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## A review on ethnomedicinal, phytochemical and pharmacological properties of *Phyllanthus niruri*

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### Abstract

*Phyllanthus niruri* Linn. Belongs to Euphorbiaceae family and it is a small herb having wide range of medicinal properties, and it is used widely across the world. In Indian ayurvedic and Unani system it is used for Jaundice, ulcers, skin diseases, diabetes, chest pain and urinary complications. Its taste is bitter and acts as astringent and show laxative effect. This review covers information about ethno medicinal uses of *Phyllanthus niruri* in different countries with various pharmacological profile of the plant. The phytochemical studies were characterized and the presence of various compounds such as lignans, phyllanthin, hypophyllanthin, flavonoids, glycosinoids & tannins was mentioned. The extracts of *Phyllanthus niruri* have a wide range of pharmacological activities like antimicrobial, antiviral, hepato protective, antioxidant, anticancer, anti-inflammatory, antiplasmodial and diuretic. This review summarizes the information about its botanical, morphological, ethnomedicinal, pharmacological and biological activities of the plant. In addition this review provides information about the structure of the phytochemical compounds that promotes better commercial exploitation.

**Keywords:** *Phyllanthus niruri*, phytochemical, pharmacological, hepatoprotective

### 1. Introduction

Bhumaamalaki (*Phyllanthus niruri* Schum. & Thonn., Euphorbiaceae), which is widely spread throughout the tropical and subtropical countries of the world including India is most commonly used in the Indian Ayurvedic system of medicine in problems of stomach, genitourinary system, liver, kidney and spleen. *Phyllanthus niruri* has been described in Ayurveda by the Sanskrit name – Bhoomyaamalakee, Taamalakee and Bhodhatree. It was described to have the properties of Rasa, Guna, Veerya and Vipaka. The Ayurvedic literature has shown its uses as Kaasahara (antitussive), Shwaasahara (antispasmodic, antidyspnoic), Kaphapittahara (which relieves the Kapha Pitta Dosha), Pipaasaaghna (which relieves Polydipsia), Raktapittahara (hemorrhage disease), Paanduhara (antianemic), Kaamalaahara (which cures jaundice), Kushthaghna (indicated in leprosy), Daahaghna (refrigerant, relieves burning sensation), Kshatakshayaghna (indicated in Trauma) and Mootrarogahara (which cures urinary disorders). The use of *Phyllanthus niruri* is gaining momentum because of its novel antiviral activity against hepatitis B virus and for several other biological activities such as kidney and gallbladder stones, for cold, flu, tuberculosis, and other viral infections; liver diseases and disorders including hepatitis, jaundice and liver cancer<sup>[1]</sup>. It also acts against liver cell toxicity and improves the immune system of patients and has been found effective against hepatitis A. *Phyllanthus niruri* is often used in the traditional system of medicine for a variety of ailments including dropsy, diabetes, jaundice, asthma and bronchial infections<sup>[2]</sup>. In the Ayurvedic system of medicine it is used in problems of stomach, genitourinary system, liver, kidney and spleen. It is bitter, astringent, stomachic, diuretic, febrifuge and antiseptic. The whole plant is used in gonorrhoea, menorrhagia and other genital affections. It is useful in gastropathy, diarrhoea, dysentery, intermittent fevers, ophthalmopathy, scabies, ulcers and wounds. It is also used as a good tonic. The Spanish name ‘chanca piedra’ means “stone breaker or shatter stone.” In South America, ‘chanca piedra’ has been used to eliminate gall bladder and kidney stones, and to treat gall bladder infections, cardiovascular problems, and also a remedy around the world for influenza. *Phyllanthus niruri* has a long history of use in the treatment of liver, kidney and bladder problems, diabetes and intestinal parasites. In Suriname (Northeastern part of South America), *Phyllanthus niruri* is always sold as fresh and dry plant material in the herb markets. Decoctions are used in herbal baths and after labor, cramps, asthma, uterus complaints and to treat stomachache<sup>[3]</sup>.

