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An Ayurvedic and Modern Aspects of Bhumyamalaki (*Phyllanthus niruri*): An Overview

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Abstract

Phyllanthus niruri L. also known as Phyllanthus amarus Schum and Thonn (belonging to Euphorbiaceae family) is called as Bhumi amla or Bhui Amla in Hindi. And Bhumyamalaki in Sanskrit. It is a well-known medicinal plant in *Ayurvedic* classical medicine. It grows on its own in rainy season (kharif) and is available throughout the year in shady moist places. Ayurvedic classical texts have mentioned its use in cough, asthma, haemorrhagic disorder, anaemia, jaundice, skin disorders, urinary disorders etc. Phytochemical screening reported the existence of various phytocompounds such as alkaloid, flavonoid, terpenoids, cardiac glycoside, saponins, tannins, cyanogenic glycosides. It possesses antioxidant, anti-inflammatory, analgesic, antinociceptive, immunomodulatory, hepatoprotective, nephro-protective, cardioprotective, hypolipidemic, anti-platelet aggregation, vasorelaxant, anti-diabetic, anti-urolithic, anti-hyperuricemic, diuretic, anti-leptospiral, anti-plasmodial, anti-nematodal, antiviral, anti-bacterial, anti-ulcer, burn wound healing, anti-venom, anti-fertility and anticancer properties. These pharmacological studies have established a scientific basis for therapeutic uses of this plant. Further research is still needed on its active components and associated structure-activity relationship and multifactorial signaling mechanisms. In this article attempts were made to review medicinal value of this plant with special reference to an ayurvedic and modern scientific aspect.

Keywords: *Phyllanthus niruri*, Phyllanthus amarus, Bhumyamalaki, pharmacological.

Introduction

The medicinal plants are used by traditional medical practitioners in day-to-day practice to cure a variety of diseases. Herbal therapies are applied throughout the world to minimize adverse drug reaction, improve the patient compliance and quality of life, and also enables it use for future research for its usage in the treatment of several diseases. *Phyllanthus niruri* L. (Family-Euphorbiaceae), which is more commonly recognized as Bhumi amla or Bhui Amla in Hindi and Bhumyamalaki in Sanskrit, is one of the important medicinal plants of Ayurvedic medicine. Its Sanskrit synonyms are Bhudhatri, Bahuphala, Tamalaki, Bahupatra etc. Its fruit looks like gooseberry and it is a very small plant, thus known as Bhui Amla or Bhumi Amla. *Phyllanthus niruri* is well known as Gale of the wind and stonebreaker.

This tropical annual herb grows as a weed in moist humid waste land [1, 2]. *Phyllanthus* means 'leaf and flower' because the flowers, as well as the fruit, seem to become one with the leaf. It is among more than 500 Phyllanthus species that are widely spread in temperate and tropical climates region [3]. Tamalaki (*Phyllanthus niruri*) grows 30-40 cm in height, has small leaves and yellow flowers; the stem has green capsule, and blooms with flowers with 5 white sepals and apical acute anther. The fruit of Bhumyamalaki has green capsules, and smooth and fruiting pedicels while seeds are longitudinally rugose [4]. It is found throughout the tropics and sub-tropics such as West Africa (including Nigeria and Ghana), Europe, Asia (including China, Pakistan, India and Malaysia Indian ocean), central and south America as medicinal plant for the treatment of various diseases [5, 6, 7, 8, 9].

Nowadays this plant has caught the attention of the researchers for its hepatoprotective activity. Its active phytochemicals include flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarins, and saponins. The useful parts of Bhumyamalaki are the whole plant with fresh leaves, and fruits. The plant has been used since antiquity, for thousands of years, in Ayurvedic medicinal practices to treat various diseases [10]. In India, Bhumyamalaki is one of the

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most significant traditional drugs administered to cure jaundice, asthma, hepatitis and urolithic disorder [11].
The Bhumyamalaki is usually used by traditional medicine practitioners for the treatment of asthma, bronchial infection, liver diseases, diabetes, gonorrhoea, inducing labour and treatment of oedema, feverish pain, sore throat, female sterility, oliguria and vaginitis. They also used the plant to manage irregular menstruation, tachycardia, dysentery, spasmodic cough, itchiness, arthritis, otitis, swelling, skin ulcer and weakness of male organ [12, 13, 14]. The folk medicine of P. amarus is used to treat diarrhoea, diabetes, otitis, swelling skin ulcer, Jaundice and gastrointestinal disturbances. In research studies this plant has revealed antimicrobial, antioxidant, anticancer, anti-inflammatory, antiplasmodial, antiviral, diuretic and hepatoprotective properties [7]. *Phyllanthus niruri* L has also shown to act as immunomodulator against Covid-19 [8]. Within this context, the present study is comprised of its botanical description, traditional uses, phytochemical analysis, pharmacological importance and medicinal value with special reference to an ayurvedic and modern aspect [7]. *Phyllanthus niruri* L has also shown to act as immunomodulator against Covid-19 [8].

