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Danladi S

Department of Pharmaceutical & Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Bayero University, Kano, Nigeria

Idris MA

Department of Pharmacognosy & Herbal Medicine, Faculty of Pharmaceutical Sciences, Bayero University, Kano, Nigeria

Umar II

Department of Clinical Pharmacy & Clinical Practice, Faculty of Pharmaceutical Sciences, Bayero University, Kano, Nigeria

Correspondence:

Danladi S

Department of Pharmaceutical & Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Bayero University, Kano, Nigeria
Email: danladisuleimen[at]gmail.com

Review on pharmacological activities and phytochemical constituents of *Phyllanthus niruri* (Amarus)

Danladi S*, Idris MA, Umar II

ABSTRACT

Phyllanthus amarus Schum and Thonn (*Euphobiaceae*); is found in tropical and sub-tropical region of the world. It grows as a weed in moist abandoned land. It has various applications in tradition and folk medicine for treatment of various diseases such as hepatitis, cough, diuretic, menstruation problem and dysentery. It is commonly used by many countries across the world. Scientific investigation revealed that *Phyllanthus amarus* has potent activity against various diseases such as hepatitis B, HIV, microbial infections, plasmodiasis, nematode infestation, lithiasis, hyperlipidemia, diabetes, hyperuricemia, nephrotoxicity, platelet aggregation, radiation exposure, algisia, unwanted pregnancy, vasoconstriction, hepatotoxicity and biological oxidation.

Phyllanthus amarus contains several phytochemical constituents such as alkaloid, flavonoid, terpenoids, cardiac glycoside, saponins, tannins, cyanogenic glycosides while proximate analysis showed that it contained high carbohydrate and fibre content.

Several important chemical compounds were isolated from *Phyllanthus amarus* such as phyllanthin, hypophyllanthin, Niranthin, Nirtetralin, phyltetralin phyllangin, nirphyllin, phyllnirurin and corilagin. Study showed that these compounds are responsible for several pharmacological activities.

Keywords: *Phyllanthus amarus*, activity, disease, constituents.

INTRODUCTION

Phyllanthus niruri also known as *Phyllanthus amarus* Schum and Thonn, is known as Dukung anak in Malaysia, Iyin Olobe by the Yoruba tribe in Nigeria. It is a member of *Euphobiaceae* family. The origin of *Phyllanthus amarus* is tropical America; from there it spread as a weed to other tropic and sub-tropics. It is a tropical annual herb shrub which grows as weed in moist humid waste land^[1, 2]. *P. niruri* is among more than 500 *Phyllanthus* species that are widely spread in temperate and tropical climates region^[3]. It grows 30 - 40 cm in height, has small leaves and yellow flowers; the stem has green capsule, and blooms with flowers with 5 white sepals and apical acute anther. The fruit has green capsules, and smooth and fruiting pedicels while seeds are longitudinally rugose^[4]. It is found throughout the tropics and sub-tropics such as West Africa (including Nigeria and Ghana), Europe, Asia (including China, Pakistan, India and Malaysia Indian Ocean), central and south America as medicinal plant for the treatment of various diseases^[5, 6, 7, 8, 9]. The plant has been used for a long period of time (thousands of years) in Ayurvedic traditional medicine for various illnesses^[10]. In India, *Phyllanthus niruri* is one of the most important traditional medicines used for the treatment of jaundice, asthma, hepatitis and urolithic disease^[11].

Traditional Use of *Phyllanthus niruri*

The aerial part of *Phyllanthus niruri* has been used by many countries in folk medicine for treatment of various disease conditions such as increase libido or fertility in men. In India, the plant is usually used by traditional medicine practitioners for the treatment of asthma, bronchial infection, liver diseases, diabetes, gonorrhoea, inducing labour and treatment of oedema, feverish pain, sore throat, female sterility, oliguria and vaginitis. They also used the plant to manage irregular menstruation, tachycardia, dysentery, spasmodic cough, itchiness, arthritis, otitis, swelling, skin ulcer and weakness of male organ^[4, 12, 13]. In Brazil, the tea of *Phyllanthus niruri* is used to treat renal calculi^[14]. In South Africa, it is used in folk medicine to treat hyperuricemia^[15]. Aqueous extract of *P. amarus* has application in Nigerian homes for elimination of waste from the body. It is also used to restore liver activity, blood tonic and enhance body defence system^[16]. In Thailand, *Phyllanthus amarus* is used in traditional medicine as

antipyretic, a diuretic, to treat liver diseases and viral infections [17].