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It is a restoration herb and used as an appetizer and as tonic. It is also used as colic. The plant, when boiled with the leaves, is considered to be a diuretic and is used in treatment of diabetes, dysentery, hepatitis, menstrual disorders, and skin disorders. Plant extracts are used as blood purifiers, for light malaria fevers and anemia. It helps to release phlegm and to combat fever. This herb can be used for constipation also. *Phyllanthus niruri* elaborates different classes of organic compounds of medicinal importance including alkaloids, flavonoids, hydrolysable tannins (Ellagitannins), major lignans, polyphenols, triterpenes, sterols and volatile oil. Many lignans were isolated from the plant viz., phyllanthin (a bitter constituent) and hypophyllanthin (a non bitter constituent) [4]. The highest amounts of phyllanthin (0.7% w/w) and hypophyllanthin (0.3% w/w) have been reported in leaves whereas, in the stem these are in minor quantities present [5]. Lignans isolated from *Phyllanthus niruri* are phyllanthin, hypophyllanthin, niranthin, phyltetralin, nirtetralin, isonirtetralin, hinokinin, lintetralin, isolintetralin, demethylenedioxy-niranthin, 5-demethoxyniranthin etc., flavonoids such as gallic acid, gallic acid, quercetin-3-O-glucopyranoside, phyllanthusiin, quercetin, kaempferol 3-O-glucopyranoside, kaempferol etc., ellagitannins include geraniin, amariin, furosin, geraniinic acid B, amariinic acid, amarulone, repandusinic acid A, corilagin, isocorilagin, elaeocarpusin, phyllanthusiin A, B, C, D and melatonin; securiniga-type alkaloids such as isobubbialine and epibubbialine and sterol such as amarosterol A, amarosterol B. *Phyllanthus niruri* had been reported to have pharmacological effects such as antimicrobial, antiviral activities against hepatitis B, chemoprotective, antimutagenic and hypoglycaemic agent. Methanolic extract of *Phyllanthus niruri* exhibited immunomodulatory activity. Ellagitannins (geraniin and corilagin) were shown to be the most potent mediators of the antiviral HIV activity. Phyllanthin and hypophyllanthin present in *Phyllanthus niruri* exhibited antitumor activities against EAC in Swiss albino mice, cytotoxic effects on K-562 cells, and hepatoprotective and antioxidant effects. The present review assesses the potential of *Phyllanthus niruri* in relation to its traditional uses and in terms of findings based on modern bioscientific research. The link between conventional remedies and recent research in various areas has been well established in other plants which facilitate to determine effective mode of action of plant derived products. The plant is known to contain several pharmacological important biomolecules whose efficacy is well established by several biochemical and pharmacological studies. This review intent to compile various studies on this plant and critically evaluates the issues related to ethnopharmacology, phytochemistry, pharmacology, clinical studies and toxicology of *Phyllanthus niruri*.

## 2. General Features

*Phyllanthus niruri* may be found in profusely branched condition along with crops of gram, wheat, pea, etc. In the wild it is found growing along road sides, in street corners, and dumps of building materials. Taxonomically, the annual herb *Phyllanthus niruri* belongs to the family *Phyllanthaceae* of the order Malpighiales under class Magnoliopsida of the Division Magnoliophyta. In the Ayurvedic System of medicine the whole plant of *Phyllanthus niruri* can be used for medicinal purposes. It has been accepted as acrid, cooling, alexipharmic. Ayurveda recommends its use for bronchitis, leprosy, anaemia, urinary discharge, asthma etc. Local people of Chhattisgarh and Jharkhand use it for the treatment of skin diseases, indigestion, cough, ulcers etc. Maharshi Charak has considered

this herb to be most effective in the treatment of asthma, increasing appetite, improving digestion, stimulating liver, and producing laxative effects. In the Unani System of medicine this herb is good for sores and chronic dysentery. Its seeds are used in the treatment of ulcers, wounds, scabies and ringworms. The root of this plant is considered to be an excellent remedy for liver diseases.



Fig 1: *Phyllanthus niruri* plant.

