Phyllanthus Engleri and other Species: Traditional and Medicinal Values

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ABSTRACT
Phyllanthus Engleri an annual plant of the kingdom Plantae is one of the most popular traditional herbal medicines, and its fruits are used to cure a wide range of illnesses, including fever, stomachaches, kidney cancer, and digestive disorders. Phyllanthus Engleri contains various phytochemicals, with screening mainly identifying constituents like flavonoids, phenols, saponins, alkaloid, Tannins etc. These compounds contribute to plants potential medicinal properties. Among their many advantageous qualities are their anti-inflammatory, anti-mutation, anti-carcinogenic, and ability to regulate key cellular enzyme functions. Phenols often contribute to the medicinal properties of plants. Alkaloids are another class of compound found in various plants. According to preliminary research, Phyllanthus Engleri may also be useful in treating cancer, diabetes, hypertension, and a host of other illnesses. However more research is required to confirm its efficacy and safety for specific medical applications including liver treatment. Conducting research on Urolithic with Phyllanthus Engleri because their gap in the existing studies, and previous research has specifically explored the nephroprotective potential of Phyllanthus Engleri extract which could potentially lead to development of nephroprotectivity treatments or therapies using this extract.

Keywords: Phyllanthus Engleri, flavonoids, phenols, saponins, alkaloid, Tannins, nephroprotective.

INTRODUCTION
Phyllanthus Engleri is a member of the Phyllanthaceae family and is widely utilized in African traditional medicine to cure a variety of ailments. The common name of Phyllanthus Engleri is Spurred Phyllanthus, Spurred potato-bush. The most abundant species are used in different country have a beneficial role in Ayurveda for the treatment of digestive, genitourinary, respiratory, and skin diseases.[1] Fruit and leaves have been used to treat jaundice in traditional medical systems like Ayurvedic and Unani medicine. Sometimes people with chronic dysentery use an infusion made from the young shoots of this herb. Historically, plants have been used extensively to cure a wide range of illnesses and conditions in humans.[2] Its life span is quite brief. Field weed Phyllanthus Engleri belongs to the genus Phyllanthus, which has 600–700 species with little characteristics that set them apart. Phyllanthus Engleri plant extract is used as medication in the Indian ayurvedic system and is suggested for urinary diseases, anemia, leprosy, asthma, and bronchitis, among other conditions. Phyllanthus Engleri pax specimens were gathered on February 6, 1989 by James Lovett and Roy Gereau of the Missouri Botanical Garden Conventional medical systems, including.[3]

Morphological Description
Glabrous, dioecious, up to eight meters tall as a small tree or shrub. Fissured and grey bark. Up to 30 centimeters of leafy branchlets are produced by robust spur-branchlets that are 2-3 centimeters long and contain scale leaves that eventually harden into thick, sturdy spines. Foliage leaves typically have a rounded or obtuse apex, are suborbicular, dull to yellowish green above, and are ± glaucous below. Stipules are lancelate, caducous, and measure 1-4
millimeters. There are fascicles of flowers. The ovate, highly imbricate sepals of male flowers feature five disk glands, and the stamens are free. We don't know anything about female flowers. The fruit is yellowish-green, three-lobed, and subglobose, measuring 1.5–2 × 2-2.5 cm. Up to six seeds, each measuring one centimeter, can be found.\[4\]

Phyllanthus Engleri is spur potatoe bush, Kamulya kamuseka is flowering in the reserve and the fruits are appearing. A many branched tree rough bark and sharp spur like thorns in clusters; the flowers are small in many clusters. The small fruit is edible when dark purple and has a nice taste. It is found in bunches along the stems. Reputed to be an aphrodisiac. The leaves are chewed to relieve indigestion and constipation. The bark is highly toxic all parts of the tree above ground are non-poisonous.\[5\]

**Fig. 1: Plant of Phyllanthus Engleri**

**Botanical Description and Vernacular Names**

**Leaves:** Numerous, small, green, sub sessile, closely arranged, elliptic along shaped, obtuse, having short petiole and stipules present, they are arranged alternatively on each side of the stem.\[6\]

**Flowers:** As figure 3 describe the flowered fascicles. Male flowers have five firmly imbricate, ovate sepals, five disk glands, and free stamens. We don't know about female flowers. Sub globose, 1.5–2 × 2-2.5 cm, three lobes, yellowish-green in colour, up to six seeds.\[7\]