Ayurvedic Aspect
Charak Samhita: Kasahara, Shwasahara Mahakashay [15].
Synonyms: Tamalaki, jata, vira, uccata.

Vernacular Names
Sanskrit: Bhumyamalaki, Bhudhatri, Tamlaki, Bahupatra, Bahuphala [16].
Hindi: Bhui amla
Marathi: Bhuiawala
Guajarati: Bhonya Awala Assamese: Holpholi.
Poram: Lokhi.
Bengali: Noar.
Hindi: Chalmeri, Harfarauri, Bhuiaonla.
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, Bhumyamlaki, Sukshmadala, Vitunika, Bhoodatri.

Habitat
The plant is distributed throughout India mainly in trophical and subtropical parts of country [16].

Rasapanchak of Bhumyamalaki
Rasa-Tikta, Kashay, Madhur [16].
Vipak-Madhur
Veerya-Sheeta
Guna-Laghu, Ruksha
Karma: Kapha-pitta Shamaka.

Prayojyanga (Useful Part)
Panchanga [16].

Matra (Dose)
Swarasa-10 to 20 ml [16].
Churna-3-6 gm

Medicinal Value
The plant has been used for a long period of time (thousands of years) in Ayurvedic traditional medicine for various illnesses [17]. *Bhumyamalaki*, was at first emphasized in *Brihatrayees* for addressing respiratory system disorders, afterward found its application in hepatobiliary diseases according to Nighantus and Keraleeya textbooks. This plant is a vital ingredient in formulations such as *Chyavanaprasa, Amritaprasa Ghrita,* and *Jivantyadi Churna due to* its *Rasayana* properties, In Ayurvedic classical texts references regarding its use in cough, asthma, haemorrhagic disorder, anaemia, jaundice, skin disorders, urinary disorders etc. are available. It is used in the Indian Ayurveda system of medicine in various problems like liver, stomach-ache, kidney, spleen, genitourinary system and various biological activities like kidney, gall bladder, stones, cold, flu, tuberculosis, liver disease etc. [18].

Modern Aspect
One of the potential herbal medications used in Indian medicine for a variety of liver illnesses is "Bhumyamalaki", a plant medicinal made by *Phyllanthus niruri* Lin, a member of the Euphorbiaceae family [19]. Traditionally, *Phyllanthus niruri* is used as an antiurolithiasis, antidiabetic, and antihyperuricemic agent [20]. In Asia, it is used in traditional medicine for liver protection and anti-hepatitis B. This plant is also traditionally used to treat kidney stones [21]. *Phyllanthus niruri* Schum. & Thon was used traditionally in Indian ayurvedic medicine to treat various disorders, stomach problems, genitourinary system, liver, kidney and spleen, diuretic, febrifuge, antiseptic, gonorrhea, menorrhagia, gastropathy, diarrhea, dysentery, ophthalmopathy, scabies, ulcers and wound [22]. *Phyllanthus niruri* is not found in India it is limited to the West Indies. Among the Phyllanthus species referred to as "Bhumyamalaki" are *P. amarus* Schum and *Thonn*, P. *fraternus* Web, *P. maderaspatensis* Linn., P. simplex Retz, and *P. urinaria* Linn. The main focus of Phyllanthus is its capacity to inhibit viruses, particularly the hepatitis B virus. Studies show that Phyllanthus can reduce the extent of hepatitis B virus in the circulation and prevent the virus's development and replication. While its ability to eradicate viruses has not been verified, it has demonstrated efficacy in mitigating symptoms and combating the hepatitis B virus. It is an important medicinal plant because of its antiviral activity against hepatitis-B virus as it blocks DNA polymerase in hepatitis-B Virus during reproduction [22].

Scientific Classification [23]
Domain: Eukaryota
Kingdom: Plantae
Family: Phyllanthaceae
Order: Malpighiales
Clade: Angiosperms, Eudicots, Rosids
Genus: Phyllanthus
Species: P. *niruri*
Latin Name: *Phyllanthus niruri* Linn
English Name: Gulf leaf flower.

Chemical Composition
The plant consist many of the active constituents such as glycosides, flavonoids, alkaloids, ellagitannins, phenyl propanoid, Amarin, germanin, corilagin found in the leaves, stem and root of the plant[24].P. amarus is reported to contain many chemical constituents like lignans, phyllanthin, hypophyllanthin, nortiphyllin phylline; Flavanone glycoside such as niranthin, nirtetralin, phyltetralin and lintetralin; steroid hormone estradiol, triterpenes like phyllanthus,

phyllanthenone, and phyllanthenol; flavonoids such as quercetin, quercitrin, and astragalin.