## 3. Botanical description

*Phyllanthus niruri* are erect annual herbs, 10–60 cm tall; main stem simple or branched, terrete smooth or scabridulous in younger parts. Cataphylls, stipules 1.5–1.9 mm long, deltoid acuminate blade 1–1.5 mm long, subulate acuminate. Leaves 3–11×1.5–6 mm elliptic oblong obovate, oblong, or even obovate, obtuse, or minutely apiculate at apex, obtuse or slightly inequilateral at base, petioles 0.3–0.5 mm long, stipules 0.8–1.1 mm long triangular acuminate. Flowers minutes, proximal 2–3 axis with unisexual cymules, each consisting of 1 male and 1 female or 2–3 males and female or 1 male and 2 females flower or combination thereof; male flowers pedicels at anthesis ca 1 mm long. Calyx lobe 5, subequal each ca 0.7×0.3 mm elliptic or oblong elliptic and abruptly acute at apex hyaline with unbranched mid ribs. Disc segments 5, roundish stamens 3 (rarely 2); filaments connate into a column 0.2–0.3 mm high antheros sessile a top dehiscent longitudinally. Female flowers; pedicels 0.8–1 mm long, obtusely 4-gonous, dilated above, ca 1.5 mm in fruits, calyx five lobes, subequal. Lobes sometimes toothed at apex. Styles 3, free, more or less spreading, and shallowly bifid at apex; arms divergent [6]. The seed capsules on stalks are 1–2 mm long, round, smooth, 2 mm wide, with six seeds. When the fruits burst open the seeds are hurled away. Seeds are triangular (like an orange segment); light brown, 1 mm long, with 5–6 ribs on the back [7].

## 4. Geographical Distribution

It is a field weed which is found proliferating throughout tropical and subtropical regions of Asia, America, and China. The genus *Phyllanthus* (L) Murr. Comprises from 600 to 700 species with minor distinguishing features among them. *Phyllanthus niruri* is an annual herb which grows in the wild after first showers of monsoon in Jharkhand, Bihar, Chhattisgarh, etc. states of India. However, it has also been reported to grow commonly in coastal areas. In Indian states it usually grows during second week of June and starts bearing fruits up to mid-July or August. It remains in the wild up to the end of the rainy season. However, under safe conditions it can grow and survive up to mid-winter.

### 5. Botanical classification

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

### 6. Vernacular names

Assamese	:	Holpholi; Poram-lokhi
Bengali	:	Bhui amla
Hindi	:	Chalmeri, Harfarauri, Bhuaionla.
Kannada	:	Kirunelli, Nela Nelli,
Konkani	:	Bhuin-avalae
Telugu	:	Ratsavusirike, Nela Usiri,
Tamil	:	Arunelli, Keela Nelli,
Malayalam	:	Arinelli, Kizhanelli, Nellipuli
Marathi	:	Rayavali, Bhuiavli,
Oriya	:	Narakoli
Sanskrit	:	Amala, Bhumymlaki, Sukshmadala, Vitunika, Bhoodatri.

### 7. Unani Description

Unani name	:	Bhui Amla, Amlaye Jamen.
Botanical name	:	<i>Phyllanthus niruri</i>
Synonyms	:	Amala, Bhumymlaki, Chalmeri, Harfarauri, Bhuaionla, Bhoodatri.
Mizaz	:	Cold & dry in 1 <sup>st</sup> degree.
Maza	:	Slightly in sour.
Boo	:	Slightly in sourish smelling.
Muzir	:	Due to high dosages, it has bad effect on spleen & urinary bladder.
Mukhrij	:	Expels Safra (Bile).
Nafa-e-Khas	:	Especially it is effective in hepatic disorders.

### 8. Ethnobotany

*Phyllanthus niruri* has extensive medicinal properties and has long history in the health care system of tropical countries. The plant is known in traditional health care systems. *P. niruri* is commonly known as “Chanca pedra” (or) “stone breaker”. However there is a lot of confusion about this species identification. *Phyllanthus niruri* is used as a folk medicine for treating kidney stones, gallbladder stones, liver related diseases such as liver cancer & jaundice, apart from these it is also administered for diuretic, hypoglycemic and hypertension cases and it also shows anti-inflammatory, anti-tumor, antinociceptive and anti-oxidant properties [9].

### 9. Chemical constituents

The medicinal plant *Phyllanthus niruri* Linn. (Euphorbiaceae), its wide variety of phytochemicals and their pharmacological properties. The active phytochemicals, flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarins and saponins, have been identified from various parts of *Phyllanthus niruri*. Extracts of this herb have been proven to have therapeutic effects in many clinical studies [10].

**9.1 Uses of Isolated Phytochemical Constituents Bioassay**  
guided fractionation of boiled aqueous extracts from the whole plant of *Phyllanthus niruri* (Euphorbiaceae) led to the isolation of 1-o-galloyl-6-o-luteoyl-a-Dglucose, which IC<sub>50</sub> values of 4.7mg/ml against *Babesia gibsoni* and 1.4mg/ml against *Plasmodium falciparum* in vitro. The known compounds b

glucogallin, quercetin 3-o-b-Dglucopyranosyl-(2 to 1)-o-b-D-xylopyranoside, b-sitosterol and gallic acid were isolated. Structures of these compounds were elucidated on the basis of their chemical and spectroscopic data.