Phyllanthus amarus has various pharmacological activities against various diseases, and it contains important phytochemical constituents that have been studied and proven to be effective and valuable therapeutic compounds. This study aims to review the studies conducted on various activities of *Phyllanthus amarus*.

Pharmacological activities of *Phyllanthus amarus*

Antidiabetic activity

Ethanol extract of *Phyllanthus niruri* was found to have significant antidiabetic activity in insulin-dependent diabetes mellitus rat, but showed no effect on non-insulin-dependent diabetes mellitus rat [18]. Additionally, the ethanol extract was found to lower lipid profiles (decrease in plasma cholesterol, triglycerides, Low density lipoprotein cholesterol, very low density lipoprotein cholesterol and atherogenic index, while there is increase in high-density lipoprotein cholesterol) in both insulin-dependent diabetes mellitus and non-insulin-dependent diabetes mellitus animals [18]. Concordantly, a one week study carried out on non-insulin dependent diabetic patients using aqueous extract of aerial parts of *Phyllanthus amarus* showed that, it is not effective in lowering both fasting blood glucose and postprandial blood glucose level in untreated non-insulin dependent diabetic patients [19]. Aqueous extract of *Phyllanthus niruri* demonstrated significant hypoglycemic activity in streptozotocin-induced diabetic rats [20]. Relatedly, the methanol extract of the plant has also been found to reduce blood sugar level in alloxan-induced diabetic rats [21].

Hyperlipidemic activity

Scientific studies have shown that *Phyllanthus niruri* has antihyperlipidemic effect. It was also reported that the aqueous extract exhibited antihyperlipidemic activity [20]. Hydro-alcoholic extract of leaves of *Phyllanthus amarus* was also found to have antihyperlipidemic potential in hyperlipidemic rats [22]. Additionally, phyllanthrin which is a bioactive compound of *Phyllanthus niruri* was administered for twelve weeks to mice co-fed with High Fat Diet (HFD); there was protection against HFD induced weight gain and adiposity, reduced mRNA expression of adipogenic genes and increased expression of lipolytic genes in white adipose tissue, reduced liver triglyceride accumulation, restoration of HFD induced serum lipid disturbances as well as reduced serum triglycerides and free fatty acids in HFD fed mice [23]. The lipid-lowering activity of *Phyllanthus niruri* was found to be mediated through inhibition of hepatic cholesterol biosynthesis, enhanced catabolism of LDL, increased faecal bile acids excretion and activation of LCAT and tissue lipases [24].

Hyperuricemic effect

It was reported that the methanol extract of the leaves of *Phyllanthus niruri* exhibited anti hyperuricemic activity in hyperuricemic rats. Lignans isolated from *Phyllanthus niruri* (Phyllanthin, hypophyllanthin, phylltetralin and niranthin) were also found to increase the urinary excretion of uric acid in hyperuricemic rat. Therefore, the uricosuric effect of this plant may be the attributed mechanism of anti hyperuricemic action [25].

Lithiasis

Phyllanthus niruri has shown inhibitory effect against calcium oxalate crystal growth and aggregation in human urine. This medicinal plant exhibited antiurolithic activity in both *in vitro* and *in vivo* studies [6]. The aqueous extract of *Phyllanthus niruri* inhibits the growth of the matrix calculus as well as decrease the number of stone satellites in Wistar rats [26]. Oral administration of *Phyllanthus niruri* extract by calcium stone forming patients reduced urinary calcium in hypercalciuric patients [27].