Pharmacognostical Studies

Habit and Habitat

The leaves are 3.0-11.0x1.5-6.0 mm in height, with an elliptical oblong shape. The oval, oblong leaves range in height from 10 to 60 cm [3]. The leaves are 3.0-11.0 x 1.5-6.0 mm, and the stem is upright and treaded. The younger sections are rough. Axillary flowers have bisexual blooms in the following axils after the initial 2-3 axils of unisexual, 1-3 male flowers. The male flowers have a pedicel that is 1 mm long, a calyx that is 5 oblongs, elliptic, with an acute apex and hyaline, and an unbranched midrib. The disc segments are 5 rounded and contain 3 stamens, 3 filaments that are connate, and 5 rounded and stamens, 3 filaments connate.

Description [25]

a) Macroscopic

Root: Small, 2.5-11.0cm long. Nearly straight, gradually tapering, with a number of fibrous secondary and tertiary roots, external surface light brown, fracture, short.

Stem: Slender, glabrous, light brown, cylindrical, 20-75 cm long, branching profuse towards upper region bearing 5-10 pairs of leaves, internode, 1-3.5 cm long, odour, indistinct, taste, slightly bitter.

Leaf: Compound and leaf-let arranged in two rows with a rachis, alternate, opposite and decussate almost sessile, stipulate, oblong, entire, upto 1.5 cm long and 0.5 cm wide, greenish-brown in colour, odour, indistinct, taste, slightly bitter

b) Microscopic

Root: Transverse section shows, 4-6 layers of cork consisting of thin-walled, rectangular, tangentially elongated and radially arranged cells, filled With reddish-brown content, secondary cortex consists of 8-10 layers of thin-walled, tangentially elongated parenchymatous cells, secondary phloem narrow consisting of sieve elements, phloem parenchyma and traversed by narrow phloem rays, secondary xylem represented by a broad zone of tissues, composed of vessels, tracheids, fibres and parenchyma, all elements being thick-walled and lignified having simple pits, xylem rays uniseriate.

Stem: Transverse section shows, a single layered epidermis composed of thick-walled, flattened, tangentially elongated cells, older stem shows 4-5 layers of cork, composed of thin-walled, tabular, tangentially elongated and radially arranged cells, filled With reddish-brown content, cortex composed of 4-6 layers of oval, tangentially elongated, thin-walled, parenchymatous cells, some cortical cells filled with yellowish-brown content, endodermis quite distinct, pericycle represented by a discontinuous ring, composed of several tangentially elongated strands of lignified fibres with thick walls and narrow lumen, secondary phloem narrow, composed of sieve elements, dispersed in mass of phloem parenchyma, secondary xylem composed of vessels, fibres, parenchyma and traversed by numerous uniseriate rays, vessels mostly simple pitted, a few show spiral thickenings, fibres narrow elongated, with narrow or sometimes blunt ends with simple pits, centre, occupied by a pith composed of thin-walled, circular to oval parenchymatous cells, occasionally cluster crystals of calcium oxalate present in parenchymatous cells of ground tissue.

Leaf: Transverse section of leaf shows, a biconvex outline, epidermis on either side, single layered covered externally by a thick cuticle, a palisade layer present beneath upper epidermis, intercepted by a few parenchymatous cells in the middle, meristele composed of small strands of xylem towards upper surface and phloem towards lower surface, rest of tissue of leaf composed of thin-walled, parenchymatous cells some having cluster crystals of calcium oxalate, lamina shows a dorsiventral structure, mesophyll differentiated into palisade and spongy parenchyma, epidermis on either side composed of thin-wa1led, tangentially elongated cells, covered externally by a thick cuticle, anisocytic type stomata present on both epidermises, palisade single layered, mesophyll composed of 3-5 layers of loosely arranged cells having a number of veins traversed in this region, a few cluster crystals of calcium oxalate present in spongy parenchyma.

Phyllanthus amarus possesses both anisocytic and paracytic stomata, but P. fraternus and *P. maderaspatensis* solely have anisocytic stomata, according to microscopic examination of the Phyllanthus species. *P. maderaspatensis* possesses smooth epidermal cell walls, whereas *P. amarus* and P. fraternus have wavy ones.

Powder: Powder of the drug, brown coloured, under microscope shows, fragments of cork cells, vessels and fibres.

Identity, Purity and Strength

Foreign matter not more than 2 per cent, Appendix 2.2.2.
Total Ash Not more than 16 per cent, Appendix 2.2.3.
Acid-insoluble ash not more than 7 per cent, Appendix 2.2.4.
Alcohol-soluble extractive not less than 3 per cent, Appendix 2.2.6.
Water-soluble extractive not less than 13 per cent, Appendix 2.2.7.