### 10. Traditional uses

*Phyllanthus* has been used in Ayurvedic medicine for over 2,000 years and has a wide number of traditional uses. This includes employing the whole plant for jaundice, gonorrhoea, frequent menstruation and diabetes and using it topically as a poultice for skin ulcers, sores, swelling and itchiness. The plant is bitter, astringent, cooling, diuretic, stomachic, febrifuge and antiseptic. It is useful in dropsy, jaundice, diarrhoea, dysentery, intermittent fevers, and diseases of urogenital system, scabies ulcers and wounds. The young shoots of the plant are administered in the form of an infusion for the treatment of chronic dysentery. Its efficacy in the field of gastro intestinal disorders like dyspepsia, colic, diarrhoea, constipation and dysentery is undisputed. In females it is used as a galactagogue, in leucorrhoea, menorrhagia and mammary abscess. In skin conditions, especially scabby or crusty lesions, bruises, wounds, scabies, offensive ulcers and sores, oedematous swellings, tubercular ulcers and ringworm, it has been utilized with good effect since many years. It is applied effectively in intermittent fevers and gonorrhoea as well as in ophthalmia and conjunctivitis. It has a urolithic property, dissolving renal calculi. Also, used in cough, asthma and other bronchial affections. Its antifungal, antiviral and anticancerous properties have also been demonstrated in experimental animals. The powdered leaves of *Phyllanthus niruri* (Bahupatra) were used in clinical studies evaluating its usefulness in patients suffering from chronic damage to the liver due to the protracted hepatitis B virus infection. This type of infection results in inability of the body's immune system to eliminate the virus from the liver cells. This condition is described as a carrier state, because a continuously harbors the virus. Some of the components of the virus detectable in the carrier state in the blood are: HBsAg or the surface antigen of the virus and HBeAg or the envelope antigen of the virus. In addition, the carrier state may be confirmed by the presence of antibodies directed against the core of the virus or the anti-HBc antibodies. The powdered leaves of *Phyllanthus niruri* were given in form of capsules to the patients with chronic viral hepatitis B in a dose of 200 mg three times a day for 30 days. *Phyllanthus niruri* treated patients tested negative for the viral antigen 15-20 days after the end of the treatment. Due to its antiseptic, styptic, carminative, deobstruent, coolant, febrifugal, stomachic, astringent and diuretic properties of this plant it is very much utilized in traditional medicine.

### 11. Pharmacological activity

*Phyllanthus niruri* is an important plant of Ayurvedic and Unani system of medicine in which it is used for problems of the stomach, genitourinary system, liver, kidney, spleen etc. The medicinal traits and pharmacological activities endorsed to various parts of *Phyllanthus niruri* are detailed as follows:

#### a) Hepatoprotective Effect

Hepatitis B is one of the major diseases inflicting human population. Conventional treatment with interferon –alpha is very expensive and has many serious side effects. Alternative herbal medicine using extracts of *Phyllanthus niruri* and *Phyllanthus urinaria* have been reported to be effective against Hepatitis B and other viral infections. A study reports quantitative determination of the anti-viral effect of these