Nephroprotective effect of *Phyllanthus amarus*

The aqueous extract of *Phyllanthus amarus* at doses of 200 mg and 400 mg/kg/day for 14 days, were found to protect against the nephrotoxic effect of paracetamol and gentamicin in rat, by maintaining the level of blood urea nitrogen and serum creatinine within the normal range compared to control group [1]. In another study, the ethanol extract of the leaves of the plant was investigated for its nephroprotective activity against gentamicin induced nephrotoxicity in rats. Co-administration of the extract with gentamicin prevented kidney and improved all nephrotoxic parameters (physical, urinary and blood) observed [28]. The extracts of *Phyllanthus amarus* prepared by dissolving the leaves in olive oil for fourteen and seven days were tested for their ability to protect the kidney against cisplatin induced nephrotoxicity. The study revealed significant decrease ($p < 0.05$) in plasma concentrations of K^+ , Cl^- , creatinine and urea in extract treated groups when compared to negative control (Cisplatin-treated only) value and significant increase ($p < 0.05$) in plasma concentrations of Na^+ and HCO_3^- when compared to negative control value [29].

Antiplasmodial activity

Ethanol extract of *Phyllanthus niruri* was found to have potential anti plasmodial activity *in vitro* by inhibition of the developmental stage of trophozoite to schizonts [7]. Similar *in vitro* study also showed that the callus extract and intact *Phyllanthus niruri* extract inhibited the development of trophozoites to schizonts (developmental stage of *Plasmodium falciparum*) in a dose-dependent manner. The anti plasmodial activity of extract of *Phyllanthus niruri* (whole plant) exhibited a higher anti plasmodial activity than all calli and intact fresh apical stem extracts [30]. It was reported that the water extraction of *Phyllanthus niruri* gives better results of antiplasmodial activities than ethanolic extraction and only leaves and stems parts of the plant were active *in vitro* against plasmodium [31]. 1-O-galloyl-6-O-luteoyl-R-D-glucose isolated from the *Phyllanthus niruri* was found to have inhibitory effect against Chloroquine-susceptible *P. falciparum* strain *in vitro* [32]. Chloroform/ethanol extract of *Phyllanthus niruri* showed significant inhibition of *P. falciparum* growth at different concentrations [33].

Antinematodal activity

Two compounds isolated from *Phyllanthus amarus*, 8-(3-methyl-but-2-enyl)-2-phenyl chroman-4-one and 2-(4-hydroxyphenyl)-8-(3-methyl-but-2-enyl)-chroman-4-one were found to have antinematodal activity against *Meloidogyne incognita* and *Rotelenchulus reniformis* [34].

Antibacterial activity

Phyllanthus amarus has broad spectrum antibacterial activity on both gram positive and gram negative bacteria. A study carried out on different bacterial isolates; *Bacillus stearothermophilus*, *Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus leuteus*, *Salmonella typhi*, *Enterobacter aerogens*, *Proteus mirabilis*, and *Proteus vulgaris* revealed that *P. amarus* showed the least MIC on all bacteria tested [35]. Similarly, the methanolic extract of *Phyllanthus amarus* was found to have potent inhibitory effect against drug-resistant pathogenic gram-negative bacteria; *Shigella spp.*, *E. coli*, *V. cholerae*, *S. aureus*, *S. typhimurium*, *P. aeruginosa*, *B. subtilis*, *Klebsiella* and *Streptococcus sp.* in a dose-dependent manner [36].

