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Review Article

Phyllanthus Niruri: A magic Herb

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Medicinal herbs are significant source of pharmaceutical drugs. Latest trends have shown increasing demand of phytodrugs and some medicinal herbs have proven hepatotprotective potential. Inflammation describes a coordinated series of molecular, cellular, tissue, organ, and systemic responses that drive the pathology of various diseases Inflammation is a finely tuned, dynamic, highly-regulated process that is not inherently detrimental, but rather required for immune surveillance, optimal post-injury tissue repair, and regeneration. The inflammatory response is driven by cytokines and chemokines and is partially propagated by damaged tissue-derived products (Damage-associated Molecular Patterns; DAMP's). DAMPs perpetuate inflammation through the release of pro-inflammatory cytokines, but may also inhibit anti-inflammatory cytokines.

Key-words: *Phyllanthus niruri*, phytochemistry, pharmacological profile.

Phyllanthus niruri originated in India, usually occurring as a winter weed throughout the hotter parts. The *Phyllanthus* genus contains over 600 species of shrubs, trees and annual or biennial herbs distributed throughout the tropical and subtropical areas. *Phyllanthus niruri* is a herb of Euphorbiaceae family that grows upto 60 cm. Phyllanthus means "leaf and flower" because the flower, as well as the fruit, seem to become one with the leaf. *Phyllanthus nirui* is a common kharif (rainy season) weed found in both cultivated fields and wastelands. Recently it has attracted the attention of researchers, because of its hepatoprotective properties. No effective specific therapy is available for viral hepatitis but *P. niruri* has shown clinical efficacy in viral Hepatitis B. It is known for its liver healing properties so used in Chinese medicine for treatment of liver diseases. *Phyllanthus niruri* (Euphorbiaceae) is a small herb distributed throughout the tropical and subtropical regions of both hemispheres. This plant is popular in folkmedicine, whole plant, fresh leaves and fruits are used inthe treatment of various diseases, particularly hepatitis and other viral infection. 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 *P. niruri*. Extracts of this herb have been proven to have therapeutic effects in many clinical studies. The plant is of medicinal importance for numerous ailments like dysentery, influenza, vaginitis, tumors, diabetes, diuretics, jaundice, kidney stone, dyspepsia, antihepatotoxic, antihepatitis-B, antihyperglycemic and also as antiviral and antibacterial *P. niruri* extract has been shown to inhibit DNA *Phyllanthus niruri*, (family-

Euphorbiaceae) is a herb found in many parts of the world. It is known for a variety of uses viz. hepatoprotective action, lipid lowering action, antidiabetic action, antifungal action to name a few. It holds a reputed position in both Ayurvedic and Unani systems of medicine.

Geographical Distribution

It is a field weed which is found proliferating throughout tropical and sub-tropical 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 upto mid-winter.

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 Magnolio-phyta. The Plant *Phyllanthus niruri* has different names in different names in different language – Assamese: Holpholi, Bengali:Noe, Hindi: Chalmeri, Bhumyalaki, Konka: Bhuin- avalae, Malayalam-Kijhandli, Marathi – Ray avail, Oria – Narakoli, Sanakrit – Bhoo datri, and Tamil –Aru. 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.

Description:

The annual herb is 30-60 cm high, quite glabrous, stem often branched at the base. Leaves: Numerous, sbsessile distichous often imbricating, elliptic oblong obtuse. Stipules present, very acute. Flowers: Yellowish, very numerous, axillary. The male flowers are one to three in number while the female flowers are solitary in nature. Capsules: 2.5mm in diameter, depressed globose, smooth scarcely lobed (Prajapati *et al*.).

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 *P. niruri*. Extracts of this herb have been proven to have therapeutic effects in many clinical studies. (O'Neil *et al*.).

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-D-glucose, which IC_{50} values of 4.7mg/ml against *Babesia gibsoni* and 1.4mg/ml against *Plasmodium falciparum invitro*. The known compounds b glucogallin, quercetin 3-o-b-D-glucopyranosyl-(2 to 1)-o-b-D- xylo-pyranoside, b-sitosterol and gallic acid were isolated. Structures of these compounds were elucidated on the basis of their chemical and spectroscopic data (Matsuura Subeki *et al*, 2005).

