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A Review over Pharmacognostic study and Pharmacological study over Phyllanthusniruri.

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ABSTRACT --
This review discusses the medicinal plant Phyllanthus niruri Linn. (Euphorbiaceae), its wide variety of phytochemicals and their pharmacological properties. Phytochemical screening of such plants is of high importance to establish the claims of medicinal uses by traditional and folkmedicine practitioners. The phytochemical screening reveals the presence of potent bioactive compounds that can be effectively used for the preparation of better herbal drugs. The study aims at determining the potent bioactive compounds present in the leaf extract of Phyllanthus niruri L. The active phytochemicals, flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarins and saponins, have been identified from various parts of Phyllanthus niruri. Extracts ofthis herb have been proven to have therapeutic effects in many clinical studies. Some of the most intriguing therapeutic properties include anti-ulcer, anti-hepatotoxic, anti-lithic, anti-hypertensive,anti-HIV and anti-hepatitis B.
This review summarized the pharmacognostic characters in a simple form with high specification hence the present investigations performed. In the present study evaluation of various pharmacognostical parameters such as macroscopic, microscopy, physicochemical and in detail phytochemical studies of the Phyllanthus niruri performed.
The extracts of Phyllanthus niruri have a wide range of pharmacological activities like anti-ulcer and gastric-ulcer, antimicrobial, antiviral, hepato protective, antioxidant, anticancer, anti-inflammatory, antiplasmodial and diuretic. This review summarizes the information about its botanical, morphological, ethanobotanical, pharmacological and biological activities of the plant.

Keywords : Phyllanthus niruri , pharmacognostic, phytochemical, macroscopic, microscopy, physicochemical, pharmacological action, antiviral, antibacterial, anti-plasmodial, anti-malarial, antimicrobial, anticancer, anti-diabetic, hypolipidemic, anti-oxidant,

I. INTRODUCTION

Chanka piedra (Phyllanthus niruri Linnaus.,Euphorbiaceae), is sparsely spread throughout the tropical and subtropical countries of the world. This is an annual herb and widely spread in coastal areas of India. It is used in the Indian ayurvedic systems from the ancient times (more than 2000 years), It is having very short life. P.niruri is a field weed and its genus Phyllanthus comprises of 550-750 species with minor distinguishing features among them. In Indian ayurvedic system Phyllanthus niruri plant extract is used as a medicine and is recommended for Bronchitis, Anaemia, Leprosy, Asthma, Urinary disorders etc., In Chraka Samhita book Phyllanthus niruri is used in effective treatment of asthma, stimulating liver, improving digestion, increase apetite and produce laxative effects. Maharshi Charaka has categorized it as Kasahara: alleviates cough, Swasahara: relieves asthma, mootrarogahara: cures urinary disorders, Kaphapittahara: relieves the kaphapitta dosha, Kaamalaahara: cures jaundice, and Bhava prakasa Nighantu: cures cough and blood disorders. It is bitter in taste but sweet in the post digestive effect (vipaka) and it is also used as astringent. Phyllanthus niruri have shown a wide spectrum of pharmacological activities including antiviral, antibacterial, anti-plasmodial, antimalarial, antimicrobial, anticancer ,antidiabetic, hypolipidemic, antioxidant, hepatoprotective, nephroprotective, and diurectic properties. A number of preclinical and clinical studies have confirmed the medicinal properties ofvarious Phyllanthus niruri species that have been mentioned in traditional system of medicine[1-5]. However, there is no specific and detailed review of .Phyllanthus niruri To providescientific proof for Phyllanthus niruri ethno pharmacological and traditional uses, recent scientific studies focus on

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its chemical constituents and their biological properties. Therefore, this review provides information about .Phyllanthus niruri including comprehensive information about the traditionaluse of Phyllanthus niruri, its phytochemicals and their biological activities. It also includes biological studies both in vitro and in vivo on various extracts of .Phyllanthus niruri analysis of pure compounds and clinical trial information.

Ethnobotany

Phyllanthus niruri has extensive medicinal properties and has long history in the health care system of tropical countries. The plant is known in traditional health care systems. . Phyllanthus niruri is commonly known as"Chanca pedra" (or) "stone breaker". However there is a lot of confusion about thisspecies Identification. Phyllanthus niruri is used as a folk medicine for treating kidney stones, gallbladder stones, liver related diseases such as liver cancer & jaundice, apart from these it is also administered for diuretic, hypoglycemic and hypertension cases and it also shows anti inflammatory, anti tumor, anti-nociceptive and anti oxidant properties[6.]

