International Journal of Biomedical And Advance Research

ISSN: 2229-3809 (Online)
Journal DOI:10.7439/ijbar
CODEN:IJBABN

Review Article

A review on pharmacognostical, Phytochemical, Pharmacological properties of *Phyllanthus amarus*

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Abstract

Phyllanthus amarus Schum. & Thonn. (Euphorbiaceae) is a small herb well known for its medicinal properties and widely used worldwide. *P. amarus* is reported to contain variety of phytoconstituents like lignans namely phyllanthin, hypophyllanthin, nirphyllin and phyllnirurin; flavanone glycosides like niranthin, nirtetralin, phyltetralin and lintetralin; a steroidal hormone estradiol; flavanoids like quercetin, quercitrin, and astragalin; triterpenes like phyllanthenol, phyllanthenone and phyllantheol are some of the important constituents. *P. amarus* is an important plant of Indian Ayurvedic system of medicine which is used in the problems of stomach, genitourinary system, liver, kidney and spleen. It is bitter, astringent, stomachic, diuretic, febrifuge and antiseptic. The whole plant is used in gonorrhea, menorrhagia and other genital affections. It is useful in gastropathy, diarrhoea, dysentery, intermittent fevers, ophthalmopathy, scabies, ulcers and wounds. *P. amarus* show a wide spectrum of pharmacological activities including antiviral, antibacterial, antiplasmodial, anti-inflammatory, antimalarial, antimicrobial, anticancer, antidiabetic, hypolipidemic, antioxidant, hepatoprotective nephroprotective and diurectic properties. The present work is therefore an effort to give an detailed survey of literature on pharmacognostical, traditional, phytochemical and pharmacological properties of *P. amarus.*

Keywords: *Phyllanthus amarus,* euphorbiaceae, phyllanthin, hypophyllanthin, pharmacological activities

1. Introduction

The plant genus *Phyllanthus* (Euphorbiaceae) is widely distributed in most tropical and subtrobical countries. It is a very large genus consisting of approximately 550 to 750 species and is subdivided into 10 or 11 subgenera: *Botryanthus*, *Cicca*, *Conani*, *Emblica*, *Ericocus*, *Gomphidium*, *Isocladus*, *Kirganelia*, *Phyllanthodendron*, *Phyllanthus*, and *Xylophylla.*[1]

Plant picture

Phyllanthus amarus Schum. and Thonn.

(a) Taxonomy :

Kingdom **:** Plantae

Division **:** Angiospermae

Class **:** Dicotyledoneae

Order **:** Tubiflorae

Family **:** Euphorbiaceae

Genus **:** *Phyllanthus*

Species **:** *amarus* Schum. & Thonn.

(b) Vernacular name:

Hindi : Jamgli amli, Jaramla

Kannada : Kirunelli

Malayalam : Kilarnelli, Kilukanelli

Tamil : Kilanelli, Kilakkainelli

Sanskrit : Bhumyamalaki

Bengali : Bhuiamla, sadahazurmani

Marathi : Bhuivali

Telugu : Nela usirika

(c) Part used : Whole plant

(d) Botanical description: *Phyllanthus amarus* is a herb that grows upto 10-60 cms tall, erect, stem terete, younger parts rough,cataphylls 1.5-1.9 mm long, deltoid acuminate; leaf 3.0-11.0 x 1.5-6.0 mm, elliptic oblong to obvate, obtuse or minutely apiculate at apex, obtuse or slightly inequilateral at base; Flowers axillary, proximal 2-3 axils with unisexual 1-3 male flowers and all succeeding axils with bisexual cymules. Male flowers -pedicel 1mm long, calyx 5, sub equal 0.7 x 0.3 mm, oblong, elliptic, apex acute, hyaline with unbranched mid rib; disc segments 5, rounded, stamens 3, filaments connate. Female flowers-pedicel 0.8-1.0 mm long, calyx lobes 5, 0.6 x 0.25 mm, ovate-oblong, acute at apex; disc flat deeply 5 lobed, lobes often toothed at apex, styles 3, free, shallowly bifid at apex. Capsule 1.8 mm in diameter, oblate and rounded, seeds about 0.9mm long, triangular with 6-7 longitudinal ribs and many transverse striations on the back[2].

(e) Geographical distribution: Widespread throughout the tropics and subtropics in sandy regions as a weed in cultivated and wastelands[1].

(f) Traditional use: 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[2-4].