**Fig. 2: Leaves of Phyllanthus Engleri**

**Fig. 3: Flowers of Phyllanthus Engleri**
**Fruit:** Fruit is a capsule, very small, depressed globose and more over capsule is smooth, 2-3mm in diameter.\[^{[8]}\]

**Stem:** As figure 5 Steam is having horizontal branches and height of 30-60cm, 1-2.5mm width.\[^{[9]}\]

Following are different species of *Phyllanthus* plant

**Phyllanthus niruri:** Herbal medicine traditions, including Indian Ayurveda, Indonesian Jamu, and Traditional Chinese Medicine, have long used *Phyllanthus niruri*. Numerous ailments, including influenza, vaginitis, diarrhoea, tumours, diabetes, jaundice, kidney stones, diuretics, and dyspepsia, are treated with the entire plant.\[^{[10]}\] According to Chopra et al. (1986), the plant is also effective in treating bacterial and viral infections, hyperglycaemia, hepatotoxicity, and hepatitis B. For more than 2000 years, *Phyllanthus niruri* has been utilized in Ayurvedic medicine to treat diabetes, gonorrhoea, jaundice, and irregular menstruation. It is a significant medicinal plant used in jamu; a popular traditional herbal remedy used in Indonesia to cure a wide range of illnesses. The herb is utilized as a hepatoprotective and antiviral ingredient in jamu treatments. In Malaysia, *P. niruri*, known as Duking Anak, is used internally for diarrhoea, kidney disorders, gonorrhoea and coughs.\[^{[11]}\]

**Phyllanthus urinaria:** Medicinal plants are a gift from nature that help people live healthy, disease-free lives. Numerous medicinal plants that are part of the Rasayana family of herbal remedies from the Indian traditional medical system (Ayurveda) are suggested to have intriguing antioxidant properties. *Phyllanthus emblica* Linn.,\[^{[12]}\] *Emblica officinalis/* commonly known as Indian gooseberry or amla, family Euphorbiaceae, is an important herbal drug used in unani (Graceo - Arab) and ayurvedic systems of medicine.\[^{[13]}\]

**Phyllanthus Fraternus:** One of the richest, oldest, and most varied cultural traditions pertaining to the use of medicinal herbs is found in India. Thousands of medical articles and texts have provided access to this information. These traditional medical knowledges, which include Ayurveda, Unani, Siddha, and Swa-riga (Tibetan) systems, constitute the codified medical systems. The flora and fauna are used for medicinal purposes and they have important cultural roles and as well as vital roles in
forest ecology, such as pollination, seed predation and dispersal, seed germination, herbivory and predation on potential pest species.\[14\]

**Phytoconstituents of Phyllanthus Engleri**

**Flavonoids**- Rutin is a flavanol glycoside it comprised the flavanol quercetin and disacharide rutinose, belongs a large group of phenolic secondary metabolites of plants it includes more than 2000 different acknowledge chemicals \[15\]. Free radicals are proving to be responsible for as much as 90% of all human diseases, such as cancer, arteriosclerosis, senility and stroke, due to ageing, and recent all studies have shown the rutins are powerful anti-oxidants that fight to free radical.\[16\]

An ever-expanding amount of scientific evidence supports a protective effect of polyphenols on chronic degenerative diseases.\[17\] Over the past decade, a significant amount of short duration human intervention studies has been conducted with the goal of establishing the exact bio efficacy of various polyphenol subclasses.\[18\] there was insufficient consistent evidence to provide conclusions regarding most other subclasses of flavonoid.\[19\] Flavonoids are among the most studied phytochemicals found in plant foods and include a large number of different molecules which may result in diverse biological activities.\[20\]

Quercetin is most important in nutrition due to its ability to strengthen and modulate the permeability of the walls of the blood vessels including capillaries.\[21\] Quercetin is one of the major bio flavonoids and forms the backbone of many other flavonoids.\[22\] It is frequently studied dietary flavonoid, distributed in onion, apple, berries, tea and brassica vegetables, as well as many nuts, seeds, barks, flowers, and leaves.\[23\] Glycosylation of least one hydroxyl group of quercetin derivatives result in an increase of its hydrophilicity it may be transported to various parts of the plant and stored in vacuoles.\[24\] Widely investigated chemical property of phenolic compounds is their anti-oxidant activity, and it is capable of neutralizing free radicals, which are at all times there in the food within cells of the human body.\[25\] The amplified hydrophilicity of quercetin glycosides changes the coefficients of the distribution among the aqueous and lipid phase, which is of immense implication in lipid systems such as β-carotene or TEAC emulsion.\[26\] Additionally, it has been observed in a variety of therapeutic plants, including Solanum trilobatum perforatum and Ginkgo biloba. The predictable standard daily dietary intake of quercetin by a person.\[27\]