herbs in well-defined *in vitro* systems <sup>[11]</sup>. *Phyllanthus niruri* has been reported to exhibit marked anti-hepatitis B virus surface antigen activity in *in-vivo* and *in-vitro* studies. Infectious hepatitis is due to the inability of the bodies' immune system to eliminate the virus from the liver cells; hence the "carrier state". An infection with the virus is documented by detectable levels of various viral antigens in the blood, including HbaAg (the surface antigen of the virus) as well as antibodies to the core of virus (Hbc antibodies). In one study, 37 patients with chronic viral hepatitis B were treated with a daily dose of 600mg of *Phyllanthus niruri* for 30 days. 59% of the patients lost the HBsAg two weeks after the end of the treatment. Furthermore, none of the cases followed for up to 9 months had any symptoms of HBsAg. The authors postulated that *Phyllanthus niruri* might inhibit proliferation of the virus by inhibiting replication of the genetic material of the virus <sup>[12]</sup>. Hepatoprotective effect of an ayurvedic medicine; herbal preparation HPN – 12 (containing *Glycyrrhiza glabra*, *Picrorhiza kurroa*, *Berberis aristata*, *Piper longum*, *Phyllanthus niruri*, *Solanum dulcamara*, *Zingiber officinale*, *Curculigo orchoides*, *Elettaria cardamomum*, *Tinospora cordifolia*, *Desmodium triflorum* and *Saccharum officinarum*) orally administered to male albino rats at 1ml/100g body weight was found to be effective against liver damage <sup>[13]</sup>. Animals with Carbon Tetrachloride induced hepatopathy were treated with catliv (contains extracts of *Swertia chirata*, *Eclipta alba*, *Fumaria vaillantii*, *Picrorhiza kurroa*, *Andrographis paniculata* and *Phyllanthus niruri*) at 25ml twice daily orally for six days starting at 48 hours after administration of Carbon tetrachloride. On basis of result obtained it was concluded that the ingredients in catliv, effectively helped in regeneration of hepatic cells and is an effective liver tonic for calves <sup>[14]</sup>. Research in Japan and India in the 1980's has demonstrated the liver -healing properties of *Phyllanthus niruri*. The primary compounds responsible are phyllanthin, hypophyllanthin and triacontanol. Glycosides found in *Phyllanthus niruri* demonstrated Aldose reductase (AR) inhibitory activity in studies conducted by a Japanese research group in 1988 and 1989 <sup>[15]</sup>.

#### b) Anti-viral activity

Alcoholic, hexane, chloroform, butanol and water extract of *Phyllanthus niruri* were tested for *in vitro* effects on HbsAg, HBeAg and HBV-DNA in serum samples positive for HBV antigen followed by the screening of the respective antigen by Elisa. The extract was effective against HBV antigen, the butanol extract being the most potent <sup>[16]</sup>. Further studies were conducted on mice infected with wood chuck hepatitis virus when administered with extract was effective in three animals in reducing the virus within 3-6 weeks eliminating both the surface antigen titer and DNA polymerase activity in serum <sup>[17]</sup>. An aqueous extract on human hepatocellular carcinoma derived cell at 1 mg mL<sup>-1</sup> concentration on a single dose. Inhibition of the secretion of HBsAg for a period of 48 h was observed <sup>[18]</sup>. Disruption of hepatitis B virus polymerase activity, mRNA transcription and replication supported the role of *Phyllanthus niruri* being used as an antiviral agent <sup>[19]</sup>.

#### c) Anti cancerous & cellular protective actions

*Phyllanthus niruri* has high potential to inhibit the growth and initiation of cancerous cells which were introduced into mouse skin cells with 7, 12 dimethyl benz (a) anthracene (100µg/100ml acetone) and croton oil (1%) <sup>[20]</sup> and there is drastic increase in the catalase, reduced glutathione and protein levels in the skin. In albino mice the chemopreventive action

of *Phyllanthus niruri* with DMBA induces skin papillomagenesis <sup>[21]</sup>.

#### d) Action of kidney stones & uric acid

Kidney stone is a common problem that accumulates calcium oxalate crystals, and it includes urinary calculi formation, nucleation, growth, and aggregation of crystals. *Phyllanthus niruri*'s extract interferes in the growth and aggregation of calcium oxalate [CaOx] crystals in the calculi. The extract inhibits CaOx crystal aggregation in the early stages of stone formation in the urine samples of male wister rats. It is advisable to treat stone formation in the early stages <sup>[22]</sup>. The CaOx metastable limit was decreased by the treatment of *Phyllanthus niruri* [5% [v/v]] extract and it can also deprive the CaOx crystals and formation of nucleation <sup>[23]</sup>. The extract has the ability to prevent the growth of calculi and also change the shape and texture of the calculi. When treated on the preformed calculi it can form a matrix like material on its surface and it can modify the appearance and texture of the calculus <sup>[24]</sup>. The extract is also administered in hyper calcemic patients; it can decrease the urinary calcium levels <sup>[25]</sup> and also reduces the excess uric acid in hyperuricemic people by the lignans with uricosuric action in the extract <sup>[26]</sup>.

#### e) Anti-Inflammatory activity

The Hexane Extract (HE), the Lignan-Rich Fraction (LRF), or the lignans phyltetralin, nirtetralin, niranthin of *Phyllanthus niruri* when given orally inhibited carrageenan (Cg)-induced paw oedema and neutrophil influx. The HE, the LRF or nirtetralin also inhibited the increase of IL1-β tissue levels induced by Cg. Bradykinin (BK)-, Platelet Activating Factor (PAF)- and endothelin-1 (ET-1)-induced paw oedema were significantly inhibited by the HE or LRF. Finally, nirtetralin or phyltetralin caused inhibition of paw oedema induced by PAF or ET-1. These results show that the HE, the LRF and the lignans niranthin, phyltetralin and nirtetralin exhibited marked anti-inflammatory properties <sup>[27]</sup>.

