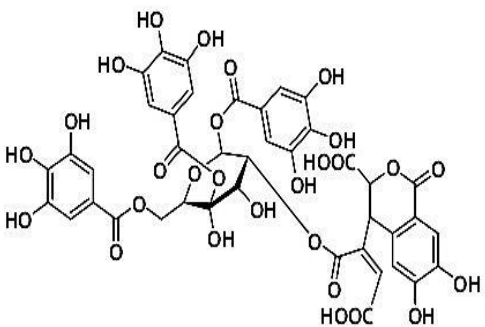
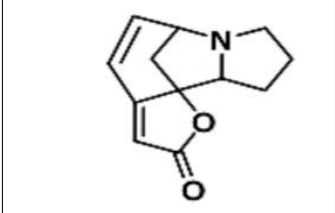
Pharmacological functions of *Phyllanthus niruri*



Mechanism of action of *P. niruri* Phytoconstituents of *P. niruri*

Class	Compound	Function	References
Alkaloid	4-methoxy-nor-securinine	Antimalarial	Zhang <i>et al.</i> , 2011
	Nirurine	Anti-cancer	Chirkin <i>et al.</i> , 2015
	Ent-norsecurinine		
Benzenoid	Gallic acid		
Flavonoid	Quercetin	Strengthen and modulate the permeability of the walls of blood vessels, Anticancer, anti-inflammatory, Antioxidant	Chromie and Gao 2015
	Rutin	Antioxidant, Strengthen the capillaries	
	Astragalin	Diuretic, Immunomodulatory	Kim <i>et al.</i> , 2012
	Quercitrin	Anti-leishmanial Anti-nociceptive, Anti-inflammatory	Kaur <i>et al.</i> , 2017
	Quercetol		Khachatorian <i>et al.</i> , 2012
Tannin	Geraniin	Anti-nociceptive	Jia <i>et al.</i> , 2013
	Repandusinic acid	Inhibited HIV-1-RT	
	Corilagin		
Sterol	B-sitosterol		Bagalkotkar <i>et al.</i> , 2006 [40]
	Estradiol		
	Isopropyl-24-cholesterol		
Lipid	Ricinoleic acid		Lee <i>et al.</i> , 2015
Saponins	Diosgenin	Antifungal	Raju and Rao <i>et al.</i> , 2012

Class	Compound	Function	References
Flavonoids	 Rutin	Rutin a flavonol glycoside made up of the flavonol quercetin and the disaccharide rutinose, 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. Anti-aggregant, anti-cancer, anti-fungal (particularly anti-dermatophytic), anti-feedant, anti-glaucomic, anti-inflammatory, anti-oxidant, antiseptic, and anti-spasmodic action are all properties of this bioactive molecule (Khachatoorian <i>et al.</i> , 2012). Catechin Gallo catechin was extracted from <i>P. niruri</i> 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 Cu ²⁺ (Kaur <i>et al.</i> , 2017).	
	 Quercetin		
	 Gallo catechin		
Terpenes	 Limonene	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 a useful topical treatment for both cutaneous and subdermal injuries (Bagalkotkar <i>et al.</i> , 2006) [40]. Lupeol 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. Lupeol, 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 <i>et al.</i> , 2017).	
	 p-Cymene		
	 Lupeol		

<p style="text-align: center;">TANNINS</p>  <p style="text-align: center;">Repandusinic acid</p>	<p>Repandusinic acid With an ID50 value of 0.05 Mm, repandusinic acid inhibited human immunodeficiency virus type-1 reverse transcriptase (HIV-1-RT). When compared to human DNA polymerase-α, it had a 10-fold higher sensitivity to HIV-1-RT, indicating good selectivity in blocking HIV replication without hurting healthy cells. Ellagic acid is anti-carcinogenic and anti-HBV. It also inhibits aldolase reductase and thus plays a major role in prevention of diabetes (Patel <i>et al.</i>, 2012).</p>
<p style="text-align: center;">Alkaloids</p>  <p style="text-align: center;">Norsecurinine</p>	<p>Norsecurinine is a securinega alkaloid with potent antispasmodic properties. Securinine, a structurally similar compound, has anti-malarial and anti-bacterial properties. Extracellular electrophysiological investigations on neurons in the cat spinal cord revealed that securinine prevented GABA inhibitory activity while having no effect on glycine inhibitory action. Securinine was also isolated from <i>P. niruri</i> and found to be a selective antagonist of GABA recognition sites on mammalian central neurons (Zhang <i>et al.</i>, 2011).</p>
<p style="text-align: center;">Lignans</p>	<p>Lignans, such as phyllanthin and hypophyllanthin, have been demonstrated to have hepatoprotective and anti-genotoxic properties. <i>In vitro</i> and <i>in vivo</i> studies have shown that these chemicals can inactivate hepatitis B. By inhibiting reverse transcriptase, phyllanthin, an aryl tetrahydro naphthalene lignan, has anti-viral action against HIV (Gautam <i>et al.</i>, 2013).</p>