Others- From englerin, quercitol, flavanone-5-O-rutinoside, and prenylated flavanone glycoside were also extracted. Niruriflavone is a flavone sulfonic acid and was shown to exhibit potent radical scavenging properties in 2, 2′-azinobis(3-ethylbenzthiazoline-6-sulfonate) (ABTS) cation radical reduction assay.\[28\]

**Tannins**- They are light brown to reddish-brown to dark brown spray-dried amorphous powders.\[29\] They are natural astringent materials commonly found in many parts of plants where they participate in defending the plant from fungal, bacterial and insects attack as well as to the plant survival in periods of drought.\[30\] Although oil-sourced materials became widespread in the past few decades, they have at present subject to lots of questioning due to the fluctuating oil price, to problems of reserves depletion, to the pollution. Nowadays, sustainable materials.\[31\] Analysis of condensed tannins is complicated by the diversity of structures found within this group of compounds.\[32\]

Human immunodeficiency virus type-1 reverse transcriptase (HIV-1-RT) was suppressed by repandusic acid with an ID50 value of 0.05 mM (Ogata et al 1992). In the same investigation, the synthesis of HIV-1 specific p24 antigen in the Clone H9 cell system was suppressed by this drug at 2.5 mM. The compound also showed strong inhibitory activity against HIV-1 protease, with an IC50 value of 12.5mM.\[33\] It is also possessed the ability to lower systemic blood pressure through the reduction of noradrenaline release in spontaneously hypertensive rats.\[34\]

**Alkaloids**- Alkaloids are usually extracted from plants and are mostly produced biosynthetically from amino acids, resulting in a range of chemical configurations. Approximately 20% of plant species contain alkaloids in very minute amounts, and research and development is still focused on producing, extracting, and processing alkaloids.
Alkaloids are crucial for human health as well as an organism's inherent defenses, among other things. Alkaloids are particularly well-known as anesthetics, anti-inflammatory, and cardioprotective drugs when used therapeutically. Known alkaloids that are utilized in therapeutic settings include nicotine, ephedrine, quinine, strychnine, and morphine. Alkaloids have given dynamic biological activities in human body as well animal body. Increases activity in the thalamus, prefrontal cortex, and visual system, anti-cholinergic effect as competitive inhibitor of the muscarinic acetylcholine receptor.[35]

Natural products are considered as important sources of new drugs, leads as well as new chemical substances.[36] The outcome of plant-based drug exploration is mainly concerned with the development of various anticancer agents from alkaloids.[37] Alkaloids are generally found in plants, and they are especially prevalent in some families of flowering plants. In excess of 3000 distinct kinds of alkaloids have been recognized.[38] Alkaloids generally represent a highly diverse group of compounds containing cyclic structures with at least one basic nitrogen atom being incorporated within.[39]

Saponins- Saponins are composed of high-molecular-weight glycosides that combine a steroid aglycone triterpene molecule or a sugar with a triterpene molecule. With an IC50 of 4.7 mgmL−1 for the intra-erythrocytic parasite and 7.5 mgmL−1 for Babesia gibsonii, respectively, Dios-genie is a steroid glycoside that exhibits action. Canine babesiosis, such as hemolytic illness, is brought on by these parasites. With IC50 values of 1.4 mgmL−1 and 4.6 mgmL−1, respectively, these compounds demonstrated activity against the malaria-causing Plasmodium falciparum. Englerin was also used to separate complicated and linear acidic hetero Xylans.[40] These agents, referred to as biological response modifiers, have the capacity to mediate a variety of therapeutic outcomes, such as anti-tumor action. By preventing the binding of the viral protein REV (regulation of virion expression) to RRE (REV response element), niruriside, a phenyl propanoid, demonstrated anti-HIV action. Triacontanal showed to be protective against galactosamine-induced toxicity in rat's hepatocytes primary culture.[41] In natural resources, all triterpenoids mostly appear as aglycones in triterpenoid saponins that may be considered glycoconjugates.[42-46]