Internal Uses

Bhumyamalaki root is diuretic and it is used to remove bladder stones, and is a remedy for jaundice. Fresh roots of Bhumyamalaki are valuable in the treatment of chronic dysentery. The leaves are also used as a treatment for dysentery. This herb is stomachic and useful in the treatment of sores and chronic dysentery. The root and leaves of *Phyllanthus niruri* are a good tonic and diuretic when taken cold in repeated doses. The milky juice is a good application to treat offensive sores.[26, 27].

It is used medicinally for treating diabetes, diarrhea, jaundice, and menstruation. Phyllanthus is particularly important in the fight against Hepatitis B and supports liver health in general. In addition, the plant has therapeutic value for ailments including gonorrhea, dyspepsia, fever, flu, tumours, jaundice, vaginitis, dyspepsia, diarrhea, and colic.

Adulterants and Substitutes

Phyllanthus niruri (Bhumyamalaki) is adulterated with Phyllanthus amarus and vice versa. Market samples of *Phyllanthus niruri* (Linn.) are often adulterated with Phyllanthus amarus Linn. Two plants are the bases of two different Ayurvedic drugs *Phyllanthus niruri* and *Phyllanthus amarus* possibly with analogous therapeutic effects [28]. Phyllanthus amarus possesses both anisocytic and paracytic stomata, but P. fraternus and *P. maderaspatensis solely* have anisocytic stomata, according to microscopic examination of the Phyllanthus species. *P. maderaspatensis possesses* smooth epidermal cell walls, whereas *P. amarus* and P. fraternus have wavy ones. India refers to all of the Phyllanthus species mentioned above as "Bhumyamalaki", and they are used to cure various liver ailments. But not all Phyllanthus species

have the therapeutic ingredients that are used to cure liver ailments [29].

Five different species are combined to form *Phyllanthus niruri* Linn. These species include *P. amarus* Schum and Thonn, P. fraternus Web, *P. maderaspatensis* Linn, P. simplex Retz, and *P. urinaria* Linn. *P. amarus* Schum and Thonn, P. fraternus P. *niruri*, listed in the flora of British India, and "Bhumyamalaki," referenced in the classical literature, have lately been equated with *P. amarus* based on clinical effectiveness. *Phyllanthus niruri* Linn. is a combination of five separate species. However, because of their similar morphologies, all five Phyllanthus types are occasionally confused and offered for sale in herbal medicine markets worldwide under the same colloquial name. As a consequence of this study, which was conducted using a highly precise approach, diagnostic features for each of the five Phyllanthus species examined have been developed [30].

Pharmacological and Biological Activities

Anti-diabetic Activity

Ethanolic extract of *Phyllanthus niruri* was found to have significant antidiabetic activity in insulin-dependent diabetes mellitus rat, but showed no effect on non–insulin-dependent diabetes mellitus rat [31]. Additionally, the ethanol extract was found to lower lipid profiles (decrease in plasma cholesterol, triglycerides, Low density lipoprotein cholesterol, very low density lipoprotein cholesterol and atherogenic index, while there is increase in high-density lipoprotein cholesterol) in both insulin-dependent diabetes mellitus and non– insulin dependent diabetes mellitus animals [32]. Concordantly, a one week study carried out on non-insulin dependent diabetic patients using aqueous extract of aerial parts of Phyllanthus amarus showed that, it is not effective in lowering both fasting blood glucose and postprandial blood glucose level in untreated non-insulin dependent diabetic patients [33]. Aqueous extract of *Phyllanthus niruri* demonstrated significant hypoglycemic activity in streptozotocin induced diabetic rats [34]. Relatedly, the methanol extract of the plant has also been found to reduce blood sugar level in alloxan-induced diabetic rats [35].

Anti-hyperlipidemic Activity

Scientific studies have shown that *Phyllanthus niruri* (Bhoomyamlaki) has antihyperlipidemic effect. It was also reported that the aqueous extract exhibited antihyperlipidemic activity [30]. Hydro-alcoholic extract of leaves of Phyllanthus amarus was also found to have antihyperlipidemic potential in hyperlipidemic rats [36]. Additionally, phyllanthin which is a bioactive compound of *Phyllanthus niruri* was administered for twelve weeks to mice co-fed with High Fat Diet (HFD); there was protection against HFD induced weight gain and adiposity, reduced mRNA expression of adipogenic genes and increased expression of lipolytic genes in white adipose tissue, reduced liver triglyceride accumulation, restoration of HFD induced serum lipid disturbances as well as reduced serum triglycerides and free fatty acids in HFD fed mice [37]. The lipid-lowering activity of *Phyllanthus niruri* was found to be mediated through inhibition of hepatic cholesterol biosynthesis, enhanced catabolism of LDL, increased faecal bile acids excretion and activation of LCAT and tissue lipases [38].