Hepatoprotective effect

The Protein isolate of *Phyllanthus niruri* indicates hepatoprotective effect against acetaminophen-induced toxicity [37]. Another study also showed that the aqueous extract of *Phyllanthus niruri* inhibited paracetamol induced hepatotoxicity in mice [38]. Similarly, fishes pretreated with *Phyllanthus niruri* extract were protected against paracetamol-induced hepatotoxicity when compared to control [39]. It was also reported that a protein isolated from *Phyllanthus niruri* protects against oxidative damage of hepatocytes induced by carbon tetrachloride [40]. Both aqueous and methanol extracts of *Phyllanthus niruri* have been demonstrated to possess hepatoprotective effect [41]. The extract of *Phyllanthus amarus* was also found to increase hepatic cell function [16]. Similarly, another study reported the hepatoprotective effect of *Phyllanthus amarus* in ethanol-induced hepatotoxicity and the effect was comparable to standard hepatoprotective drug silymarin. The hepatoprotective effect of the extract was associated with its antioxidant activity [42]. *Phyllanthus amarus* extract and phyllanthin isolated from the aerial part of the plant were found to protect the human hepatoma HepG2 Cell line against carbon tetrachloride induced hepatotoxicity. Phyllanthin demonstrated the hepatoprotective effect at a lower dose compared to *Phyllanthus amarus* extract and the effect was in a dose-dependent manner [43]. Combination of ethanolic extract of *Phyllanthus amarus* and silymarin gives synergistic hepatoprotective activity against carbon tetrachloride-induced hepatotoxicity. The effect was associated with higher concentration of phyllanthin. A combination of silymarin with ethanol extract provided higher hepatoprotective activity than when combined with aqueous extract [44].

Effect on Viral Infections

It was reported that the extract of *Phyllanthus amarus* in an *in vitro* study inhibited DNA polymerase in Hepatitis B virus (HBV) and Woodchuck hepatitis virus (WHV). Also, *in vivo* study shows that the extract of *Phyllanthus amarus* has effect against Hepatitis B virus in infected human [45]. Another study revealed that the extract blocked enzymes that play an important role in the reproduction of hepatitis B virus [46]. Oral administration of *Phyllanthus amarus* was found to decrease the mortality rate and significantly increase the survival of hepatocellular carcinoma harboring animals [47]. It was also reported that an aqueous extract of *Phyllanthus niruri* inhibits endogenous DNA polymerase of hepatitis B virus and binds to the surface antigen of hepatitis B virus *in vitro*. The extract also inhibits woodchuck hepatitis virus DNA polymerase and binds to the surface antigen of WHV *in vitro* [48].

It was reported that the alkaloidal extract of *Phyllanthus niruri* inhibited the growth of both HIV-1 and HIV-2 strains cultured on human MT-4 cells [46]. Similarly, the water alcoholic extract of *Phyllanthus amarus* was found to be a potent inhibitor of HIV-1 replication in HeLaCD4+ and also inhibited the RT inhibitor-resistant HIV strains. The inhibitory effect of *Phyllanthus amarus* against HIV strain was both *in vitro* and *in vivo* [49, 50]. Niruriside, a novel compound isolated from *Phyllanthus niruri* exhibited anti-HIV activity. It was found to exert inhibitory effect against the binding of REV protein to RRE RNA with an IC₅₀ value of 3.3 μM [51].

Effect on Reproductive system

Methanol extracts of the leaves of *Phyllanthus amarus* lead to a decrease in sperm motility and count of male guinea pigs in a dose-dependent manner. The effect was comparable to the observed effects of Vitamin E on sperm parameters [52].

The ethanolic extract of *Phyllanthus amarus* significantly affected the litter size and weight of Wistar albino rats at birth in a dose-dependent manner [8].

The alcohol extract of a whole plant of *Phyllanthus amarus* was found to show reversible antifertility effect in female mice [53]. Similarly, *Phyllanthus amarus* when given orally to male albino mice induced gradual inhibition of fertility potential with a decline in epididymal sperm profiles. However, the antifertility effect was reversible upon withdrawal of medicinal plant [54].

The methanolic extract of *Phyllanthus amarus* leaves caused significant increase in the level of testosterone of male Guinea pigs in a dose- and time- dependent manner. It also caused changes in the levels of Leutenizing (LH) and Follicle stimulating (FSH) hormones. These changes caused by *Phyllanthus amarus* were comparable to the changes caused by vitamin E on Leutenizing (LH) and Follicle stimulating (FSH) hormones. [4].