Terpenes- One monoterpenoid with numerous medicinal and pharmacological uses is limonene. Through the Diels-Alder reaction, two molecules of isoprene can be converted into one of the two mirror-image forms of the limonene molecule. Orange oil contains a lot of limonen. There have been reports of limonene's anti-carcinogenic properties in liver tumor models. An increase in diclofenac permeation induced by limonene has also been described in hairless rats, which suggests that limonene is an effective topical medication for both dermal and sub-dermal injuries.[47]

Pharmacology activity of Phyllanthus Engleri

Analgesic and Anti-Inflammatory- A cation channel known as Transient Receptor Potential Canonical 5 (TRPC5) reacts to a wide range of activators, the precise nature of which is still unknown. First identified in the central nervous system, TRPC5 also forms channels in peripheral sensory nerves, either by itself or in conjunction with TRPC1 and TRPC4. TRPC5 expression had also found in joint synoviocytes where is stimulation of TRPC5 by the thioredoxin, endogenous agonist resulted in a suppression of matrix metalloproteinases (MMPs) secretion in both human and animal synoviocytes.[48]

TRPC5 has been implicated in an endogenous anti-inflammatory/analgesic pathway in a model of unilateral arthritis and, more recently, in a model of osteoarthritis (OA), as we have previously reported. In all studies, mice deficient in TRPC5 exhibited increased localized inflammation in the synovium, which was characterized by increased production of pro-inflammatory mediators, extracellular remodelling enzymes, and increased cellular infiltration, in addition to enhanced synovial vascularization. It's interesting to note that, when compared to healthy post-mortem donors, TRPC5 expression was lower in human synovial samples from osteoarthritis patients. Together, these results suggest that TRPC5 can associated with an
endogenous anti-inflammatory and analgesic pathway in inflammatory joint conditions.[49-51]

Anti-Cancer- An extract from Phyllanthus Engleri was identified in a bioinformatic of NCI 60-cell natural product extract screening data that selectively inhibited the growth of renal cancer cell lines.[52] Bioassay-guided fractionation yielded two new guaiane sesquiterpenes, englerins A, englerins B.[53] With GI50 values ranging from 1-87nM, englerin A exhibits 1000-fold selectivity against six out of eight cell lines that are associated with renal cancer. Using spectroscopy, their relative stereochemistry was determined.[54]

Cytotoxicity- Englerin A (EA) have a rapid and potent cytotoxic effect on many types of cancer cell which is mediated by plasma membrane ion channels containing transient receptor potential canonical 4 protein [55]. Because these channels have Ca2+-permeable, it had initially thought that the cytotoxicity arose as a consequence of Ca2+ overload.[56] Here we showed that this is not the case and that the effect of -EA is mediated by a heteromeric of TRPC1 and TRPC4 proteins.[57] Both TRPC1 and TRPC4 were required for EA cytotoxicity; however, although TRPC4 was necessary for the EA-evoked Ca2+ elevation, TRPC1 was not.[58-59]

Pharmacology activity of the other species of Phyllanthus

Phyllanthus niruri- Perennial tropical plant Phyllanthus niruri has been used in traditional medicine of South and Southeast Asia for a variety of ailments, including but not limited to dyspepsia, jaundice, renal stones, diarrhoea, and genitourinary infections. In Brazil, where the plant is known as ‘Chanca Piedra’ or ‘stone breaker’, preparations of P. niruri are considered folk remedies for renal and vesicular calculi.[60]

1. Antioxidant hepatoprotective activity: P. niruri may have a high concentration of antioxidative tannins, flavonoids, terpenes, and lignans, which contribute to its antioxidant hepatoprotective effect. One of the earliest in-vitro studies on the antioxidative hepatoprotective role of P. niruri demonstrated that hexane extract of P. niruri contained lignans such as phyllanthin and hypophyllanthin, which protected rat hepatocytes against carbon tetrachloride and galactosamine-induced hepatotoxicity.[61] Similar results were also replicated in a study involving IDDM and NIDDM rats administered with ethanolic extracts of P. niruri.[62] Hence, P. niruri may alleviate lipoprotein metabolism abnormalities, reduce cholesterol–phospholipid ratios, control the bio membrane damaged and decrease ROS-linked lipid peroxidation.[63-64]