Image a- Phyllanthus niruri Leaves

Image b- Phyllanthus niruri leaf, flower

Adulterants and substitutes

Many times *Phyllanthus niruri* is adulterated with Phyllanthus amarus and vice versa. Market samples of *Phyllanthurs niruri* (Linn.) are often adulterated with *Phyllanthus amarus* Linn. Two plants are the sources of two different Ayurvedic drugs *P. niruri* and P. *amarus* possibly with similar therapeutic effects (Bagalkotkar *et al*, 2006).

Pharmacological and biological activity
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 (Meixa *et al*., 1995).

Phyllanthus niruri has been reported to exhibit marked antihepatitis 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 (Thyagarajan *et al*., 1988).

Hepatoprotective effect of an ayurvedic medicine; herbal preparation HPN – 12 (containing *Glycirrhiza glabr, Pichorhiza kurroa, Berberis aristata, Piper longum, Phyllanthus niruri, Solanum dulcamara, Zingiber officinale, Curculigo orchioides, Elettaria*

cardamomum, Tinospora cordifolia, Desmodium trifolium and *Sacchrum officinarum*) orally administered to male albino rats at 1ml/100g body weight was found to be effective against liver damage (Latha *et al*., 1999).

Animals with Carbon Tetrachloride induced hepatopathy were treated with catliv (contains extracts of *Swertia chirata, Eclipta alba, Fumaria vaillanti, Picorrhiza 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 (Pradhan *et al.,* 2001). 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 triacontanal. Glycosides found in *Phyllanthus niruri* demonstrated Aldose reductase (AR) inhibitory activity in studies conducted by a Japanese research group in 1988 and 1989 (Shimizu *et al*., 1989).

HIV Replication Inhibition

Aqueous extract of *Phyllanthus niruri* is reported to have inhibitory effect on human immunodeficiency virus. The investigation examines the anti-HIV effects of the alkaloidal extract of *Phyllanthus niruri* in human cell lines. The inhibitory effect on HIV replication was monitored in terms of inhibition of virus induced cytopathogenecity in MT-4 cells. The alkaloidal extract of *Phyllanthus niruri* showed suppressing activity on strains of HIV-1 cells cultured on MT-4 cell lines. The CC_{50} for the extract was found to be 279.85µgmL^{-1} whereas the EC_{50} was found to be 20.98µgmL^{-1}. Interestingly the Selectivity Index (SI) was found to be 13.34, which showed a clear selective toxicity of the extract for the viral cells. The alkaloidal extract of *Phyllanthus niruri* was thus found to exhibit sensitive inhibitory response on cytopathic effects induced by both the strains of human immunodeficiency virus on human MT-4 cells in the tested concentrations (Naik *et al*., 2003). Extracts of five medicinal plants: *Aristolochia indica*, *Cassia occidentalis*, *Phyllanthus niruri*, *Withania somnifera and Tinospora cordifolia* were administered to 10 HIV infected patients for a period of six months to one year. The clinical status of the patient and their CD4 cell counts were periodically monitored. The results indicate that in seven of the ten patients, their CD4 count increased and the patients remained either asymptomatic or their clinical well being improved. There was no change in the CD4 cell count in one of the patient and the other two progressed to full blown AIDS (Natarraj *et al.,* 2000).

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. (Chandra *et al.,* 2000)

Anti-Diabetic Activity

An alcoholic extract of *Phyllanthus niruri* was found to reduce significantly the blood sugar in normal rats and in alloxan diabetes rats. In normal rats, administration of *Phyllanthus niruri* 200mg/kg body weight reduced the blood sugar by 34.5 percent and to 47.4 percent at the concentration of 1000mg/kg by

weight at 1 hour. However at 6th hour, values are almost similar to normal value. Continuous administration of the drug produced significant reduction in normal blood sugar in rats, which on 15th day was also found to reduce the blood sugar in alloxan diabetic rats. In short term experiment, drug was found to reduce the blood sugar at 4th hour by 6.07 percent at dose level of 200mg/kg by weight and 18.7 percent at concentration of 1000mg/kg by weight. Continuous administration of drug produced significant reduction in blood sugar in alloxan diabetic rats. On 15th day values were almost similar to normal in the group taking 1000 mg/kg by weight. Plant extract did not produce any toxicity as seen from liver and kidney function test and in hematological parameters. The results indicate potential antidiabetic action of *Phyllanthus niruri*. (Raphael *et al*., 2000).