Effect on Cardiovascular System

It was reported that methyl brevifolincarboxylate (MB) isolated from the leaves of *Phyllanthus niruri* L. exerted vasorelaxant effect on the aortic rings of rat. It also antagonised the vasoconstriction effect of Norepinephrine [55]. MB was also found to have potent inhibitory effect against platelet aggregation; the effect was comparable to known inhibitor of platelet aggregation adenosine [3]. In a recent study, the aqueous extract of *Phyllanthus amarus* was tested for its cardioprotective property against high-fructose (HF) diet induced cardiac damage in Wistar rats; the aqueous extract prevented the increase in levels of cardiac and aortic lipids *i.e.*, total lipids, triglycerides, total cholesterol and free fatty acids and decreased phospholipids after co-administration with the HF for sixty days [56]. Yao *et al.* (2018) compared the diuretic effect of the ethanolic fraction of the plant (EIPA) to that of a standard drug (frusemide); the diuretic effect of EIPA was comparable to the standard with an additional benefit of not promoting kaliuresis. Furthermore, the diuretic activity was attributed, at least in part, to the involvement of prostaglandins [57].

Analgesic, Anti-inflammatory and antiulcer activity

Studies have shown that extract of *Phyllanthus amarus* has an anti-inflammatory effect; and that it is effective in preventing persistent

neuropathic pain, as well as prevent both ipsilateral and contralateral persistent nociception [58]. Another study showed that *P. niruri* exhibited potent systemic antinociceptive actions against two models of neurogenic pain [59]. Similarly, methanol extract of *Phyllanthus amarus* significantly inhibited gastric lesions induced by intragastric administration of absolute ethanol. Aqueous and methanol extracts of *Phyllanthus amarus* were found to have anti-inflammatory activity [60].

Radioprotective effect

It was also reported that *Phyllanthus amarus* improved antioxidant activity in liver and blood of irradiated mice [61]. Similarly, *Phyllanthus amarus* prevented the genotoxic effect of radiation on mice chromosome, and it prevented the intestine from radiation induced damages as evident by decreased peroxidation level of intestinal membrane and elevated antioxidant system [62].

Cancer and cytotoxicity

Phyllanthus amarus offers protection against chemical carcinogenesis. It was reported that the aqueous extract of *Phyllanthus amarus* significantly inhibited hepatocarcinogenesis induced by N-nitrosodiethylamine (NDEA) in a dose-dependent manner in male Wistar rats [63]. *Phyllanthus amarus* extract was also found to have significant activity against chemically induced tumour. Inhibition of cell cycle regulation, topoisomerase II, P450 enzymes as well as antioxidant activity may contribute to the overall activity of the extract against carcinogenesis induced in animals and this may be relevant to human cancer as well [64]. It was reported that the extract of *Phyllanthus amarus* inhibited the mutagenicity produced by direct acting mutagens. It also inhibited the activation and mutagenicity of 2-acetaminofluorene (2-AAF), which in turn declined the mutagenesis and possibly carcinogenic potential. Oral administration of *Phyllanthus* extract was found to significantly inhibit urinary mutagenicity produced in rats by benzo- pyrene [65]. The study showed that the methanol extract of *Phyllanthus amarus* has Chemopreventive activity against N-methyl N²-nitro-N-nitrosoguanidine (MNNG) induced stomach cancer in Wistar rats [66]. The aqueous extract of *Phyllanthus amarus* has also demonstrated anti-mutagenic and anti-genotoxic properties as indicated by the extracts ability to protect against the mutagenic effects of 2-aminofluorene, 2-aminoanthracene, 4-nitroquinoline-1-oxide, N-ethyl-N-nitro-nitrosoguanidine, 2-nitrofluorene and sodium azide in test bacteria. In addition, the extract antagonizes DNA damage caused by DMN in hamster liver [67].

Effect of *Phyllanthus amarus* on metabolizing enzymes (CYP P450 3A Family)

Phyllanthus amarus significantly inhibits the Metabolism of CYP4A5 and CYP4A7 enzymes which are essential enzymes responsible for phase I drug metabolism. Co-administration of *Phyllanthus amarus* with orthodox drugs that are completely metabolized by CYP3A Family can lead to therapeutic failure, drug interaction and adverse effect since it will interfere with its metabolism [68]. Another study showed that CYP1A2, CYP2C9, CYP2D6 AND CYP3A4 enzymes were inhibited by aqueous extract of *Phyllanthus amarus* similarly human and rat glutathione S-transferases (GSTs) liver cytosolic enzyme was strongly inhibited by *Phyllanthus amarus* [69].