Botanical Description and Vernacular Names

Phyllanthus niruri is an erect annual herb, growing 40 - 70cm height having ascending herbaceous branching; it is quite glabrous and branching at the base. The genus Phyllanthus means "leaf and flower" because the flower and fruit can be associated with the leaf. It is a plumose leaf that carries flower and fruit[7].

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

Flowers : The flowers are yellowish, small, numerous, axillary. These are unisexual, monoecious flowers, male flowers having 1-3 sessile stamens and female flowers were solitary in nature.

Fruits : Fruit is a capsule, very small, depressed globose and more over capsule is smooth, 2- 3mm in diameter,

Botanical classification: Phyllanthus niruri L. Kingdom – Plantae Division – MagnoliophytaClass – Magnoliopsida Order – Euphorbiales Family – Euphorbiaceae Genus – Phyllanthus Species – Niruri

Vernacular names: In India

Assamese: Holpholi;
Hindi: **Bhumi amla**, Chalmeri, Harfarauri,English : Gale of the wind
Telugu: Ratsavusirike, Nela Usiri,Tamil: Arunelli, Keela Nelli, Marathi: Rayavali, Bhuiavli,
Sanskrit: Amala, Bhumyamlaki, Sukshmadala, Vitunika, Bhoodatri

Phytochemical

Properties: Phytochemistry is regarded as the heart of herbal therapy and the phytochemical research plays an importantrole in the development of green medicines, which are safer to use (**Table 1**). The major class of bioactive compounds like alkaloids,

Stem : It is having horizontal branches and height of30-60cm, 1-2.5mm width.

Root : It is somewhat branched and large.

flavonoids, lignans, phenols, tannins, terpenes and volatile oils has been isolated. These bioactive compounds further include their respective phytoconstituents

Table 1; Phytochemicals present in Phyllanthus niruri [15-29]

S. NO.	Secondary Metabolite	Structural Definition	Some ImportantPhytochemicals	References
1.	Alkaloids	Alkaloids are a group of naturally occurring nitrogenous organic compounds of plant origin.	Securinine, nor-securinine, epibubbialine,isobubbialine, dihydrosecurinine.	8, 9

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2.	Flavonoids	Flavonoids are polyphenolic molecules containing 15 carbon atoms and are soluble in water.	Quercetin, kaempferol, astragalin, quercetin-3- O-glucoside, quercitrin.	10. 11, 12, 13.
3.	Tannins	Tannin is a polyphenolic biomolecule that binds to precipitate proteins and various other organic compounds like amino acids and alkaloids.	Amarulone, geraniin, amariin, furosin, corilagin, melatonin, phyllanthusin D.	14, 15.
4.	Lignans	Plant lignans are also polyphenolic compounds derived from phenylalanine via dimerization of substituted cinnamic alcohols.	Phyllanthin,hypo- phyllanthin,5-dimethoxy- niranthin, nirtetralin, phyltetralin, hinokinin, 4- (3,4-diethoxyphenyl)-1-7 methoxybenzo[1,3] dioxol-5-yl)-2,3-bismethoxy methyl-butan-1-ol	16, 17, 18
5.	Sterols	Phytosterols, which encompass plant sterols and stanols, are phytosteroid similar to cholesterol which occur in plants and vary only in carbon side chains and/or presence or absence of a double bond.	Amarosterol A,Amarosterol B.	19
6.	Triterpenes	Triterpenes are a class of chemical compounds having three terpene units with the molecular formula C30H48 or consists of six isoprene units.	Phenazine and phenazine derivatives, 2Z, 6Z, 10Z, 14E, 18E, 22E-farnesyl farnesol.	20, 21,

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7.	VolatileOils	A volatile oil is a concentrated hydrophobic liquid containing volatile aroma compounds from plants.	Linalool, Phytol.	22

Pharmacognostic studies

Morphologic study of Phyllanthus species - Morphological study carried out as per the reported methods. Organoleptic evaluation wan done by means of sense organs, which provide the simplest as well as quickest means to establish the identity and purity to ensure quality of a particular drug. Organoleptic characters such as shape, size, colour, leaf structure like margin, apex, base surface, venation and inflorescence were evaluated.[23-24]