Anti-hyperuricemic Activity

It was reported that the methanol extract of the leaves of *Phyllanthus niruri* exhibited anti hyperuricemic activity in hyperuricemic rats. Lignans isolated from *Phyllanthus niruri* (Phyllanthin, hypophyllanthin, phyltetralin and niranthin) were also found to increase the urinary excretion of uric acid in hyperuricemic rat. Therefore, the uricosuric effect of this plant may be the attributed mechanism of anti hyperuricemic action [39].

Antiurolithic Activity

Phyllanthus niruri has shown inhibitory effect against calcium oxalate crystal growth and aggregation in human urine. This medicinal plant exhibited antiurolithic activity in both *in vitro* and *in vivo* studies [40]. The aqueous extract of *Phyllanthus niruri* inhibits the growth of the matrix calculus as well as decrease the number of stone satellites in Wistar rats [26]. Oral administration of *Phyllanthus niruri* extract by calcium stone forming patients reduced urinary calcium in hypercalciuric patients [41].

Hepatoprotective Activity

The Protein isolate of *Phyllanthus niruri* indicates hepatoprotective effect against acetaminophen-induced toxicity [42]. Another study also showed that the aqueous extract of *Phyllanthus niruri* inhibited paracetamol induced hepatotoxicity in mice [43]. Similarly, fishes pretreated with *Phyllanthus niruri* extract were protected against paracetamol-induced hepatotoxicity when compared to control [44]. It was also reported that a protein isolated from *Phyllanthus niruri* protects against oxidative damage of hepatocytes induced by carbon tetrachloride [45]. Both aqueous and methanol extracts of *Phyllanthus niruri* have been demonstrated to possess hepatoprotective effect [46]. The extract of Phyllanthus amarus was also found to increase hepatic cell function [47]. Similarly, another study reported the hepatoprotective effect of Phyllanthus amarus in ethanol-induced hepatotoxicity and the effect was comparable to standard hepatoprotective drug silymarin. The hepatoprotective effect of the extract was associated with its antioxidant activity [48]. *Phyllanthus niruri* extract and phyllanthin isolated from the aerial part of the plant were found to protect the human hepatoma HepG2 Cell line against carbon tetrachloride induced hepatotoxicity. Phyllanthin demonstrated the hepatoprotective effect at a lower dose compared to Phyllanthus amarus extract and the effect was in a dose-dependent manner [49]. Combination of ethanolic extract of *Phyllanthus amarus* and silymarin gives synergistic hepatoprotective activity against carbon tetrachloride-induced hepatotoxicity. The effect was associated with higher concentration of phyllanthin. A combination of silymarin with ethanol extract provided higher hepatoprotective activity than when combined with aqueous extract [50].

Antiplasmodial Activity

Ethanolic extract of *Phyllanthus niruri* was found to have potential anti plasmodial activity *in vitro* by inhibition of the developmental stage of trophozoite to schizonts [51]. Similar *in vitro* study also showed that the callus extract and intact *Phyllanthus niruri* extract inhibited the development of trophozoites to schizonts (developmental stage of Plasmodium falciparum) in a dose-dependent manner. The anti plasmodial activity of extract of *Phyllanthus niruri* (whole plant) exhibited a higher anti plasmodial activity than all calli and intact fresh apical stem extracts [30]. It was reported that the water extraction of *Phyllanthus niruri* gives better results of antiplasmodial activities than ethanolic extraction and only leaves and stems parts of the plant were

active *in vitro* against plasmodium [31]. 1-O-galloyl-6-O-luteoylR-D-glucose isolated from the *Phyllanthus niruri* was found to have inhibitory effect against Chloroquine-susceptible P. falciparum strain *in vitro* [32]. Chloroform/ethanol extract of *Phyllanthus niruri* showed significant inhibition of P. falciparum growth at different concentrations [33].

Antibacterial Activity

Phyllanthus niruri (Bhumyamalaki) has broad spectrum antibacterial activity on both gram positive and gram negative bacteria. A study carried out on different bacterial isolates; Bacillus stearothermophilus, Staphylococcus aureus, Bacillus subtilis, Micrococcus luteus, Salmonella typhi, *Enterobacter Aerogenes*, Proteus mirabilis, and Proteus vulgaris revealed that P. amarus showed the least MIC on all bacteria tested [52]. Equally, the methanolic extract of *Phyllanthus niruri* was found to have potent inhibitory effect against drug resistant pathogenic gram-negative bacteria; Shigella spp., E. coli, V. cholerae, S. aureus, S. typhimurium, P. aeruginosa, B. subtilis, Klebsiella and Streptococcus sp. in a dose-dependent manner [53].