#### f) Antioxidant activity

The Total Phenolic Content (TPC) and antioxidant activity of fresh and dried *Phyllanthus niruri* were evaluated by Folin-Ciocalteu method, 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging activity and Ferric Reducing Antioxidant Power (FRAP) assays. Different drying treatments led to significant reduction ( $p < 0.05$ ) in antioxidant properties of *Phyllanthus niruri* methanolic extracts, with microwave drying causing the highest decrease in TPC and antioxidant activity exhibited by the reduction in both radical scavenging activity and FRAP, the boiling water extracts appeared to exhibit stronger antioxidant potentials ( $p < 0.05$ ) even in dried plant materials. This proves its strong free radical scavenging activity <sup>[28]</sup>.

#### g) Anti-spasmodic activity

Research done in Brazil at the Federal University of Santa Catarina in 1984 on *Phyllanthus niruri* revealed an alkaloid (phyllanthoside) in the leaves and stem with strong antispasmodic activity. It served as a relaxing agent for smooth muscles and they concluded that its spasmolytic action probably accounted for the efficacy of *Phyllanthus niruri* in expelling stones <sup>[29]</sup>.

#### h) Analgesic activity

Methanol extract of dried callus tissue at a concentration of 10mg/kg, administered intraperitoneally to mice was active vs.

acetic acid induced writhin and vs. formalin – induced pedal edema. The extract, at 50mg/kg was inactive vs tail flick response to radiant heat. Ethanol/ water (1:1) extract of dried entire plant at a dose of 50mg/kg, administered intragastric to male mice was active. The extract also administered intraperitoneally to male mice at a dose of 0.3mg/kg was active. In both cases antinociceptive effects were demonstrated using 5 different models of nociception <sup>[30]</sup>.

#### i) Antibacterial activity

The antibacterial activity of extracts of the root and leaf was assessed against extend spectrum lactamase (ESBL) producing *Escherichia coli* isolated from the stool samples of HIV sero-positive patients using Bauer disc diffusion method. The strains isolated from both HIV sero-positive patients were susceptible to various concentrations of the extracts (5, 10, 20, 40 and 80 mg mL<sup>-1</sup>). This proves the antibacterial activity of the extract <sup>[31]</sup>.

#### j) Immune modulatory actions

An arabinogalactan (AG) which was obtained from *Phyllanthus niruri* tea preparations was found to have immunological properties and is tested with peritoneal mice macrophages. The glycoside showed the same activity when subjected to acidic and neutral gastric conditions using human gastric fluids and aq. HCL solution <sup>[32]</sup>.

#### k) Aphrodisiac activity

The effect of methanolic extract of the leaves of *Phyllanthus niruri* on the hormonal parameters of male guinea pigs was investigated. The hormonal parameters investigated were testosterone, leutinizing and follicle stimulating hormone. Methanolic extract of *Phyllanthus niruri* leaves (50–800 mg/kg) caused a statistically significant increase in the level of testosterone of the male guinea pigs, from  $2.3 \pm 0.06$  to  $3.9 \pm 0.05$ ,  $4.3 \pm 0.6$  and  $2.8 \pm 0.6$  after the 7th, 14th and 21st day of the administration of the extracts, respectively. Furthermore, the methanolic extract of *Phyllanthus niruri* (800 mg/kg) caused an insignificant change in the level of luteinizing (LH) and follicle stimulating (FSH) hormones from  $3.1 \pm 0.22$  and  $1.6 \pm 0.50$  to  $3.0 \pm 0.08$  and  $1.5 \pm 0.13$ , respectively <sup>[33]</sup>.

#### l) Anti-ulcer activity

The acidic heteroxylyan and another polysaccharide showed anti-ulcer activity. These compounds reduced the gastric lesions induced by 65% and 78% ethanol. *Phyllanthus niruri* proved to be efficient against peptic ulcers <sup>[34]</sup>.