Microscopic study of Phyllanthus species - For the microscopic studies, the dried plant materials [root and stem] boiled for 10-15 minutes in distilled water to become soft and then the transverse section obtained. The leaves were soaked in normal water for two hours. For microscopic studies, freehand transverse sections of root, stem and leaf taken. The staining and mounting of the sections performed following usual procedures of plant micro techniques. The sections of the plant materials stained mainly by phloroglucinol and HCL and mounted with help of few drops of glycerine.[25]

3. **Physico-chemical analysis** - Physico-chemical values such as the percentage of total ash, acid- insoluble ash, water-soluble ash as well as water soluble and alcohol soluble extractives were calculated as per the standard procedures and were in accordance with procedures mentioned in Indian Pharmacopoeia.[26]

Determination of total ash: Five grams of the ground plant material was taken in a silica crucible previously ignited and weighed. The ground plant material was then spread in a fine even layer on the bottom of the crucible. It was then incinerated in a muffle furnace by gradually increasing the heat not exceeding dull red heat until free from carbon and then cooled and weighed. If a carbon free ash could not be obtained in this way, the charred mass was exhausted with hot water. The residue was collected on an ashless filter paper which was then incinerated. The ash percentage was calculated with reference to the air dried material [27]

Where, w1 = weight of crucible (g); w2 = weight of crucible with the ash (g); w = weight of dried sample (g) **Determination of Water Soluble Ash:** 100 mg of ash was boiled for five minutes with 10 ml of distilled water. The insoluble matter was collected in a silica crucible or on an ash less filter paper. It was washed with hot water and then ignited to constant weight at low temperatures. The weight of the insoluble matter was subtracted from the weight of the ash. The percentage of water soluble ash was calculated with reference to the amount of ash taken .

Determination of Acid Insoluble Ash: The total ash was boiled for five minutes with 25 ml of 10% HCl. The insoluble ash was collected in a silica crucible or on an ash less filter paper. It was washed with hot water and then ignited and weighed. The weight of the insoluble matter was subtracted from the weight of ash. The difference in weight represents the acid insoluble ash. The percentage of acid insoluble ash was calculated with reference to the amount of ash taken.

Determination of extractive value with different solvents: Estimation of extractive value was done according to the method of A known quantity of powdered drug was taken. Extraction was made in soxhlet apparatus with different solvents i.e. petroleum ether, ethyl acetate, benzene, methyl alcohol, chloroform and ethyl alcohol. The extract was filtered and the solvent was evaporated, accurate weight of the extract was taken. The percentage (%) was calculated with reference to air dried drug[28]

1. **Morphologic characters**- Phyllanthus niruri is an herb that grows up to 10-75 cm high and is erect.

Stem and secondary branches: Stem is cylindrical with 2 to 3 mm in diameter. Internodes are 5 to 15 mm in length, branching from the base. Each branch is 4 to 5 cm in length. Longitudinally ridged at places; fracture is short, fractured surface is hollow in the centre; main stem branches from the base bears 4 to 5 cm long deciduous branches which are about 1 mm in diameter having scarious lanceolate small stipules at the base and 8 to 12 more pairs of leaves on either side. Fruits, flowers and leaves get detached on drying and then branches appear like rachis of unipinnate compound leaf.

Leaves: They are simple, alternate, distichous, arranged very closely, obovate to oblong. They are lanceolate 4- to 9 mm in length and 3 to 4 mm in width. Leafs are shortly petiolate or subsessile,

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obtuse, entire, glabrous, reticulate, pinnate, lateral veins less conspicuous on the upper surface.

Flowers: They are small, unisexual axillary, solitary or in clusters. There 3 united stamens with 5 sepals.

Fruits: They are tricarpellary globose capsule, 3 to 5 mm in diameter, pedicel is short, fruiting perianth is acute. 6 seeds are present in a fruit and are trigonous.

