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## RESEARCH ARTICLE

### **PHYLLANTUS NIRURI: ETHNOBOTANY, CHEMISTRY AND PHARMACOLOGICAL PROPERTIES TOWARDS DRUG FORMULATIONS**

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#### ABSTRACT

The plants of the genus *Phyllanthus* (Euphorbiaceae) have been used as traditional medicinal materials for a long time in China, India, Brazil, and the Southeast Asian countries. They can be used for the treatment of digestive disease, jaundice, and renal calculus antimicrobial, antioxidant, anticancer, antiinflammatory, antiplasmodial, antiviral, diuretic and hepatoprotective. Particularly, *Phyllanthus niruri* found throughout the tropical and subtropical regions of both hemispheres showing an impressive list of medicinal uses in many countries around the world. In this review, we highlight the properties of the specie about ethnobotanical, phytochemical, pharmacological, biological and toxicological activities as it has been described in the scientific journals of the last 10 years. The emphasis is centered to liver disorders and kidney stones, different ways of drug formulations, dosage and the precaution uses.

**Key words:** *phyllanthus niruri*, Hepatitis, Gallstones, Drug Formulations.

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#### INTRODUCTION

*P. niruri* is called Chanca Piedra in Spanish, which means stone breaker, because it has been used as an effective remedy to eliminate gallstones, kidney stones and other kidney disorders (Narendra, 2012). It is a typical member of family Euphorbiaceae. Small annual herb found throughout the tropical and subtropical regions of both hemispheres, the genus *Phyllanthus* has been used in traditional medicine for its wide range of pharmacological activities like antimicrobial, antioxidant, anticancer, antiinflammatory, antiplasmodial, antiviral, diuretic and hepatoprotective (Harish and Shivanandappa, 2006); (Patel, 2011). *Phyllanthus* species are extensively used in traditional medicines for the treatment of hepatic diseases due to their bioactive hypophyllanthin and phyllanthin, but *P. niruri* species is certainly one the most used of *Phyllanthus* genus in world folk medicine. The reason could probably be the fact that it is so widely distributed, both in tropical and subtropical countries (Calixto, Santos, Filho, and Yunes, 1998); (Syamasundar et al., 1985). *P. niruri* has enormous pharmacological activities such as antiviral (against Hepatitis B), antimicrobial, hepatoprotective, anticancerous and hypocalcemic agent.

Recently, it has been used as a treatment for diabetes mellitus type 2 diabetes in Sprague–Dawley rats was achieved by a low dose of streptozotocin (STZ) (25 mg/kg bw *via* metabolomics approach (Mediani, 2016). In this review, we highlight the properties of the specie about ethnobotanical, phytochemical, pharmacological, biological and toxicological activities as it has been described in the scientific journals of the last 10 years, and the different formulations are suggested for drug making.

**Ethnobotany:** The plants of the genus *Phyllanthus* (Euphorbiaceae) have been used as traditional medicinal materials for a long time in China, India, Brazil, and the Southeast Asian countries. *Phyllanthus niruri* is a medicinal plant (commonly known as stone breaker) found in the tropics and other parts of the world. It is known for its capacity to block the formation of calcium oxalate crystals and kidney stone formation in urolithiasis. This plant has been used to treat hyperglycemia, hypertension, pain, and mild cases of malaria (Khoo, W. K., Adnan, M. A., Mahalingam, T. P., Fernandez, A. R. and Jeevaratnam, K., 2016). *Phyllanthus niruri*, as said in introduction, 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 for mostly liver disorders and gallstones". Apart from these, *Phyllanthus niruri* is also used and administered for diuretic, hypoglycemic and hypertension cases. And it also shows anti-inflammatory (Lee, 2016), anti-tumor (Zheng, 2016), antinociceptive and anti-

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oxidant properties (Giribabu, 2014). The table 1 describes the different ethnobotanical uses across the world.