Analgesic, Anti-inflammatory and antinociceptive activity

Studies have shown that extract of Phyllanthus amarus has an anti-inflammatory effect; and that it is effective in preventing persistent neuropathic pain, as well as prevent both ipsilateral and contralateral persistent nociception [48]. Another study showed that P. *niruri* exhibited potent systemic antinociceptive actions against two models of neurogenic pain [54]. Aqueous and methanol extracts of Phyllanthus amarus were found to have anti-inflammatory activity [55].

Antiulcer and Burn Wound Healing Activity

The methanol extract of Phyllanthus amarus significantly inhibited gastric lesions induced by intragastric administration of absolute ethanol. A rat study involving the oral administration of ethanolic extract of the herb showed significant inhibition of the development of indomethacin-induced ulcers. The anti-ulcer activity has been attributed to gallic acid, beta-sitosterol, ellagic acid and alkaloids-4-methoxy-securinine.…[56]….Extracts of P. *niruri* also protect against ethanol-induced gastric mucosal ulceration in rats and reverse dexamethasone-suppressed burn wound healing. The exact mechanism have not been elicited to date.56. Abdulla MA *et al*. Gastroprotective effect of *Phyllanthus niruri leaf extract* against ethanol-induced gas-tric mucosal injury in rats. African J Pharm Pharmacol 2010; 4: 226–230

Anti-Platelet Aggregation, Vasorelaxant and Diuretic Activity

It was reported that methyl brevifolincarboxylate (MB) isolated from the leaves of *Phyllanthus niruri* L. exerted vasorelaxant effect on the aortic rings of latvia inhibition of noradrenaline-induced vasoconstriction mediated by a decrease in calcium ion influx through receptor-operated Ca2+ channels.. It also antagonised the vasoconstriction effect of Norepinephrine [57]. MB was also found to have potent inhibitory effect against platelet aggregation; the effect was comparable to known inhibitor of platelet aggregation adenosine. In a recent study, the aqueous extract of Phyllanthus Amarus was tested for its cardioprotective property against high-fructose (HF) diet induced cardiac damage in Wistar rats; the aqueous extract prevented the increase in levels of cardiac and aortic lipids i.e., total lipids, triglycerides, total cholesterol and free fatty acids and decreased phospholipids after co-administration with the HF for sixty days [58]. Yao *et al*. (2018) compared the diuretic effect of the ethanolic fraction of the plant (EEPA) to that of a standard drug (frusemide); the diuretic effect of EEPA was comparable to the standard with an additional benefit of not promoting kaliuresis. Furthermore, the diuretic activity was attributed, at least in part, to the involvement of prostaglandins [59]. Aqueous extract of *Phyllanthus niruri* (200 mg/kg and 400 mg/kg. p.o. single dose) was tested for its diuretic activity and compared with the standard drug hydrochlorothiazide (10 mg/kg p.o.; single dose). Significant increase in the volume of urine and excretion of sodium, potassium and chloride was recorded when aqueous extract of *Phyllanthus niruri* was administered to hydrated albino rats [60].

Nephroprotective Activity

The aqueous extract of *Phyllanthus niruri* doses of 200 mg and 400 mg/kg/day for 14 days, were found to protect against the nephrotoxic effect of paracetamol and gentamicin in rat, by maintaining the level of blood urea nitrogen and serum creatinine within the normal range compared to control group [61]. In another study, the ethanol extract of the leaves of the plant was investigated for its nephroprotective activity against gentamicin induced nephrotoxicity in rats. Co-administration of the extract with gentamicin prevented kidney and improved all nephrotoxic parameters (physical, urinary and blood) observed [62]. The extracts of *Phyllanthus niruri* prepared by dissolving the leaves in olive oil for fourteen and seven days were tested for their ability to protect the kidney against cisplatin induced nephrotoxicity. The study revealed significant decrease ($p<0.05$) in plasma concentrations of K+, Cl-, creatinine and urea in extract treated groups when compared to negative control (Cisplatin-treated only) value and significant increase ($p<0.05$) in plasma concentrations of Na+ and HCO3 when compared to negative control value [63].

Antifertility Activity

Methanol extracts of the leaves of *Phyllanthus niruri* lead to a decrease in sperm motility and count of male guinea pigs in a dose dependent manner. The effect was comparable to the observed effects of Vitamin E on sperm parameters [64]. The ethanolic extract of *Phyllanthus niruri* significantly affected the litter size and weight of Wistar albino rats at birth in a dose-dependent manner [65]. The alcohol extract of a whole plant of *Phyllanthus niruri* was found to show reversible antifertility effect in female mice [66]. Similarly, Phyllanthus amarus when given orally to male albino mice induced gradual inhibition of fertility potential with a decline in epididymal sperm profiles. However, the antifertility effect was reversible upon withdrawal of medicinal plant [67]. The methanolic extract of *Phyllanthus niruri* leaves caused significant increase in the level of testosterone of male Guinea pigs in a dose-and time-dependent manner. It also caused changes in the levels of Luteinizing (LH) and Follicle stimulating (FSH) hormones. These changes caused by *Phyllanthus niruri* were comparable to the changes caused by vitamin E on *Luteinizing* (LH) and Follicle stimulating (FSH) hormones [68].