Microscopic characters - The observations of the studied microscopic characters compiled in a comparative manner with respect to three important parts of the plant viz. root, stem and leaf.

a) **Root** - The TS of root shows epidermis a single layer of thin walled cells. The cortex region with 6-8 layers of parenchymatous cells without intercellular spaces. The inner cortex consists of patches of macrosclereids. The vascular cylinder consisting of 5-8 layers secondary phloem cambium and25- 40 layers of secondary xylem along with fibers (pits rare, bordered; ends tapering; wall tetra-to hexagonal), vessel members (long with tails at both ends, pits circular, bordered; perforation plate simple). The xylem parenchyma is thin-walled with uniseriate rays, 3-8 cells high, usually heterogenous type while the pith is parenchymatous.

b) **Stem** - The TS of the stem is circular in outline and shows central pith occupying the major area of the section, encircled by continuous band of xylem and a ring of discontinuous periclyclic fibers, narrow parenchymatous cortex, a layer of epidermis and collenchymatous narrow hypodermis. The detailed TS at 40x shows a layer of epidermis, embedded with stomata, at places bearing papilla and covered with thick cuticle, a narrow band of chlorenchymatous hypodermis lies underneath this followed by 2 to 3 rows of chlorenchymatous cortex, pericycle is characterized by discontinuous ring of groups of thin walled fibers. Phloem is narrow, parenchymatous, cambium is distinct, xylem consists of radial rows of vessels tracheids, thinwalled fibres, parenchyma and uniserate to biseriate medullary rays; pith is wide and parenchymatous; cells getting disintegrated on drying developing cavity in the centre, cluster and rosette crystals of calcium oxalate throughout the parenchymatous cells of the cortex and the pith.

c) **Leaf-** The transverse section of the leaf passing through midrib is slightly elevated on the lower side and flat on the upper side. It shows layer of upper epidermis, its cells being bigger in size than the lower one and cover with thin cuticle. At places it is papillose and embedded with stomata, underneath the upper epidermis lies a layer of palisade in continuation with the midrib. Meristele of the midrib consists of radiate xylem and an arcof phloem; underneath the palisade layer of lamina lie 2 to 4 rows of spongy parenchyma traversed with obliquely cut vascular bundles and prismatic and rosette crystals of calcium oxalate.

Medicinal uses:

1) Phyllanthus has been used in Ayurvedic medicine for over 2,000 years and has awide number of traditional uses.
2) This includes employing the whole plant for

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jaundice, gonorrhea, frequentmenstruation and diabetes and using it topically as a poultice for skin ulcers, sores, swelling and itchiness.

3) The plant is bitter, astringent, cooling, diuretic, stomachic, febrifuge and antiseptic. It is useful in dropsy, jaundice, diarrhoea, dysentery, intermittent fevers, diseases of urino- genital system, scabies ulcers and wounds.
4) The young shoots of the plant are administered in the form of an infusion for the treatment of chronic dysentery. Its efficacy in the field of gastro intestinal disorders like dyspepsia, colic, diarrhoea, constipation and dysentery is undisputed.
5) In females it is used as a galactogogue, in leucorrhoea, menorrhagia and mammary abscess.
6) In skin conditions, especially scabby or crusty lesions, bruises, wounds, scabies, offensive ulcers and sores, oedematous swellings, tubercular ulcers and ringworm, it has been utilized with good effect since many years.

It is applied effectively in intermittent fevers and gonorrhoea as well as in ophthalmia and conjunctivitis[29].

Traditional uses:

1. For jaundice: The whole plant juice with 10-20ml of dose is recommended three times daily.
2. The fresh roots (10gms) powder is mixed with fresh milk. This is recommended to take in the early mornings for effective cure forjaundice.
3. The leaves were crushed with salt andapplied for skin diseases.
4. The plant decoction was very effective for diabetes and chest pain.
5. The decoction of leaves or roots is usedfor ulcers.
6. The dried powder of the plant mixed with gruel water is applied over ulcers and wounds.
7. The juice of whole plant can be taken as a dose of 45-50 ml in the early morning for leucorrhea, gonorrhea, menorrhea and other urinary complains[30]

Pharmacology Studies ;-

Anti-oxidant or Gastrointestinal protective - There is concerning the involvement of reactive oxygen species in different gastrointestinal (GI) diseases. Although a number of synthetic agents in treating diverse GI disease are available, use of herbal medicine has received increasing consideration due to their low side effects, and proven curative/preventive benefits. In-take of herbs, vegetables, and fruits with high level of antioxidant is found to be inversely associated with the risk of several chronic diseases.