**Phytochemistry of *P. Niruri*:** 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.*). *Phyllanthus niruri* has several bioactive molecules such as lignans, phyllanthin, hypophyllanthin, flavonoids, glycosides, tannins, alkaloids, ellagitannins, phenyl propanoids, steroids, ricinolic acid, niriside and phylltetralin. It contains also acid arabinogalactan and diterpene (Kaur, 2017). Limonene is a monoterpene and has many medical and pharmaceutical applications. It is a major component of orange oil. Its anti-carcinogenic actions in liver tumour model have been reported (Mills, 1995).

*P-Cymene* also belongs to the monoterpene category. It has a wide variety of biological actions, among them anti-oxidant and anti-microbial activity. Recent study on thyme, an essential oil with *p-cymene* as one of its components, exhibited a good anti-oxidant activity by preventing oxidation of *α-tocopherol*. *P-Cymene* was tested for anti-microbial properties using the paper disc diffusion method, in which it revealed a good anti-microbial activity (Marchese, 2017). Lupeol belongs to the pentacyclic triterpene category and can be synthesized through protosterol carbocation by backbone rearrangement reaction. The compound has proven to have anti-inflammatory and antitumour activities (Magalhães, 2017).

### Drug formulations

***P. niruri* tea:** *P. niruri* tea or chanca piedra tea is brewed from the dried leaves of the plant. Its detoxifying power is what makes it such a popular ingredient in natural health solutions, particularly in South America, as it is native to the Amazon region. While this tea is still not widely distributed around the world, its specific health effects have brought it into the spotlight for natural health practitioners in America, Europe, and Asia. It has also been a part of traditional Ayurvedic medical practices for generations (Kumar, Singh, Bajpai, Singh, and Kumar, 2017). Drinking chanca piedra tea brings a number of health benefits, particularly for the liver and preventing kidney stone formation by reducing the level of calcium, but knowing how to brew it properly is also important. Some studies have even found that drinking this tea can relax the ureter (Boim, 2010), so if the stones are too large and begin to pass, they won't be quite as painful.

**Capsules and Tablets:** Capsules and Tablets are always made with excipients, generally at the concentration of 70% and 30% of excipients. The effect of excipients was studied and reported by (de Souza, 2007)

***P. Niruri* Syrup:** Syrup is made by extraction with a solvent, then dried for processing the oral liquid. The study suggests that methanolic extract of *P. niruri* leaf possess anti-inflammatory activity and promotes ulcer protection as ascertained by regeneration of mucosal layer and substantial prevention of the formation of hemorrhage and edema (Mostofa, 2017).

**Pharmacological properties:** A good number of findings from on scientific investigations have been reported and described as responsible of various pharmacological effects and the dosage as well (Kamruzzaman, 2016). Some are summarized in table 2. For hundreds of years *P. niruri* has been used as an herbal remedy to kidney stones, viral infections, liver disorders, bacterial infections, and many other ailments. In more recent years, however, *P. niruri* has been shown in modern medicine to cure or treat multiple disorders.

**Dosage:** From the literature, showing best results, it is recommended to take one to two capsules, each containing 500 mg of *P. Niruri* two times a day after meals. However, it is best to consult an experienced physician and practitioner before taking these capsules to avoid reaction with any ongoing medication or side-effects due to any chronic ailment.

According (Kamruzzaman, 2016), the dosage is described as following:

### 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.

- 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 oral 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 *P. niruri* powder has been taken by mouth three times daily for 30-45 days;
- To treat urinary stones, 450 milligrams of *P. niruri* has been taken by mouth three times daily for three months. Children (under 18 years old);
- Children

There is no proven safe or effective dose for *P. niruri* in children.

According (Paithankar V. V., 2011), 37 patients with chronic viral hepatitis B were treated with a daily dose of 600mg of *P. niruri* for 30 days. 59% of the patients lost the HBsAg two weeks after the end of the treatment.

**Precautions:** *P. niruri* showed few negative side effects in human and animal studies, but you should still use caution. It may cause stomach upset or diarrhea. Because it hasn't been studied, there's no proven safe dose for children. This herb is not recommended for pregnant or breastfeeding women. Pregnant women should abstain from taking *P. Niruri* supplement; feeding mothers on the other hand may take this herb if medically prescribed.