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, galocatechin, 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 pappilomagenesis induced significant reductions in tumour incidence, tumour yield, tumour burden, and cumulative number of pappilomas, 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 *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). *P. niruri* methanolic extracts exhibit potent anti-diabetic properties. After 21 days of ingestion of extract of *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 *P. niruri*

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. *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, *Phyllanthus niruri* is likely safe. Blood sugar levels may be lowered by *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. *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. *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 *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 *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 *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 *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)^[15]. *P. niruri* extract, at

300 mg/kg b.wt, is typically safe for acute oral administration of *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 *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 *P. niruri* at prescribed levels. Because it has the ability to permeate the blood–testis barrier, the aqueous extract of *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^[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 *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. *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 *P. niruri*

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. *P. niruri* decoction is rich in many bioactive compounds such as alkaloids, ellagitannins, flavonoids, glycosides, hypophyllanthin, lignans, *niruriside*, 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 antiinflammatory, anti-tumour, anti-nociceptive and antioxidant properties. A protein has also been isolated from *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 *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 *P. niruri* (Kaur *et al.*, 2017). Considering the medicinal properties of the *Phyllanthus* herbs, these species should be assessed for pharmacognostics and pharmacological properties. Considering the growing popularity of ethnopharmacological value of *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)^[45].

Conclusion

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*.