Numerous medicinal herbs and phytochemicals have been investigated as complementary and alternative treatment for GI disease. Herbs are the central component of traditional formulations available around the world to cure oxidative stress-induced GI diseases. Antioxidant activity along with anti- inflammatory effect through the modulation of immune response, alteration of diverse transcription factors, or by reduction of certain cytokine release is considered as a key mechanism by which the

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herbs/phytochemicals confer GI protection. This chapter deals with the different herbs, poly-herbal traditional formulation, and phyto-chemicals in prevention or treatment of GI disorders[31].

Hepatoprotective –

Herbal-based therapeutics have been used for a long time in India for liver disorders, and most of the available drugs are taken from the Indian traditional systems of medicine: Ayurveda, Siddha, and Unani. Preclinical and human studies carried out in the last two decades have conclusively shown that some of the Indian medicinal plants (PICRORHIZA KURROA, MORINDA CITRIFOLIA, Andrographis paniculata, Phyllanthus niruri, and ECLIPTA alba) and the polyherbal formulations (Liv 52, Livergen, Octagen, Stimuliv, Tefroliv) made from these plants are effective as hepatoprotective agents [32] However, most of these agents are medicinal agents and not a part of the regular diet. From a human perspective, it is always desirable to have hepatoprotective agents that are a part of the normal diet so that special attention need not be paid by the recipient toward adhering to the therapeutic/prophylactic regimen. Studies carried out in the recent past suggest that dietary agents such as FOENICULUM VULGARE (fennel), TRIGONELLA FOENUM-GRAECUM (fenugreek), Curcuma longa (turmeric), Garcinia mangostana (mangosteen), Phyllanthus emblica (Indian gooseberry), and Zingiber OFFICINALE are effective as hepatoprotective agents in various models of study Of these, ginger, a common household spice, is arguably the most commonly used and well-studied herb for its hepatoprotective effects[33].

Antidiabetic – hypoglycaemic action - Increased oxidative stress dueto chronic hyperglycaemia is a widely accepted factor in the progression of diabetes and its complications. Animal studies using extracts of Phyllanthus niruri have demonstrated dose-dependent improvements in fasting blood sugar, improved glucose tolerance and restoration of pancreatic tissue architecture, which may be due to inhibition of enzymatic pathways in intestinal carbohydrate digestion and glucose storage.[34-36] It is thought that the bioactive agents of the extract possess insulin-mimicking activity or potentially may stimulate the production of insulin as observed by the extracts ability to improve hepatic glycogen content and increase liver hexokinase activity. Despite these findings, the antidiabetic activity of Phyllanthus remains uncertain with varying results from different members of the genus. Review of existingstudies suggest that the authors have used a variety of methods to induce diabetes, differing extraction method and dosages.This has invariably precluded the direct comparison of studies to ascertain the true functional properties of P. niruri as an antidiabetic agent although it has long been employed as a traditional treatment for alleviation of non-insulin- dependent diabetes.[37]

Anti-inflammatory, antinociceptive and analgesic activity -

Studies on the anti-inflammatory, antinociceptive and analgesic activity of P. niruri have mainly revolved around animal models. Intraperitoneally administered methanol extract of dried callus tissue of P. niruri caused antinociceptive effects on five different models of pain, suggesting that P. niruri possessed analgesic properties. However, the mechanism of action is still debated on. Currently, there are still no molecular studies on the effect of Phyllanthus niruri extracts on pain pathways.[38] deduced that the anti-inflammatory and antinociceptive action of P. niruri was mediated via the peripheral nervous system. In his study on rats, whole plant chloroform extractwas found to inhibit writhing response, reduce yeast-induced pyrexia, alleviate albumin- induced inflammation with an effect comparableto aspirin, increase pain threshold in the Randall–Selitto test but not the hot plate test for thermally induced nociception. Hence, Obidike deduced that Phyllanthus niruri chloroform extract exerted antipyretic, anti-inflammatory and antinociceptive effects " the peripheral nervous system rather than the central nervous system." However, other rat studies suggest that the hydroalcoholic and spray-dried standardized extracts may exert both significant peripheral and central analgesia. Hence, there remains a need for the further study of the effect of P. niruri extracts on major pain pathways to clarify the ambiguity that surrounds its analgesic mechanism[39].