2. Phytochemical properties of *Phyllanthus amarus*

Phytochemistry is regarded as the heart of herbal therapy and the phytochemical research plays an important role in the development of herbal medicines. It constantly addresses a challenge because of the large number of compounds present as mixture in the extract in trace amounts. However screening of prefractionated extracts allows quick identification and dereplication of extract that depicts compound whose activity is masked in crude extracts. Though, the phytochemical research is comparatively slow as compared to synthetic but by all advanced methods including dereplication, mechanism based cleaning, drug design using natural molecules, have the potential to discover and develop active new chemical entities of rich medicinal values[5]. *Phyllanthus amarus* has been reported to possess two lignans namely phyllanthin and hypophyllanthin obtained from the leaves of the plant that has been noted to enhance the cytotoxic responses with cultured multidrug-resistant cells[6-7]. Niranthin, nirtetralin, phyltetralin and lintetralin; the four flavanone glycoside has been reported to be obtained from the leaves of *Phyllanthus amarus*[8-9]. Surprisingly, a steroidal hormone namely estradiol has been noted to be present in root and bark of the plant [10]. Quercetin, quercitrin, astragalin and fisetin-41-o-beta-d-glucoside were the

two flavanoids that have been reported to be isolated from the entire plant of *Phyllanthus amarus*[11]. Phyllanthenol, phyllanthenone and phyllantheol are the three triterpenes obtained from aerial parts of plant[12]. Moreover, singh *et al*. reported nirphyllin and phyllnirurin, the two lignins that were isolated from the aerial parts of *Phyllanthus amarus*[13]. Additionally, Quercetin-3-o-beta-d-glucopyranosyl-(1-4)-alpha-lrhamno pyranoside, a flavanol was obtained from stem of the plant[14]. Moreover, the structure of three new lignans namely 2,3-desmethoxy seco-isolintetralin, 2,3-desmethoxy seco-isolintetralin diacetate and demethylenedioxyniranthin were determined from leaves of *Phyllanthus niruri*[15]. An unusual ellagitannin, Phyllanthusiin D (I), was found to be isolated from the biological active polar fraction of aerial parts of *Phyllanthus amarus* whose structure was established as 1-galloyl-2,4-(acetonyl-dehydrohexahydroxydiphenoyl)-3,6-hexahydroxy di phenoyl-glucopyranoside by chemical and spectroscopic methods[16]. In addition, novel cyclic hydrolysable tannin namely amarulone was obtained from the whole plant of *Phyllanthus amarus*[17]. Further, *Phyllanthus amarus* has been reported to possess di-dehydrohexahydroxyldiphenoyl hydrolysable tannin named amariin. In addition, geranin, corilagin, 1, 6-digalloylglucopyranoside, rutin, quercetin-3-o-glucopyranoside were isolated from the polar fraction of aerial parts of *Phyllanthus amarus*[18]. Chemical examination of the polar extractives of the aerial parts of *Phyllanthus amarus* led to the isolation of amariinic acid, a novel ellagitannin, together with 1-o-galloyl-2,4-dehydrohexahydroxydiphenyl-glucopyranose, elaeocarpus in, repandusinic acid A and geraniinic acid B[19]. In addition, two new Securinega-type alkaloids isobubbialine and epibubbialine were isolated from the leaves of *Phyllanthus amarus*. Other known alkaloids are securinine, norsecurinine, and phyllanthine the structures of which have been detected by means of UV, IR, mass and NMR spectroscopy[20]. The whole plant of *Phyllanthus amarus* has afforded new secosterols named as amarosterol-A characterized as 13, 14-seco-stigma-5(6), 14(15)-diene-3-a-ol (I) and amarosterol-B characterized as 13, 14-seco-stigma-9(11), 14(15)-diene-3-a-ol (II) whose structures have been elucidated on the basis of spectral and chemical studies [21]. In addition, 2, 3, 5, 6-tetrahydroybenzyl acetate and phyllangin are the two new compounds isolated from the whole plant of *Phyllanthus amarus* [22].

3. Pharmacological Properties

3.1 Antiviral: *Phyllanthus amarus* target different steps of the HIV life cycle, thereby presenting multiple antiviral activities. The water/alcohol extract blocks HIV-1 attachment and the HIV-1 enzymes integrase, reverse transcriptase and protease to different degrees. A gallotannin containing fraction and the isolated ellagitannins geraniin and corilagin were shown to be the most potent mediators of these antiviral activities. The *P. amarus* derived preparations blocked the interaction of HIV-1 gp120 with its primary cellular receptor CD4 at 50% inhibitory concentrations of 2.65 (water/alcohol extract) to 0.48 µg/ml (geraniin). Inhibition was also evident for the HIV-1 enzymes integrase (0.48–0.16 µg/ml), reverse transcriptase (8.17–2.53 µg/ml) and protease (21.80–6.28 µg/ml).[23] The aqueous extract of *P. amarus* was tested for its activity against WSSV in marine shrimp and fresh water crabs. *P. amarus* showed antiviral activity against WSSV at the concentration of 150 mg/kg of animal body weight.[24] An aqueous extract on human hepatocellular carcinoma derived cell at 1 mg/ml concentration on a single dose. Inhibition of secretion of HbsAg for a period of 48 h was observed[25]. Disruption of hepatitis B virus polymerase activity, mRNA transcription and replication supported the role of *Phyllanthus amarus* being used as antiviral agent.[26]