Similarly, in *in vitro* study it was also found out that the extract of *Phyllanthus amarus* significantly inhibited CYP1A1, CYP1A2,

CYP2B1/2, CYP2E1, CYP 1A, 2A, 2B, 2D and 3A enzymes activity, while in *in vivo* study indicated the activity of P450 enzymes after phenobarbitone administration elevated but oral administration of *Phyllanthus amarus* was found to reduce the activity [70]. The effect of *Phyllanthus amarus* extract on the pharmacokinetic profile of midazolam has been studied and found to interfere with CYP3A4, thereby increasing the blood level of the drug [71]. The mean maximum concentration (C_{max}), time to reach maximum concentration (T_{max}), area under curve (AUC₀₋₈), and elimination half-life (T_{1/2}) (2.9-, 1.6-, 2.8-, and 1.4-fold, respectively) were all increased when compared to control group receiving a single oral dose of midazolam [71].

Toxicity study

Toxicity study of aqueous extract of *Phyllanthus amarus* showed that the extract can cause anaemia because it is associated with decrease in the red blood cell (RBC) count, packed cell volume (PCV), haemoglobin concentration (Hb) level of alanine aminotransferase (ALT); but there is an increase in the white blood cell (WBC) count, levels of aspartate aminotransferase (AST), total conjugated bilirubin, total protein and albumin. The extract also causes a decrease in body weight of laboratory animal. Histopathology study has shown that the kidney, liver and testes are affected by the plant; these showed the toxic potential of the plant [72]. The fractions of *Phyllanthus amarus* obtained from chromatographic separation showed that the plant has toxic effect on blood products [73]. Single oral dose and sub-acute toxicity study of *Phyllanthus amarus* showed that the medicinal plant is non-toxic with an LD₅₀ > 5 g/kg; which is a clear indication that it is safe, but associated with slight cytotoxic effect to the human adenocarcinoma cell line [75]. The difference between this study and that of Adedapo *et al.* (2005a⁷² & b)⁷³ may be as a result of variation in experimental condition and procedure. However, Singh *et al.* (2016) reported an LD₅₀ of 2590.984 mg/Kg bw in Swiss albino mice model in laboratory condition when administered with aqueous extract of the plant. Doses above 2500 mg/Kg bw demonstrated a statistically significant elevation of urea level and histopathological changes were observed; with no significant increase in creatinine level [76]. Another study showed that alcohol extract of the whole plant was not toxic as it displayed no effect on blood cell counts, Hb levels and serum biochemical parameters. Moreover, the body weights of test animals were affected by the extract [53, 54].

Antioxidant

Phyllanthus niruri showed significant improvement of body antioxidant activities in both insulin and non-insulin dependent diabetes mellitus animals [18]. A protein isolated from *Phyllanthus niruri* has also been showed to act as radical scavenger, thereby scavenging the free radicals released by the toxic effect of carbon tetrachloride in hepatocytes. The hepatoprotective effect of *Phyllanthus niruri* may be associated with its action at cellular level by reducing oxidative stress as a radical scavenger and promoting antioxidative defense mechanism of the cells [40]. *In vitro* antioxidative assay showed that the plant is an effective radical scavenger [62].

High phenolic content of *Phyllanthus amarus* showed a strong correlation with its antioxidant activity. *Phyllanthus amarus* has a high antioxidant activity because of its several phenolic constituents and it inhibits chromium (VI) induced oxidative toxicity to MDA-MB-435S human breast carcinoma cells [76]. Similarly, it was also reported that *Phyllanthus amarus* has a strong free radical scavenging

activity and ferric reducing property; its strong free radical scavenging activity is associated with its high phenolic content. The methanol extract of dried *Phyllanthus amarus* has lower antioxidant property compared to fresh sample [77].

Phyllanthus amarus was found to have effective *in vivo* antioxidant activity as seen by its ability to inhibit carbon tetrachloride induce lipid peroxidation in rat liver; while *in vitro* antioxidant activity showed that the plant has high radical scavenging activity [41]. Phyllanthin was reported to have higher radical scavenging capacity than *Phyllanthus amarus*, as indicated by its higher antioxidant activity than *Phyllanthus amarus* [43].