2. Antidiabetic hypoglycaemic action: Phyllanthus niruri are demonstrated dose-dependent improvements in fasting blood sugar, improved the glucose tolerance and restoration of pancreatic tissue architecture, which can be due to inhibition of enzymatic pathways in intestinal carbohydrate digestion and glucose storage.[65-67] Despite these findings, the antidiabetic activity of Phyllanthus remains uncertain with varying results from different members of the genus.[68]

3. Anti-inflammatory: Antinociceptive and analgesic activity: Research on Phyllanthus niruri's anti-inflammatory, antinociceptive, and analgesic properties has mostly focused on animal models. Five distinct pain models may exhibit antinociceptive responses to an intraperitoneal injection of Phyllanthus niruri's dried callus tissue methanol extract, indicating the plant may have analgesic qualities. The mode of action is still up for discussion, though. As of right now, no molecular research has been done on how P. niruri extracts affect pain pathways Obidike.[69] However, other rat studies suggest that the hydroalcoholic[70-72] and spray-dried standardized.[73]

Phyllanthus urinaria- Phyllanthus urinaria (P. urinaria), commonly called chamber bitter, is an herb species in the family Euphorbiaceae.[74-75] The entire plant has therapeutic properties. As a natural product, P. urinaria have long been used in traditional oriental medicine to promote the healthy elimination of gallstones and kidney stones, as an immune system inducer, and for liver disease treatment.[76-77]
1. **Anti-diabetic effects** - Diabetes mellitus (DM) is a prevalent illness among the human population. The ethno-medicinal plant P. urinaria has been used as herbal antidiabetic remedies in Vietnam, and Trinidad and Tobago.\[78-79\]. PUE may exert hypoglycaemic effects by enhancing glucose metabolism and/ or suppressing glucose absorption in the gut.\[80\]

2. **Anti-oxidative activities** - Studies have shown that P. urinaria has potential antioxidant agents \[81-83\]. By dampening oxidative stress, this plant may serve as an alternative source of medicine for steatohepatitis alleviation \[84\], skin disorder treatment \[85\], skin aging amelioration \[86\], protection against DOX cardiotoxicity \[87-88\], and modulation of phagocyte associated innate immune response.\[89\]

3. **Hepatoprotective effects** - Phyllanthus species are well known for their hepatoprotective activities.\[90-91\]. In an animal model of CCl4-induced acute liver damage, P urinaria significantly reduces the ALT, inhibits increases membrane mobility, oxidative stress and decreases liver infiltration and focal necrosis.\[92\]

**CONCLUSION**

A thorough summary of a few chosen scientific papers involving the plant *Phyllanthus Engleri* is given in this review. Due to the plants' widespread application in complementary and traditional medicine to treat a wide range of illnesses, numerous scientific research has been conducted, many of which involve animal models. As concluded, the current review shows that *Phyllanthus Engleri* extracts have pharmacological potential under a wide range of situations. *Phyllanthus Engleri* appears to have been studied extensively for its anti-inflammatory, analgesic, anti-cancer, renal cancer, and cytotoxic effects \[93\] among other disorders.\[93\]

It is possible that the crude extracts employed in this research contained a variety of bioactive chemicals, which would account for the good results observed in the evaluated publications. Most people agree that crude extracts contain a variety of bioactive substances, each of which has a unique ability to affect bodily tissues. The majority of investigations, however, focused on the activity of methanolic and aqueous crude extracts; very few evaluated the pharmacological potential of these bioactive substances.\[95-96\]

Because researchers cannot distinguish between the effects of a single bioactive molecule and the synergy between several bioactive compounds, crude extracts used in therapeutic research have low translational utility. This has further bearing on the extraction procedure. It is well recognized that using solvents with varying polarities and various extraction techniques produce distinct bioactive chemicals, which restricts our ability to compare study results. During the course of our research, we found that study protocols varied significantly and that there were occasionally contradictory results. These findings raise the possibility that certain studies may not have produced data that could be repeated. Furthermore, some studies' lack of information makes it impossible to repeat them and conduct an impartial evaluation of the plant's therapeutic potential. It is crucial that authors give a thorough description of the experimental design and the protocol when evaluating the pharmacological potential of novel therapeutic agents in order to ensure appropriate standardization of materials and techniques. Some studies in this review don't seem to address this requirement.

**Conflicts of Interest**: The authors declare that there are no conflicts of interest.

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