Anti-Malarial Activity

The ethanolic, dichloromethane and lyophilized aqueous extracts of Cassia occidentalis root bark, Morinda morindoides leaves and whole plants of *Phyllanthus niruri* were evaluated for their antimalarial activity in vivo, in 4-day, suppressive assays against *Plasmodium berghei* ANKA in mice. No toxic effect or mortality was observed in mice treated, orally, with any of the extracts as a single dose, of 500 mg/kg body weight, or as the same dose given twice weekly for 4 weeks (to give a total dose of 4 g/kg). No significant lesions were observed, by eye or during histo-pathological examinations, in the hearts, lungs, spleens, kidneys, livers, large intestines or brains of any mouse. At doses of 200 mg/kg, all the ethanolic and dichloromethane extracts produced significant chemosuppressions of para-sitaemia (of > 60% for *C. occidentalis* root bark and *Phyllanthus niruri* whole plant, and of 30% for *M. morindoides* leaves) when administered orally. The most active ethanolic extract, that of *Phyllanthus niruri*, reduced parasitaemia by 73%. The dichloromethane extracts of *M. morindoides* and *Phyllanthus niruri* produced similar reductions (74% and 72% chemosuppression, respectively), whereas that of *C. occidentalis* was slightly less active (60% chemo-suppression). Each lyophilized aqueous extract was less active than the corresponding ethanolic extract (Neraliya *et al*., 2004).

Activity against Filarial Mosquito (*Culex quinquefasciatus*)

Eighteen plants were evaluated for juvenile hormone analogue activity against *Culex quinquefasciatus*. Of these acetone extracts of 8 plants namely *Commelina benghalensis, Ageratum conyzoides, Achyranthus aspera, Sida acuta, Euphorbia pulcherrina, Rivinia humilis, Ruellia tuberosa* and *Phyllanthus niruri* possessed significant juvenile hormone activity. The LC_{50} values of 5 most active plants namely *Phyllanthus niruri*, *Amaranthus spinosus, Antegonon leptopus, Corchorus aestuans, Corchorus benghalensis* were determined to be 13, 16, 17, 17, 14ppm respectively (Calixto *et al*., 1984).

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 (Grewal, 1984).

Analgesic activity

Methanol extract of dried callus tissue at a concentration of 10mg/kg, administered intraperitonially 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 intraperitonially 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 (Santos *et al.,* 1994).

Chromosome Aberration Inhibition

Water extract of dried fruit and leaves, at a dose of 685.0 mg/kg, administered to mice by gastric incubation was active vs. chromosome damage induced by lead nitrate and aluminium sulphate in bone marrow chromosomes. Dosing was for 7 days (Holdsworth *et al.,* 1982).

Worldwide Traditional Medicinal Uses

Hot water extract of the entire plant is administered orally, to reduce fevers, and as a laxative (Halberstein *et al.,* 1978). Decoction of dried leaves and roots is taken orally for fever, and for good health. Dried entire plant, grounded in buttermilk is administered orally for jaundice. Fresh leaf juice is used externally for cuts and bruises. For eye diseases the juice is mixed with castor oil and applied to the eye. Infusion of dried leaves is administered orally for dysentery and diarrhea. Infusion of green root is taken orally to treat heavy menstrual periods (Singh *et al.,* 1986). Hot water extract of leaves is administered orally as a cholagogue (Duke *et al.,* 1975). Decoction of dried leaves is taken orally for or used in bath for fever, and orally for indigestion (Weninger *et al.,* 1986). Hot water extract of dried entire plant is administered orally as a spasmolytic and is also against fever (Weninger *et al.,* 1982). Fresh plant juice is taken orally for genito urinary disorders (Sahu *et al.,* 1984). The fruit is used externally for tubercular ulcers, scabies and ringworm (Chauhan *et al.,* 1977). Hot water extract of dried entire plant is administered orally for diabetes (Jain *et al* 1967). For asthma in ayurvedic medicine (Sircar *et al* 1984). Fresh leaf juice or fresh root juice are taken orally for venereal diseases. Decoction of dried entire plant is administered orally to treat venereal diseases (Holdsworth *et al.,* 1989). Decoction of dried leaf when taken orally is a treatment for diarrhea. A cupful of leaf decoction is drunk daily (Holdsworth *et al.,* 1992). Decoction of dried entire plant is used as a bath for newborns. It is believed to remove disease-causing elements from the skin. Orally the decoction is used for coughs in infants (Velazco *et al.,* 1980). Hot water extract of commercial sample of the entire plant, is administered orally as an antipyretic (Mokkhasmit *et al.,* 1971). Hot water extract of dried aerial parts administered orally is used as a diuretic, as an antipyretic, and for malaria (Kitisin *et al* 1952). Hot water extract of dried entire plant is administered orally as an anti-inflammatory agent (Wasuwat *et al.,* 1967). Hot water extract of the plant is taken orally to increase the appetite (Oakes *et al* 1958). Hot water extract of roots together with hot water extract of *Citrus aurantifolia* roots is taken orally to increase appetite. Hot water extract of entire plant administered orally, is taken for malarial fever. The plant is boiled and the tea taken. Water extract of the leaves and roots is taken orally for diabetes, and as a diuretic (Asprey *et al.,* 1955).