Phyllanthus amarus demonstrated antioxidant activities as indicated by its ability to increase the activities of enzymic and non-enzymic antioxidants and reduce malondialdehyde levels [20]. The methanol extract of *Phyllanthus amarus* was found to possess potential antioxidant activity as evident by its ability to inhibit lipid peroxidation and scavenge hydroxyl and superoxide radicals *in vitro* [21]. Aqueous extract of *Phyllanthus niruri* exhibited high free radical scavenging, inhibition of reactive oxygen and lipid peroxidation [39].

Phyllanthus amarus alleviated oxidative stress induced by nimesulide in the liver as evident by the outcome of post-treatment; with *Phyllanthus amarus* rapidly restoring most of the Nimesulide-induced oxidative changes compared to those obtained by the self-recovery of liver [78].

Pharmacokinetic

The pharmacokinetic study of four lignans of *Phyllanthus amarus* showed that following intravenous administration of phyllanthin, hypophyllanthin, phylltetralin and niranthin to rat, the mean half-lives were 3.56, 3.87, 3.35 and 4.40 respectively. Furthermore, the mean clearances were found to be 0.04, 0.01, 0.03 and 0.02 l/kg respectively. Additionally, after oral administration of Phyllanthin, hypophyllanthin, phylltetralin and niranthin, the peak plasma concentrations were 0.18, 0.56, 0.12 and 0.62ug/ml respectively. One hour later, the absolute oral bioavailabilities were 0.62, 1.52, 4.01 and 2.66% respectively [79].

Phytochemical screening

The plant contains high levels of saponins and tannins with low content of cyanogenic glycosides. The proximate analysis showed that it contains high percentage of carbohydrate and fiber [16]. *P. amarus* has also been reported to have high amounts of alkaloids and phenols [35], alkaloids, tannins, and flavonoids [36], flavonoids, tannins, alkaloids, terpenoids, steroids, saponins and cardiac glycosides [4].

Isolation of Compounds

Bioassay guided fractionation of methanol extract of the leaf of *Phyllanthus niruri* lead to the isolation of niruricide, a novel specific inhibitor of REV protein/RRE RNA and other three known compounds; phyllanthin, rutin, and kaempferol- 3-O-rutinoside [51].

Acyclic triterpenes 3,7,11,15,19,23-hexamethyl-2Z,6Z,10Z,14E,18E,22E-tetracosahexen-1-ol was isolated from the *Phyllanthus niruri* by spectral and chemical method [80].

Further investigation of hexane extract of aerial part of *Phyllanthus niruri* lead to the investigation and isolation of one lignin and one neolignan; these are nirphyllin (3,3',5,9,9'-pentamethoxy-4-hydroxy-4', 5' -methylenedioxy lignan) and phyllnirurin (3,4-methylenedioxy-5'-methoxy-9'-hydroxy-4',7- epoxy-8,3'-neolignan) respectively [81].

Three lignans have also been isolated from the hexane extract of *Phyllanthus niruri* Linn; Niranthin, Nirtetralin and phylltetralin [82]. Two other lignans cubebin dimethyl ether and urinatetralin were also isolated from the cell suspension cultures of *Phyllanthus niruri* [83]. Phyllanthin, hypophyllanthin, nirtetralin are other compounds isolated from *Phyllanthus niruri* [84].

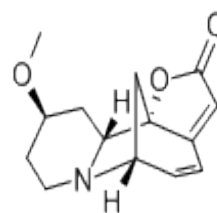
Several hydrolysable tannins were isolated from aerial part of *Phyllanthus amarus* which include Amariin, unusual ellagitannin (phyllanthusiin D), geraniin, corilagin, 1,6-digalloylglucopyranoside as well as rutin and quercetin-3-O-glucopyranoside [12, 85].