#### m) Contraceptive effect

Antifertility effect of an alcoholic extract of the whole plant of *Phyllanthus niruri* at a dose of 100 mg/kg body weight for 30 days orally was investigated in cyclic adult female mice. The results revealed no significant change in absolute body and organ weights in extract fed animals indicated no alteration in general metabolic status. Cohabited females with normal male mice were unable to become pregnant as their cyclicity was affected. These factors are related to a change in the hormonal milieu that governs female reproductive function. Upon withdrawal of feeding for 45 days, these effects were reversible. Thus, this extract manifests a definite contraceptive effect in female mice <sup>[35]</sup>.

#### n) Lipid Lowering Activity

Lipid lowering activity of *Phyllanthus niruri* alcoholic extracts in triton induced hyperlipidaemia was examined in rats. It was

observed that administration of triton in rat caused increase in serum cholesterol by 3.5 fold, phospholipid 2 fold and triglyceride 1.2 fold. Administration of *Phyllanthus niruri* at the dose of 200mg/kg simultaneously with triton lowered the level of total cholesterol, phospholipid and triglyceride by 27, 25 and 24 percent respectively. In an experiment with cholesterol fed rats, *Phyllanthus niruri* at a dose of 100 mg/kg lowered the elevated level of low-density lipoprotein lipids in hyperlipidemic and drug fed animals <sup>[36]</sup>.

#### o) Anticonvulsant Activity

Epilepsy is a major neurological disorder characterized by the occurrence of recurrent seizures. The two widely proposed mechanisms involve alterations in the voltage – dependent ion channels such as reduction in inhibitory GABA - mediated drive or increase in excitatory glutamate mediated inputs. This chronic progressive CNS disorder affects a large population of the world. In search of herbal treatment, aqueous and ethanolic extract of *Phyllanthus niruri* were evaluated for anticonvulsant effect using pentylenetetrazole (PTZ) and maximal electroshock - induced seizures (MES) in swiss albino rats. The result showed ethanolic and aqueous extract of leaves and stem of *Phyllanthus niruri* significantly effective in abolishing hind limb extension induced by MES as well as PTZ induced seizures <sup>[37]</sup>.

#### p) Chemoprotective Activity

The chemoprotective activity effect of 75% methanolic extract of the *Phyllanthus niruri* plant was studied against cyclophosphamide (CTX) induced toxicity in mice. Administration of CTX produced significant myelosuppression as seen from the decreased WBC count and bone marrow cellularity. Administration of *Phyllanthus niruri* extract at doses 250 and 750 mg/kg body weight significantly reduced the myelosuppression and improved the WBC count, bone marrow cellularity as well as the number of maturing monocytes that accounted for its chemoprotective activity. In addition, extract from the plant of *Phyllanthus niruri* was found to decrease the activity of phase I enzyme that showed potent chemoprotective potential of the plant <sup>[38]</sup>.

#### q) Diuretic Activity

The diuretic, hypotensive and hypoglycemic effects of *Phyllanthus niruri* on human subjects were assessed. Appropriate parameters have been studied in the blood as well as urine samples of the patients. In addition, the physiological profile and dietary pattern before and after the treatment period were assessed. Interestingly, a significant increase in urine volume, urine and serum Na levels was observed after treatment with *Phyllanthus niruri* extract. A significant reduction in systolic blood pressure in non-diabetic hypertensive subjects was noted that further confirmed its diuretic property <sup>[39]</sup>.

## 12. Dosage

Adults (18 years and older)

- Generally, an infusion or weak tea of *Phyllanthus niruri* has been taken by mouth. Traditionally, individuals drink 1-3 cups daily or weekly. Some pharmacies in South America sell concentrated extracts with a daily dose of 2-6 milliliters, taken twice or thrice daily.
- To treat acute viral hepatitis, 900 milligrams of powdered *Phyllanthus niruri* capsules has been taken by mouth three times daily for seven days.
- To treat diabetes, 100 milliliters of *Phyllanthus niruri*

extract has been taken by mouth twice daily for one week. Additionally, two pellets of *Phyllanthus niruri*, each 0.8 grams, have been taken three times daily by mouth for 10 days.

- To treat hepatitis B, 200-1,100 milligrams of dried *Phyllanthus niruri* has been taken by mouth three times daily for up to three months.
- To treat high blood pressure, two 0.8-gram pellets have been taken by mouth three times daily for 10 days.
- To treat liver disease, three grams of *Phyllanthus niruri* powder has been taken by mouth three times daily for 30-45 days.
- To treat urinary stones, 450 milligrams of *Phyllanthus niruri* has been taken by mouth three times daily for three months. Children (under 18 years old)
- There is no proven safe or effective dose for *Phyllanthus niruri* in children.