Conclusion

Phyllanthus niruri is an important medicinal plant. The plant is widely used for the treatment of hepatic disease, oedema, dropsical condition, and urinary troubles. A large number of publications on the chemistry, pharmacology, and several other aspects have been made, but no homogenous, pure, active principle of the plant in the form of a modern standardized drug has been

introduced. A basic protein showing high systemic resistance inducing activity against plant viruses has been isolated, but it has not yet been purified to homogeneity and commercially made available. However, the plant is abundantly available in wild form over large tracts of land. The commercial bulk of *Phyllanthus niruri represents* a heterogeneous population. Consequently, it quite often results in poor quality roots and biomass. The cardinal feature of modern cultivation of any plant with impressive uniformity and high productivity for end product is thus grossly lacking in *Phyllanthus niruri.*

Table-1.Chemical constituents present in different part of plant

Essential oil	Leaf	Root	Aerial parts	Leaf, stem
1. Kaempferol-4-o-alpha-L-rhamnoside, Aer 0.9%, Rt 2. (-) Limonine, Lf EO 4.5% 3. Ascorbic acid, Lf 0.41% 4. Cymene, Lf EO 11% 5. Hypophyllanthin, Pl 0.05-0.17% 6. Geranin, Pl .23% 7. Linoleic acid, Sd Ol 21% 8. Linolenic acid, Sd Ol 51.4% 9.Ricinoleic acid, Sd Ol 1.2% 10.Phyltetralin, Pl, Lf 0.14% 11.&Phyllanthin, Lf, Aer	1. 4-Hydroxy-lintetralin, Lf 2. 2,3-dimethoxy-iso-lintertralin, Lf 3. Astragalin, Lf 4. Beta sitosterol, Lf 5.Demethylenedioxy niranthin, Lf 6. Hydroxy niranthin, Lf 7. Hypophyllanthin, Lf Aer 8. Iso-quercitin, Lf 9. Linnanthin, Lf 10.Lintetralin, Lf 11.Niranthin, Lf 12.Quercitrin, Lf 13.Salicylic acid methyl ester, Lf EO 14.Seco-4-hydroxy-lintetralin	1. (+)-Catechin, Rt cult 2.(+)Gallocatechin, Rt Cult 3.(-)Epicate chin, Rt Cult 4.(-)Epicate chin-3-gallate, Rt Cult 5.(-) Epigalloca techin, Rt Cult 6. Gallic acid, Rt cult 7. (-)-Epigalloca techin-3-Ogalla te, Rt 8. Eriodictyol-7-o-alpha-L-rhamnoside, Rt 9. Fisetin-41-O-alpha-L-rhamo niside, Rt 10.Lupeol acetate, Rt 11.Lupeol, Rt 12.Nor-securinine, Rt	1.24-Isopropyl Cholestrol, Aer 2.Dotriacontanoic acid, Aer 3.Nirphyllin, Aer 4.Nirurine, Aer 5.Phyllanthenol, Aer 6.Phyllantheol, Aer 7.Phyllester, Aer 8.Phyllinurin, Aer 9.Phylltetrin, Aer 10.Triacontan-1-al, Aer 11.Triancontan-1-ol, Aer	1.Nirtetralin, Pl, Lf 2.4-Methoxy-nor securinine, Aer, Rt, St 3.Rutin, Pl, Lf 4. Phyllanthine, Rt, Lf, St 5. Phyllochrysine, Lf, St 6. Quercetin, Lf, Pl

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