Hypolipidaemic activity -

Studies pertaining to the lipid-lowering activity of P. niruri have all been conducted using rat models. It is interesting to note that no studies using rabbit models have been performed despite that fact that it is widely accepted that rabbits are more reliable hyperlipidaemic models. Additionally, no in-depth in-vitro or molecular

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studies have been conducted to date to elucidate the exact mechanism involves in the activity of lowering lipid levels. However, animal studies provide strong evidence that P. niruri possesses antioxidant-linked hypolipidaemic properties.

Antiviral activity

Perhaps the most prominent among the potential therapeutic effects of Phyllanthus niruri is its antiviral activity. Studies conducted on sera obtained from chronic hepatitis B patients and woodchuck hepatitis (WHV)-infected woodchucks, which were treated with Phyllanthus niruri extracts, showed decreased viral antigen levels. Overall, aqueous extracts of Phyllanthus niruri have been shown to possess significant antiviral potential and appear promising especially with regard to hepatitis B carriers[40].

Clinical studies on hepatitis B patients showed that 50–60 per cent of patients who were administered Phyllanthus niruri extract experienced HBsAg seroconversion. The reduction in HBsAg antigen may have been due to the inhibitory effect of P. niruri on hepatitis B viral genetic replication. Although not all the bioagents responsible for the anti-hepatitis B activity of P. niruri have been identified, molecular studies have determined the molecular structure of a novel lignin found in P. niruri, nirtetralin B and its two stereoisomers, nirtetralin and nirtetralin A. Nirtetralin significantly inhibited HBsAg and HBeAg levels in vitro.[41] All three lignans had a dose-dependent inhibitory effect on the in- vitro titres of HBV antigens. Moreover, inhibition ratios for nirtetralin and nirtetralin B were significant when compared with acyclovir, suggesting that these compounds were promising as novel anti-HBV antivirals. In general, lignans had low cytotoxicity on host cells, suggesting that these compounds could safely be given at non-toxic dosages without incurring undesirable adverse drug reactions[42].To date, no systematic review has been conducted on the anti-hepatitis B activity of P. niruri per However, there have been a number of reviews since the year 2000, on the utility of members of the Phyllanthus genus as potential antiviral agents for chronic hepatitis B infection. One review concluded that Phyllanthus extracts were as effective as interferon in the terms of HBsAg seroconversion. Moreover, the extracts of members of the Phyllanthus genus were more effective than other herbal preparations in eliminating hepatitis B surface antigen from patient sera and in normalizing other hepatic parameters. Phyllanthus extracts also worked more effectively when used in combination with interferon[43].

Antibacterial activity-

With the increase in antibiotic resistance rates and the need for novel antibiotics, which have optimal antimicrobial activity with minimal toxicity, there is renewed interest in exploring phytochemicals from everyday plants. A possible reason for the increased interest in extracting phytochemicals for the development of novel antibiotics is the threat of plant species extinction, hence inciting a need to explore the medicinal potential of these resources before they are lost[44].

P. niruri contains various phytochemicals, which exert antimicrobial and antiprotozoal properties. These include rutin, gallocatechin, prenylated flavanone glycosides, quercetin, quercitrin, p-Cymene, corilagin, diosgenin, Securinine and β-glucogallin. Overall, studies on the antimicrobial activity of P. niruri extracts are still limited to in-vitro models and have not advanced to animal studies as of the time of writing. These studies utilize different types of P. niruri extracts, with one study a comparison of methanolic, ethanolic and aqueous extracts, recognizing that different preparations yielded different compositions of pharmacophores[45].

It was observed that methanol extracts of P. niruri were twice as strong as that of aqueous preparations, with an MIC of approximately one-third that of aqueous extracts. In addition, both aqueous and methanolic extracts of P. niruri demonstrated significant activity against Listeria monocytogenes, the bacteria responsible for listeriosis, suggesting the potential of P. niruri as a food preservative. A subsequent disc diffusion study found that both ethanolic and aqueous extract of P. niruri failed to inhibit the growth of the Gram-negative bacilli but demonstrated statistically more significant inhibitory activity against Gram-positive bacteria[46]. The apparent difference in results between this study and that of Cheah and colleagues in 2011, could be due to the use of varying solvents. This could suggest that the aqueous extracts contained a higher content of phenolic compounds compared with the ethanolic extract.