References

- Al Zarzour RH, Ahmad M, Asmawi MZ, Kaur G, Saeed MAA, Al-Mansoub MA, et al. *Phyllanthus niruri* Standardized Extract Alleviates the Progression of Non-Alcoholic Fatty Liver Disease and Decreases Atherosclerotic Risk in Sprague-Dawley Rats. *Nutrients*. 2017;9:766. <https://doi.org/10.3390/nu9070766>
- Colpo, Elisângela, et al. Antioxidant effects of *Phyllanthus niruri* tea on healthy subjects. *Asian Pacific journal of tropical medicine*. 2014;7(2):113-118.
- Putri, Denise Utami, et al. Immune modulation properties of herbal plant leaves: *Phyllanthus niruri* aqueous extract on immune cells of tuberculosis patient-*in vitro* study. *Natural product research*. 2018;32(4):463-467.
- Mediani Ahmed, et al. Metabolic and biochemical changes in streptozotocin induced obese-diabetic rats treated with *Phyllanthus niruri* extract. *Journal of pharmaceutical and biomedical analysis*. 2016;128:302-312.
- De Araújo Júnior, Raimundo Fernandes, et al. A dry extract of *Phyllanthus niruri* protects normal cells and induces apoptosis in human liver carcinoma cells. *Experimental biology and medicine*. 2012;237(11):1281-1288.
- Kamruzzaman, Hakim MD, Obydul Hoq. A review on ethnomedicinal, phytochemical and pharmacological properties of *Phyllanthus niruri*. *Journal of Medicinal Plants Studies*. 2016;4(6):173-180.
- Ramandeep, Kaur, et al. Phytochemical screening of *Phyllanthus niruri* collected from Kerala region and its antioxidant and antimicrobial potentials." *Journal of Pharmaceutical Sciences and Research*. 2017;9(8):1312.
- Giribabu, Nelli, et al. Aqueous extract of *Phyllanthus niruri* leaves displays *in vitro* antioxidant activity and prevents the elevation of oxidative stress in the kidney of Streptozotocin-induced diabetic male rats." *Evidence-Based Complementary and Alternative Medicine*. 2014.
- Tjandrawinata, Raymond Rubianto, Liana Wijaya Susanto, and Dwi Nofiarny. The use of *Phyllanthus niruri* L. as an immunomodulator for the treatment of infectious diseases in clinical settings." *Asian Pac. J. Trop. Dis*. 2017;7(3):132-140.
- Couto, Angélica G, et al. Anti-inflammatory, antiallodynic effects and quantitative analysis of gallic acid in spray dried powders from *Phyllanthus niruri* leaves, stems, roots and whole plant." *Revista Brasileira de Farmacognosia*. 2013;23(1):124-131.
- Lee NY, Khoo WK, Adnan MA, Mahalingam TP, Fernandez AR, Jeevaratnam K. The pharmacological potential of *Phyllanthus niruri*. *Journal of pharmacy and pharmacology*. 2016;68(8):953-969.
- Paithankar VV, et al. *Phyllanthus niruri*: A magic herb. *Research in Pharmacy*, 2015, 1(4).
- Kaur, Navneet, Baljinder Kaur, Geetika Sirhindi. "Phytochemistry and pharmacology of *Phyllanthus niruri* L. A review. *Phytotherapy research*. 2017;31(7):980-1004.
- Asare, George Awuku, et al. Acute toxicity studies of aqueous leaf extract of *Phyllanthus niruri*." *Interdisciplinary toxicology*. 2011;4(4):206.
- Pucci, Nidia D, et al. Effect of *Phyllanthus niruri* on metabolic parameters of patients with kidney stone: A perspective for disease prevention. *International braz J urol*. 2018;44(4):758-764.
- Narendra K., et al. *Phyllanthus niruri*: A review on its ethno botanical, phytochemical and pharmacological profile." *Journal of Pharmacy Research*. 2012;5(9):4681-4691.
- Mediani, Ahmed, et al. Phytochemical and biological features of *Phyllanthus niruri* and *Phyllanthus urinaria* harvested at different growth stages revealed by 1H NMR-based metabolomics. *Industrial Crops and Products*. 2015;77:602-613.
- Okoli, Charles O, et al. Studies on the possible mechanisms of antidiabetic activity of extract of aerial parts of *Phyllanthus niruri*. *Pharmaceutical biology*. 2011;49(3):248-255.
- Moreira, Jeverson, et al. Anti-hyperalgesic activity of corilagin, a tannin isolated from *Phyllanthus niruri* L. (Euphorbiaceae). *Journal of Ethnopharmacology*. 2013;146(1):318-323.
- Amin, Zahra A, et al. Protective role of *Phyllanthus niruri* extract against thioacetamide-induced liver cirrhosis in rat model. *Evidence-based complementary and alternative medicine*. 2012.
- Liu, Sheng, et al. *In vitro* and *in vivo* anti-hepatitis B virus activities of the lignan niranthin isolated from *Phyllanthus niruri* L." *Journal of Ethnopharmacology*. 2014;155(2):1061-1067.
- Chandana G, Manasa R, Vishwanath S, Mahesh MS. Antimicrobial activity of *Phyllanthus niruri* (Chanka piedra). *IP Journal of Nutrition, Metabolism and Health Science*. 2021;3(4):103-108.
- Dahanayake, Jeevani Maheshika, Pathirage Kamal Perera, Priyadarshani Galappaththy, and Menuka Arawwawala. A mini review on therapeutic potentials of *Phyllanthus niruri* L." *Trends in Phytochemical Research*. 2020;4(3):101-108.
- Mehta, Manu, Sarika Gupta, Ajay Duseja, and Sandeep Goyal. Phytochemical and Antioxidants Profiling of *Phyllanthus niruri*: A Hepatoprotective Plant. *World J Pharm Pharm Sci*. 2019;8(8):1117-1127.
- Ramandeep, Kaur, Akhtar Nahid, Choudhury Neelabh, and Kumar Navneet. Phytochemical screening of *Phyllanthus niruri* collected from Kerala region and its antioxidant and antimicrobial potentials. *Journal of Pharmaceutical Sciences and Research*. 2017;9(8):1312.
- Shanmugam B, Shanmugam KR, Ravi S, Subbaiah GV, Mallikarjuna K, Reddy KS. Antibacterial activity and phytochemical screening of *Phyllanthus niruri* in