Figure 1. Aerial parts of the *P. niruri*

Table 1. Worldwide Ethnobotanical uses (Narendra, 2012)

Country/ Region	Ethnobotanical uses
Amazonia	Apertif, anodyne, colic, carminative, digestive, diabetes, dropsy, diuretic, dyspepsia, dysentery, flu, fever, gonorrhoea, gallstones, itch, kidney stones, jaundice, malaria, laxative, proctitis, stomachache, vaginitis, tumor, vermifuge.
Bahamas/ Caribbean	Antiviral, aperitif, antispasmodic, antihepatotoxic, appetite stimulant, bactericidal, constipation, cold, diuretic, fever, typhoid, flu, laxative, hypoglycemic, stomachache
Brazil	Analgesic, Abortifacient, aperient, anti-bacterial, anti-inflammatory, anticancerous, antiviral, arthritis, ache (joint), antilithic, albuminuria, antispasmodic, bladder stones, calculi, cystitis, catarrh (liver and kidney), diabetes, digestion stimulant, diaphoretic, diuretic, fever, gout, gastrointestinal problems, hepato-protective, hepatitis, hydropsy, hypoglycemic, hypertension, jaundice, kidney stones, malaria, obesity, muscle relaxant, purgative, prostatitis, renal problems, stomachic, tonic, uric acid excess, uterine relaxant, urinary problems.
Haiti	Colic, carminative, diuretic, digestive, indigestion, fever, spasmolytic, malaria, stomachache.
India	Asthma, anemia, astringent, conjunctivitis, bronchitis, cough, dropsy, diarrhea, diabetes, dysentery, diuretic, eye disorders, galactagogue, gonorrhoea, genitourinary disorders, jaundice, hepatitis, menorrhagia, leucorrhoea, ringworm, oligogalactia, stomachic, scabies, tuberculosis, thirst, urogenital tract infections, tumor (abdomen). In Chhattisgarh state, it has medicinal tradition of this weed mainly for the snake bite.
Malaya	Caterpillar sting, diarrhea, dermatitis, diuretic, itch, piscicide, miscarriage, renosis, purgative, vertigo, syphilis.
Peru	Diuretic, calculus, gallstones, emmenagogue, hepatitis, kidney problems, kidney pain, kidney stones, urinary infections, renal problems, vermifuge.
United States	Bronchitis, analgesic, deobstruent, chologogue, fever, diabetes, gallstones, gallbladder problems, hepatitis, gout, hypertension, kidney stones, kidney problems, uric acid excess, liver disease, urinary tract infections.

Table 2. Specific diseases cured by *P. Niruri*

Diseases	Actions	References
Liver Diseases	It helps cure several liver related ailments like jaundice, liver cancer and hepatitis.	(Mekha Mohan, 2015); (Li, 2017)
Gastrointestinal problems	The herb is used as a medication to treat flatulence as well as, aid digestion. This herb is also often prescribed to patients suffering from stomach pain and intestinal parasites as well	(Melo, 2015); (Sousa, 2018)
Kidney and gall bladder stones	This herb is primarily used to prevent formation of calcium stones in the kidney and gall bladder. The name 'stone-breaker' was in fact given to this plant because of its ability to cure as well as, prevent the formation of gall bladder and kidney stones.	(Paithankar, 2015); (Pucci, 2018)
Anti-HIV and anti-hepatitis B properties	It possesses hepato-protective qualities and helps treating Hepatitis B. Its effectiveness in relieving acute symptoms of HIV has also been established through many studies. Research conducted in this field has also shown that <i>Phyllanthus Niruri</i> helps treat Hepatitis B to a great extent.	(Bagalkotkar, Sagineedu, Saad, & Stanslas, 2006)
Diabetes:	The herb effectively helps cure and manage diabetes.	(Asare et al., 2012); (Najari Beidokhti et al., 2017)
Anti-ulcer activity		(Okoli et al., 2009)
Other disorders	Leucorrhoea and menorrhagia in women, Urinary disorder, chronic fever, excessive thirst, as diuretic and immunity booster, blennorrhagia, dysmenorrhoea and menorrhagia	(Narendra, Swathi, Sowjanya, & Satya, 2012).