Agar diffusion assays in a study on Helicobacter pylori and three species of probiotic Lactobacilli revealed.

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That Phyllanthus niruri inhibited H. pylori in a dose-dependent manner while it did not affect the growth of lactic acid bacteria[47]. The addition of proline to H. pylori agar did not reverse the inhibiting activity of P. niruri aqueous extract, suggesting that the anti-H. pylori property of P. niruri did not involve the inhibition of proline dehydrogenase, a membrane-associated protein linked with prokaryotic energy production. The anti-H. pylori activity recorded in this study could be due to ellagitannins such as geraniin and corilagin contained in the aqueous extract, which have also been previously shown to act in a concentration- dependent manner against various antibiotic- resistant H. pylori strains by rapidly precipitating agglutination of H. pylori cells. The lack of activity against lactobacilli implies that the ellagitannins-rich aqueous extract was selective for the targeted pathogen (E. coli) instead of probiotic organisms. In terms of its anticoliform activity, methanolic extracts of Phyllanthus niruri followed by its seeds, displayed greatest inhibition of E. coli activity. Overall, root extracts displayed the weakest antibacterial activity[48]. The optimal bacteriostatic action against E. coli, S. viridans, S. aureus and Phyllanthus aeruginosa observed with methanolic leaf extract could be due to the action of flavonoids.

Methanolic extracts of P. niruri leaves acted directly on the cell wall in a concentration-dependent trend. There is a possibility that certain morphological or molecular features of Gram-positive cell walls are targets of the activeagents of P. niruri methanolic extracts.These binding sites have yet to be identified[49].

Anti-plasmodial and nematicidal properties- In-vivo and in-vitro studies show that Phyllanthus niruri extracts display

II. DISCUSSION AND CONCLUSION-

The present review provides a comprehensive overview of selected scientific studies using the plant P. niruri. The plants' extensive use in traditional and complementary medicine for variety of diseased condition has led to a significant amount of scientific studies particularly using animal models. The positive findings seen in the articles reviewed here is likely due to the fact that there may bemultiple bioactive compounds within crude extracts used in these studies. It is widely accepted that crude extracts are made up of a range of bioactive compounds and each compound may exert differing activity on body tissues. The active phytochemicals, flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarins and saponins, have been antiplasmodial properties. This may be due to the terpene-rich content of P. niruri extracts. Of interest, methanolic extracts displayed chemosuppressive action comparable with chloroquine and demonstrated better prophylactic activity than pyrimethamine. Of note, a study on the nematicidal activity of P. niruri against Meloidogyne incognita and Rotylenchulus reniformis identified two prenylated flavanones as being responsible for the nematicidal activity of P. niruri.[50] identified from various parts of Phyllanthus niruri.

Therapeutic findings using crude extracts havelimited translational value as investigators are unable to determine whether the findings are related to the action of a single bioactive compound or that of synergy between multiple bioactive compounds. This additionally relates to the extraction process used when preparing crude extracts. It is widely known that different extraction methods and use of solvents with different polarity yield different bioactive compounds and as such limits our ability to compare findings between studies. In performing our review, we observed that there was significant heterogeneity in study protocols and in some instances conflicting results, which suggest that some studies may not provide reproducible data. Additionally, the lack of information in some studies prevents our ability to replicate these studies to make an independent assessment of the therapeutic potential of the plant. When assessing pharmacological potential of novel therapeutic agents, it is essential that authors provide a comprehensive account of the experimental design and protocol and ensure proper standardization of material and techniques, an aspect that appears to be lacking in some studies in this review. Thus while the overall findings suggest an abundance of therapeutic potential of P. niruri, such findings must be interpreted with caution. There are still many aspects of research on this herb that need to be considered such as larger sample sizes, toxicological studies, mechanism studies and molecular analyses. Current evidence is largely limited to correlation between identified phytochemicals and their biological activities. There is a lack of mechanisms of action studies to understand the interaction of bioactive phytochemicals from P. niruri and their respective

molecular targets. Essentially, more robust scientific methodologies are necessary before confirmatory decisions can be made on the potential of P. niruri. A key step before clinical trials may be considered.

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