Methyl brevifolincarboxylate was isolated from the leaves of *Phyllanthus niruri* L [55]. Tissue culture of *Phyllanthus niruri* resulted in isolation and production of six phenolic compounds; gallic acid, (-)-epicatechin, (+)-gallocatechin, (-)-epigallocatechin, (-)-epicatechin 3-O-gallate and (-)-epigallocatechin 3-O-gallate [11]. An alkaloid named ent-norsecurinine was also isolated from *Phyllanthus niruri* [86].

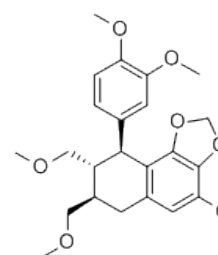
It was also reported that the highest amount of these four lignans; Phyllanthin, hypophyllanthin, phylltetralin and niranthin were found to be in leaves than fruit, followed by branches and stem of *Phyllanthus niruri* using High-performance liquid chromatography method with fluorescence detection. (Murugaiya & Chan, 2007^B)⁸⁰. 1-O-galloyl-6-O-luteoyl-R-D-glucose, β -glucogallin, quercetin 3-O- β -D-glucopyranosyl-(2-1)-O- β -D-xylopyranoside, β -sitosterol, and gallic acid were isolated from *Phyllanthus niruri* [32].

Three compounds were isolated from *Phyllanthus niruri* Linn; 2,3,5,6-tetrahydroxybenzyl acetate, 2,4,5-trihydroxy-3-(4,6,7-trihydroxy-3-oxo-1,3-dihydroisobenzofuran-5-yl)-benzoic acid methyl ester (phyllangin) and corilagin [87].

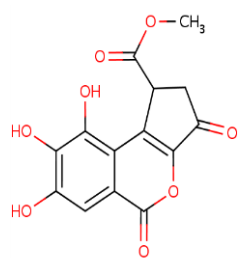
Chemical Structure of some isolated compound of *Phyllanthus amarus*



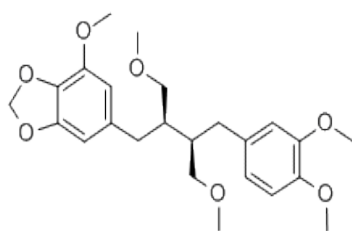
Phyllanthin



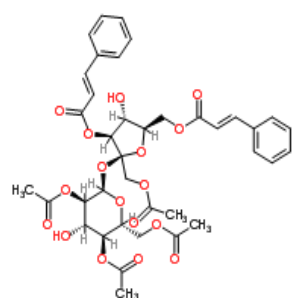
hypophyllanthin



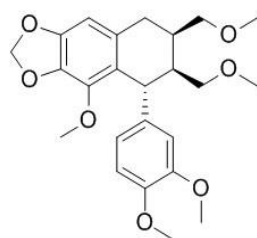
Methyl brevifolincarboxylate



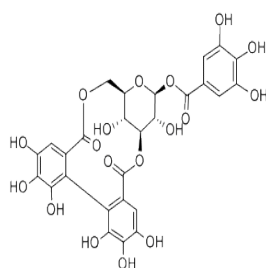
niranthin



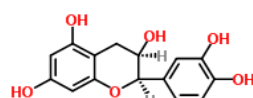
niruriside



nirtetralin



corilagin



epicatechin

DISCUSSION AND CONCLUSION

Phyllanthus niruri is an important medicinal plant which has been used in ayurvedic medicine in the treatment of diseases for over 2000 years [10]. The plant is also used in traditional medicine for treatment of diseases. Scientific investigation revealed the therapeutic value of this medicinal plant; showed that the plant contains several chemical constituents which have been isolated and characterized, and were found to be active against some diseases. For example; phyllanthin is a chemical compound isolated from *Phyllanthus niruri*, and reported to have hepatoprotective activity. This activity is associated with its radical scavenging activity [43]. *Phyllanthus niruri* has been used for years in different parts of the world for liver problem. The Aqueous extract of *Phyllanthus niruri L.*, has also been used by Brazilians as traditional medicine for the treatment of stone disease [6] as well as for jaundice and hepatitis [11]. Scientific investigation has proven that the plant has positive effect against hepatitis B virus as well as kidney stone.

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