### 13. Side Effects and Warnings

- In general, side effects were lacking in human studies. *Phyllanthus niruri* is likely safe when taken up to 400 milligrams three times daily for one month, under the care of a healthcare practitioner.
- *Phyllanthus niruri* may lower blood sugar levels. Caution is advised in people with diabetes or hypoglycemia, and in those taking drugs, herbs, or supplements that affect blood sugar. Blood glucose levels may need to be monitored by a qualified healthcare professional, including a pharmacist and medication adjustments may be necessary.
- *Phyllanthus niruri* may increase the risk of bleeding. Caution is advised in people with bleeding disorders or those taking drugs that may increase the risk of bleeding. Dosing adjustments may be necessary.
- *Phyllanthus niruri* may cause low blood pressure. Caution is advised in people taking agents that lower blood pressure.
- Drowsiness or sedation may occur. Use caution if driving or operating heavy machinery.
- Use cautiously in people with liver disease.
- Use cautiously people taking diuretics, agents that lower cholesterol or agents that affect the immune system.
- Avoid in pregnant or breastfeeding women, or in those trying to become pregnant.
- Avoid in people with known allergy or sensitivity to *Phyllanthus niruri* their parts, or members of the Euphorbiaceae family.
- *Phyllanthus niruri* may also cause abdominal pain or discomfort; altered immune system function; altered levels of certain white blood cells; anorexia; chills; diarrhea; disturbed sleep; dizziness; enlarged lymph nodes; fatigue; fever; headache; hives; increased sodium, potassium, and chloride in the urine; increased urine volume; joint pain; lung disease; malaise (discomfort); muscle pain; nausea; rash; skin prickling; and sore mouth.

### 14. Pregnancy and Breastfeeding

- There is a lack of scientific evidence on the use of *Phyllanthus niruri* during pregnancy or breastfeeding.

### 15. Interactions with Drugs

- *Phyllanthus niruri* may lower blood sugar levels. Caution is advised when using medications that may also lower blood sugar. People taking drugs for diabetes by mouth or insulin should be monitored closely by a qualified

healthcare professional, including a pharmacist. Medication adjustments may be necessary.

- *Phyllanthus niruri* may increase the risk of bleeding when taken with drugs that increase the risk of bleeding. Some examples include aspirin, anticoagulants (blood thinners) such as warfarin (Coumadin®) or heparin, antiplatelet drugs such as clopidogrel (Plavix®), and nonsteroidal anti-inflammatory drugs such as ibuprofen (Motrin®, Advil®) or naproxen (Naprosyn®, Aleve®).
- *Phyllanthus niruri* may cause low blood pressure. Caution is advised in people taking drugs that lower blood pressure.
- *Phyllanthus niruri* may increase the amount of drowsiness caused by some drugs. Examples include benzodiazepines such as lorazepam (Ativan®) or diazepam (Valium®), barbiturates such as phenobarbital, narcotics such as codeine, some antidepressants, and alcohol. Caution is advised while driving or operating machinery.
- *Phyllanthus niruri* may interact with agents for inflammation, pain relief, or wound healing; agents that alter immune function; agents that damage the liver; agents that increase urine output; agents that inhibit angiotensin-converting enzyme (ACE), angiotensin-converting enzyme receptor (ARB), or endothelin; agents that mimic acetylcholine (a neurotransmitter); agents that protect against radiation; agents that protect against toxic effects of chemotherapy; agents that treat disorders of the blood, digestive tract, eyes, heart, or kidneys; agents that treat gout or inhibit xanthine oxidase (enzyme that breaks down purine); agents that widen blood vessels; agents used for cancer, diarrhea, fever, HIV/AIDS, malaria, obesity, or urinary stones; antibiotics, antivirals, cholesterol-lowering agents, fertility agents, interferons (man-made version of an immune system protein), and nonsteroidal anti-inflammatories (NSAIDs, medications that reduce swelling and pain).

### 16. Toxicology

*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.

### 17. Conflicts of Interest

The authors declare no conflict of interests.

### 18. Conclusion

*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. Coupled with improvements in approaches for natural-product isolation, characterization and synthesis, this could be opening the door to a new era in the investigation of natural products in academia and industry.

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