- ethanolic, methanolic and aqueous extracts. International Journal of Pharmaceutical Sciences Review and Research. 2014;27(2):85-89.
28. Cordelia ON. Evaluation of chemical constituents of *Phyllanthus niruri*. African Journal of Pharmacy and Pharmacology. 2012;6(3):125-128.
29. Colpo E, Vilanova CD, Pereira RP, Reetz LGB, Oliveira L, Farias IL, *et al.* Antioxidant effects of *Phyllanthus niruri* tea on healthy subjects. Asian Pacific journal of tropical medicine. 2014;7(2):113-118.
30. Shanmugam B, Shanmugam KR, Ravi S, Subbaiah GV, Mallikarjuna K, Reddy KS. Antibacterial activity and phytochemical screening of *Phyllanthus niruri* in ethanolic, methanolic and aqueous extracts. International Journal of Pharmaceutical Sciences Review and Research. 2014;27(2):85-89.
31. Kaur N, Kaur B, Sirhindi G. Phytochemistry and pharmacology of *Phyllanthus niruri* L.: A review. Phytotherapy research. 2017;31(7):980-1004.
32. Shilpa VP, Muddukrishnaiah K, Thavamani BS, Dhanapal V, Arathi KN, Vinod KR, *et al.* *In vitro* immunomodulatory, antifungal, and antibacterial screening of *Phyllanthus niruri* against to human pathogenic microorganisms. Environmental Disease. 2018;3(3):63.
33. Ranilla LG, Apostolidis E, Shetty K. Antimicrobial activity of an Amazon medicinal plant (*Chancapiedra*) (*Phyllanthus niruri* L.) against *Helicobacter pylori* and lactic acid bacteria. Phytotherapy research. 2012;26(6):791-799.
34. Pucci ND, Marchini GS, Mazzucchi E, Reis ST, Srougi M, Evazian D, *et al.* Effect of *Phyllanthus niruri* on metabolic parameters of patients with kidney stone: A perspective for disease prevention. International braz J urol. 2018;44:758-764.
35. Boim MA, Heilberg IP, Schor N. *Phyllanthus niruri* as a promising alternative treatment for nephrolithiasis. Int Braz J Urol. 2010 Nov-Dec;36(6):657-64.
36. Tan WC, Jaganath IB, Manikam R, Sekaran SD. Evaluation of antiviral activities of four local Malaysian *Phyllanthus* species against herpes simplex viruses and possible antiviral target. Int J Med Sci. 2013;10(13):1817-1829. Published 2013 Oct 31.
37. Cíntia RC, Porto, Luiz AL, Soares Tatiane P. Souza, Pedro R. Petrovick, Ibson L. Lyra, Raimundo F. Araújo Júnior, Silvana Maria Zucolotto Langassner, Aurigena A.A. Ferreira, Gerlane C.B. Guerra, Anti-inflammatory and antinociceptive activities of *Phyllanthus niruri* spray-dried standardized extract, Revista Brasileira de Farmacognosia, 2013, 23(1).
38. Mostofa R, Ahmed S, Begum MM, Sohanur Rahman M, Begum T, Ahmed SU, *et al.* Evaluation of anti-inflammatory and gastric anti-ulcer activity of *Phyllanthus niruri* L. (Euphorbiaceae) leaves in experimental rats. BMC Complement Altern Med. 2017 May 16;17(1):267.
39. Satya A, Narendra Kumara, Swathi J, Sowjanya KM. *Phyllanthus niruri*: A Review on its Ethno Botanical, Phytochemical and Pharmacological Profile. Journal of pharmacy research. 2012;5:4681.
40. Bagalkotkar G, Sagineedu SR, Saad MS, Stanslas J. Phytochemicals from *Phyllanthus niruri* Linn. and their pharmacological properties: A review. J Pharm Pharmacol. 2006 Dec;58(12):1559-70. doi: 10.1211/jpp.58.12.0001. PMID: 17331318.
41. Couto, Angélica G, *et al.* Anti-inflammatory, antiallodynic effects and quantitative analysis of gallic acid in spray dried powders from *Phyllanthus niruri* leaves, stems, roots and whole plant. Revista Brasileira de Farmacognosia, 2013.
42. Ezzat MI, Okba MM, Ahmed SH, El-Banna HA, Prince A, Mohamed SO, Ezzat SM. In-depth hepatoprotective mechanistic study of *Phyllanthus niruri*: *In vitro* and *in vivo* studies and its chemical characterization. 2020 Jan 15.
43. Zheng ZZ, Chen LH, Liu SS, Deng Y, Zheng GH, Gu Y, Ming YL. Bioguided Fraction and Isolation of the Antitumor Components from *Phyllanthus niruri* L, 2016 Sep 29.
44. Amin ZA, Bilgen M, Alshawsh MA, Ali HM, Hadi AH, Abdulla MA. Protective Role of *Phyllanthus niruri* Extract against Thioacetamide-Induced Liver Cirrhosis in Rat Model. Evid Based Complement Alternat Med, 2012.
45. Sarin, Bharti, Verma, Nidhi & Martín, Juan & Mohanty, Aparajita. An Overview of Important Ethnomedicinal Herbs of *Phyllanthus* Species: Present Status and Future Prospects. The Scientific World Journal, 2014.
46. Giribabu N, Karim K, Kilari EK, Salleh N. *Phyllanthus niruri* leaves aqueous extract improves kidney functions, ameliorates kidney oxidative stress, inflammation, fibrosis and apoptosis and enhances kidney cell proliferation in adult male rats with diabetes mellitus. J Ethnopharmacol, 2017 Jun 9.
47. Nisar MF, He J, Ahmed A, Yang Y, Li M, Wan C. Chemical Components and Biological Activities of the Genus *Phyllanthus*: A Review of the Recent Literature. Molecules, 2018 Oct 8.
48. Bello I, Usman NS, Dewa A, Abubakar K, Aminu N, Asmawi MZ, Mahmud R. Blood pressure lowering effect and vascular activity of *Phyllanthus niruri* extract: The role of NO/cGMP signaling pathway and β -adrenoceptor mediated relaxation of isolated aortic rings. J Ethnopharmacol, 2020 March 25.
49. Ezzat MI, Okba MM, Ahmed SH, El-Banna HA, Prince A, Mohamed SO, *et al.* In-depth hepatoprotective mechanistic study of *Phyllanthus niruri*: *In vitro* and *in vivo* studies and its chemical characterization, 2020.
50. Porto Cíntia, Soares Luiz, Souza Tatiane, Petrovick Pedro, Lyra Ibson, Júnior Raimundo, *et al.* Anti-inflammatory and antinociceptive activities of *Phyllanthus niruri* spray-dried standardized extract. Revista Brasileira de Farmacognosia. 2013.
51. Gautam K, Kumar P, Jain C. Comparative study of alpha amylase inhibitory activity of flavanoids of *Vitex negundo* Linn. and *Andrographis paniculata* Nees. Int J Green Pharm. 2013;7(1):25-28.
52. Cromie MM, Gao W. Dangi AS, Sharma M, Yadav A. Epigallocatechin-3-gallate enhances the therapeutic effects of leptomycin B on human lung cancer A549 cells. Oxid Med Cell Longev 2015: 217304. <https://doi.org/10.1155/2015/217304>.2015.
53. Khachatoorian R, Arumugaswami V, Raychaudhuri S, *et al.* Divergent antiviral effects of bioflavonoids on the hepatitis C virus life cycle. Virology. 2012;433:346-355.
54. Patel P, Harde P, Pillai J, Darji N, Patel B. Antidiabetic herbal drugs: A review. Pharmacophore. 2012;3(1):18-29.2012.
55. Zhang W, Li JY, Lan P, *et al.* Chemical synthesis and