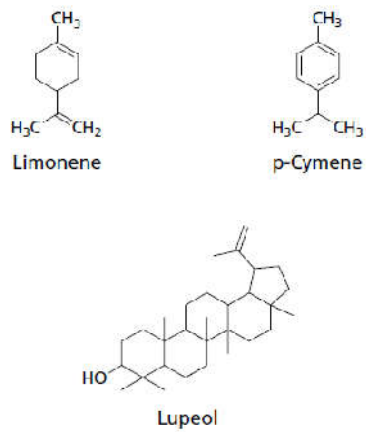


Figure 2. Chemical structures of Terpenoids

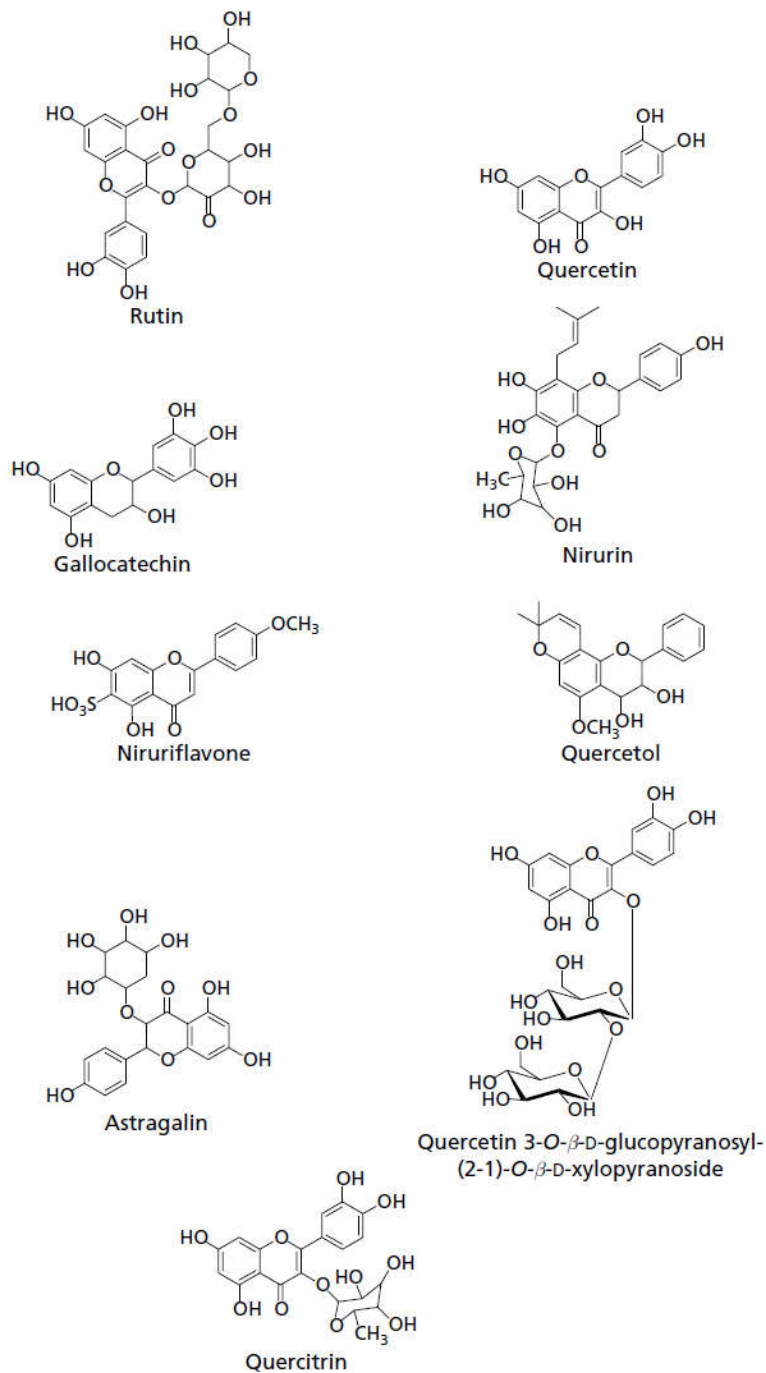


Figure 2. Chemical structure of Flavonoids

## Flavonoids

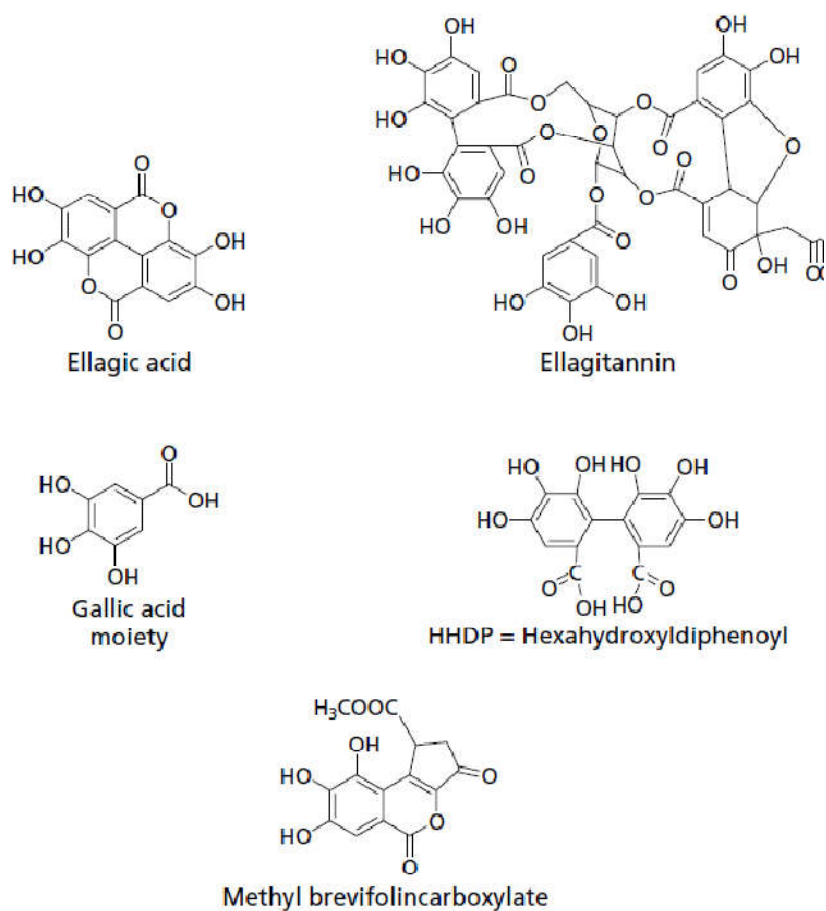


Figure 3. Chemical structures of ellagic acid, gallic acid, ellagitannin hexahydroxyldiphenoyl moiety and methyl brevifolincarboxylate



Figure 4. Different Ayurveda formulations of *P. niruri*: powder (a), tablets (b), Syrup(c), capsules (d) and tea (e).

Heart patients too are advised to take *P. niruri* only after consulting their doctors, as this herb may contradict the medication being taken for the heart already. Similarly people on diabetes medication should also consult their GP before taking this herb, as their ongoing medication may require modifications if this herb is consumed alongside. This product may at times result in increased need to urinate. It is advised that this product be stored in a cool dry place and away from hot and cold temperatures; as well as reach of children.

## Conclusion

A large number of features on the chemistry, pharmacology, and several other aspects on *P. niruri* have been discussed in several scientific papers. The specie has undoubtable medicinal properties supported by the evidences from scientific investigations. Those properties are due to all its active compounds such as quercetin rhamnoside, gallic acid, geraniin and quercetin glucoside. They were identified and proved with the properties of anti-viral and anti-hepatotoxic effects. As the specie is safe and can be used alone without associate other ingredients, the drug formulation is recommendable for alleviating liver disorders and kidney stones.

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