Antinematodal Activity

Two compounds isolated from Phyllanthus amarus, 8-(3-methyl-but2–enyl)-2-phenyl chroman-4-one and 2-(4-hydroxyphenyl)-8-(3-methyl-but-2–enyl)-

chroman-4-one were found to have antinematodal activity against Meloidegyne incognita and Rotylenchulus Reniformis [69].

Antioxidant Activity

Phyllanthus niruri showed significant improvement of body antioxidant activities in both insulin and non-insulin dependent diabetes mellitus animals [70]. A protein isolated from *Phyllanthus niruri* has also been showed to act as radical scavenger, thereby scavenging the free radicals released by the toxic effect of carbon tetrachloride in hepatocytes. The hepatoprotective effect of *Phyllanthus niruri* may be associated with it action at cellular level by reducing oxidative stress as a radical scavenger and promoting antioxidative defense mechanism of the cells [71]. *In vitro* antioxidant assay showed that the plant is an effective radical scavenger [72]. High phenolic content of Phyllanthus amarus showed a strong correlation with its antioxidant activity. Phyllanthus amarus has a high antioxidant activity because of its several phenolic constituents and it inhibits chromium (VI) induced oxidative toxicity to MDAMB-435S human breast carcinoma cells [73]. Similarly, it was also reported that Phyllanthus amarus has a strong free radical scavenging activity and ferric reducing property; its strong free radical scavenging activity is associated with its high phenolic content. The methanol extract of dried Phyllanthus amarus has lower antioxidant property compared to fresh sample [74]. *Phyllanthus niruri* was found to have effective *in vivo* antioxidant activity as seen by its ability to inhibit carbon tetrachloride induce lipid peroxidation in rat liver; while *in vitro* antioxidant activity showed that the plant has high radical scavenging activity [75]. Phyllanthin was reported to have higher radical scavenging capacity than Phyllanthus amarus, as indicated by its higher antioxidant activity than Phyllanthus amarus [76]. Phyllanthus amarus demonstrated antioxidant activities as indicated by its ability to increase the activities of enzymic and non-enzymic antioxidants and reduce malondialdehyde levels [77]. The methanol extract of Phyllanthus amarus was found to possess potential antioxidant activity as evident by its ability to inhibit lipid peroxidation and scavenge hydroxyl and superoxide radicals *in vitro* [78]. Aqueous extract of *Phyllanthus niruri* exhibited high free radical scavenging, inhibition of reactive oxygen and lipid peroxidation [79]. Phyllanthus amarus eased oxidative stress induced by nimesulide in the liver as evident by the outcome of post-treatment; with Phyllanthus amarus rapidly restoring most of the Nimesulide Induced oxidative changes compared to those obtained by the self-recovery of liver [80].

Anti-cancer Activity

Phyllanthus amarus offers protection against chemical carcinogenesis. It was reported that the aqueous extract of Phyllanthus amarus significantly inhibited Hepatocarcinogenesis induced by N Nitrosodimethylamine (NDEA) in a dose-dependent manner in male Wistar rats [81]. Phyllanthus amarus extract was also found to have significant activity against chemically induced tumour. Inhibition of cell cycle regulation, topoisomerase II, P450 enzymes as well as antioxidant activity may contribute to the overall activity of the extract against carcinogenesis induced in animals and this may be relevant to human cancer as well [82]. It was reported that the extract of Phyllanthus amarus inhibited the mutagenicity produced by direct acting mutagens. It also inhibited the activation and mutagenicity of 2-acetaminofluorene (2-AAF), which in turn declined the mutagenesis and possibly carcinogenic potential. Oral administration of Phyllanthus extract was found to significantly inhibit urinary mutagenicity produced in rats by benzo-pyrene [83]. The study showed that the methanol extract of Phyllanthus amarus has Chemopreventive activity against N-methyl N'-nitro-N-nitrosoguanidine (MNNG) induced stomach cancer in Wistar rats [84]. The aqueous extract of Phyllanthus amarus has also demonstrated anti-mutagenic and antigenotoxic properties as indicated by the extracts ability to protect against the mutagenic effects of 2-aminofluorene, 2-aminoanthracene, 4-nitroquinoline-1-oxide, N-ethyl-N-nitro-nitrosogua-nidine, 2-nitrofluorene and sodium azide in test bacteria. In addition, the extract antagonizes DNA damage caused by DMN in hamster liver [85]. 3.7. Anti-cancerous activity It is reported that and the extract of P. amarus was shown to be capable of apoptosis-(Inducing Programmed cell death) with its anti-metastatic action, 3-fold increase of caspases-3 and-7 presence of DNA fragmentation and terminal deoxynucleotidyl transferase enzyme mediated dUTP nick end labelling assay (TUNEL)-positive cells. The anti-metastatic activity is associated to the presence of polyphenol compounds in its extracts.