- biological activities of Securinega alkaloids. *J Chin Pharm Sci.* 2011;20:203-217.
56. Jia L, Jin H, Zhou J, *et al.* A potential anti-tumor herbal medicine, corilagin, inhibits ovarian cancer cell growth through blocking the TGF- β signaling pathways. *BMC Complement Alternat Med* 13: 57. Chirkin E, Atkatlian W, Poree FH. 2015. The Securinega alkaloids. *Alkaloids Chem Biol.* 2013;74:1-120.
57. Raju J, Rao CV. Diosgenin, a steroid saponin constituent of yams and fenugreek: emerging evidence for applications in medicine. In: *Bioactive Compounds in Phytomedicine*, Rasooli I (ed), 2012.
58. Shanmugam BSKR *et al.* Antibacterial activity and phytochemical screening of *Phyllanthus niruri* in ethanolic, methanolic and aqueous extracts. *Int J Pharmaceut Sci Rev Res.* 2014;27:85-89.
59. Ghiasi M, Azadnia A, Arabieh M, Zahedi M. Protective effect of rutin (vitamin p) against heme oxidation: A quantum mechanical approach. *Comp Theor Chem.* 2012;996:28-36.
60. Hidanah S, Sabdoningrum EK, Sudjarwo SA. Formulation and Characterization of Meniran (*Phyllanthus niruri* Linn) Extract Nanoparticle on Antibacterial Activity against Salmonella Pullorum. *Pharmacognosy Journal*, 2022, 14(2).