Cardioprotective Activity

Individual one major animal study has been conducted to investigate the reducing action of *Phyllanthus niruri* extracts in preventing doxorubicin-associated cardiotoxicity. Pre-treatment of rats with *P. niruri* extract significantly protected rat myocardia from doxorubicin toxicity by normalizing cardiac biomarkers, restoring intracellular levels of enzymatic and non-enzymatic antioxidants and decreasing rat cardiac tissue peroxidation [86].

Anti-viral Activity

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 [87]. 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 papillomatosis induced significant reductions in tumour incidence, tumour yield, tumour burden, and cumulative number of papillomas, according to the data [88]. 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.

Anti-venom Activity

The blend of Andrographis paniculata plant and extract of P. amarus possess potent venom neutralizing capability and used for therapeutic functions in case snake bite. The Phyllanthus extracts of Di-herbal possess effectively neutralize cobra snake venom induced lethal activity. The di-herbal plant extract (about 0.24 mg) is fully able to neutralize the lethal activity of 2 LD50 of genus N. naja Venom [89].

Antileptospiral Activity

Human meet with the infected animal's urine or urine contaminated environment is called Leptospirosis which is globally important disease. P. amarus have been looked for the antileptospiral activity by micro dilution tests and tube dilution technique and results revealed the inhibitory action of

methanolic and extract of whole plant P. amarus against leptospira.

Immunomodulatory Activity

Extracts of P. *niruri* have proven to be potent murinelymphocytes mitogens and are able to induce surface activation maker (CD69), B and T lymphocyte proliferation. The production of interferon-gamma (IFN-gamma) and interleukin-4 (IL-4) by P. *niruri* extract-stimulated naive splenocyte cultures was also increased in a concentration-dependent manner. Various indices of activation and functions of murine bone marrow-derived macrophages, such as phagocytosis, lysosomal enzymes activity and TNF-alpha release, were significantly enhanced by pre-treatment with P. *niruri* extract, which also modulated macrophage nitric oxide release [90]. P. *niruri* also increased the expression of major histo-compatibility complex-II and markers for dendritic cell maturation (CD40), activation (CD83) and costimulation (CD86) in a concentration-dependent manner. In a transgenic T-cell activation model, P. *niruri*-treated den-dritic cells also presented Ova antigen to Ova-specificCD8(+) T cells more efficiently [91].

Conclusion

It is a commonly used herb in Ayurvedic medicine. This evaluation ropes all updated information on its phytochemical and pharmacological activities, traditional uses and scientific approach. The plant extract have been widely used for the treatment of a large number of human ailments. The chemical entities of this plant have been used as an antidiabetic, antibacterial, anti-inflammatory, antinociceptive, anti-androgenic, anticonvulsant, antioxidant, and anti-tumor, anti-ulcer agents. Scientifically proved activities are related with traditional concept. s. M. pudica has a variety of bioactive compounds with a variety of pharmacological effects. Scientific suggestion exists with respect to their major and minor constituents. *M. pudica* is the most important controversial and effective natural origin that has a tremendous future for research. The novelty and applicability of *M. pudica* are hidden. Such things should be overcome through modern scientific concept. Bhumi Amla (Phyllanthus *niruri*) possess predominant tikta, kashaya, madhura rasa, sheeta veerya and Madhur Vipak.

Phyllanthus niruri (Bhudhatri) contains several phytochemical constituents such as effective natural origin that has a tremendous future for research. The novelty and applicability of *M. pudica* are hidden. Such things should be overcome through modern scientific concept. Numerous investigations on *M. pudica* have now established that it is an important medicinal plant having a plethora of chemical constituents effective against a large number of ailments. Summarized studies which shows antioxidant, anti-inflammatory, analgesic, antinociceptive, immunomodulatory, hepatoprotective, nephro-protective, cardioprotective, hypolipidemic, anti-platelet aggregation, vasorelaxant, anti-diabetic, anti-urolithic, anti-hyperuricemic, diuretic, anti-leptospiral, anti-plasmodial, anti-nematodal, antiviral, anti-bacterial, anti-ulcer, burn wound healing, anti-venom, anti-fertility and anticancer properties. However, the diverse pharmacological activities of the plant extract and isolated phytochemicals have only been assayed in laboratory, and very few clinical studies were available. So it is necessary to take clinical trials according to its studies carried out and the exploit the full medicinal potential of *Mimosa pudica.*

Therefore, advanced research is needed on *M. pudica* active constituent's isolation and exploration as well as their beneficial therapeutic effects on the human body.

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