3.2 Hepatoprotective: Aflatoxin was administered orally (66.6 µg kg^{-1} BW 0.2 ml^{-1} day^{-1}) to the mice of each group except control to which normal saline and ascorbic acid (0.1 g kg^{-1}BW 0.2 ml^{-1} day^{-1}) were given, respectively. Ethanolic extract of *Phyllanthus amarus* (0.3 g kg^{-1} BW 0.2 ml^{-1} day^{-1}) was given to all groups except control groups (gp. I and gp. V) after 30 min of aflatoxin administration. The entire study was carried out for 3 months and animals were sacrificed after an interval of 30 days till the completion of study. *Phyllanthus amarus* extract was found to show hepatoprotective effect by lowering down the content of thiobarbituric acid reactive substances (TBARS) and enhancing the reduced glutathione level and the activities of antioxidant enzymes, glutathione peroxidase (GPx), glutathione-*S*-transferase (GST), superoxide dismutase (SOD) and catalase (CAT).[27] In-vivo methanolic and aqueous extracts of the seeds of *P. amarus* 250mg/kg were found to have protective properties in rats with CCl4 induced liver damage as judged from serum biochemical enzyme marker activities and histopathological studies.[28] *P. amarus* (1–4 mg/ml) shows the beneficial roles against ethanol-induced liver injury in rats. Possible mechanism may involve their antioxidant activity.[29]

3.3 Antiarthritic: The standardized aqueous extract of *P. amarus* extract (PAE) was tested against Freund's complete adjuvant (FCA) induced arthritic rats. Arthritis assessment, paw volume, joint diameter, mechanical hyperalgesia and nociceptive threshold were measured. On day 28, the animals were sacrificed, tibiotarsal joint was extracted for

histopathology. PAE significantly decreased the arthritis which was evident with arthritis index, paw volume and joint diameter. It also significantly increased the mechanical hyperalgesia and nociceptive threshold.[30]

3.4 Antimicrobial: *P. amarus* showed the most promising antibacterial properties, inhibiting all of the strains tested with minimum inhibitory concentrations (MICs) ranging from 0.25 to 16 mg/ml. [31] The strains isolated from both HIV sero-positive patients were susceptible to various concentrations of the P. amarus extracts (5, 10, 20, 40 and 80 mg ml-1) which were assessed against extend spectrum β-lactamase producing Escherichia coli isolated from the stool samples of HIV sero-positive patients with or without diarrhoea.[32]

3.4 Antiallodyanic: In the rat model of PAF-induced allodynia, both niranthin (30 nmol/paw) and WEB2170 (a PAF receptor antagonist, 30 nmol/paw) treatment significantly inhibited PAF-induced allodynia. In addition, niranthin had a rapid onset and long-lasting antiallodynic action when compared with WEB2170.[33]

3.5 Anticancer: Aqueous extract of *P. amarus* treatment exhibited potent anticarcinogenic activity against 20-methylcholanthrene (20-MC) induced sarcoma development and increased the survival of tumour harboring mice. The extract administration (p.o) was also found to prolong the life span of Dalton's Lymphoma Ascites (DLA) and Ehrlich Ascites Carcinoma (EAC) bearing mice and reduced the volume of transplanted solid tumours.[34] A mixture (1:1) of Phyllanthin and Hypophyllanthin isolated from *P. amarus* extract at a dose of 25mg/kg, 50nmg/kg, 100mg/kg body weight exhibited antitumor activities against Ehrlich Ascites Carcinoma in Swiss albino mice. [35]

3.6 Antifertility: Antifertility effects of an alcohol extract of the whole plant, *P. amarus* a dose of 100 mg/kg body weight for 30 days orally was investigated in cyclic adult female mice. The results revealed no- significant change in absolute body and organ weights in extract-fed animals, indicating no alteration in general metabolic status. Further, feeding had no effect on haematological and clinical biochemical tests reflecting its non-toxicity. Similarly, uterine and ovarian biochemical tests showed no change except in 3β and 17β hydroxy steroid dehydrgenase (HSDs) levels, probably affecting hormonal conversions in the latter. Cohabited females with normal male mice were unable to become pregnant as their cyclicity was affected. Upon withdrawal of feeding for 45 days, these effects were reversible.[36]

3.7 Antiinflamatory: *P. amarus* EtOH/H_2O and hexane extracts showed an inhibition of LPS-induced production of NO and PGE_2 in KC and in RAW264.7. The extracts also attenuated the LPS-induced secretion of tumor necrosis factor (TNF-α) in RAW264.7 as well as in human whole blood. Both extracts reduced expression of iNOS and COX-2 and inhibited activation of NF-κB, but not of AP-1. *P. amarus* inhibited induction of interleukin (IL)-1β, IL-10, and interferon-γ in human whole blood and reduced TNF-α production *in vivo*.[37] The effects of methanol extract of *P. amarus* on different phases of inflammation were examined. Investigations were performed using different phlogistic agents-induced paw edema, carrageenan-induced air-pouch inflammation and cotton pellet granuloma in rats. Methanol extract of *P. amarus* significantly inhibited carrageenan, bradykinin, serotonin and prostaglandin E1-induced paw edema, but failed to inhibit the histamine-induced paw edema. Maximum inhibition was observed in prostaglandin E1-induced paw edema. In carrageenan air-pouch model, methanol extract of *P. amarus* significantly reduced the volume of exudate and migration of neutrophils and monocytes. The extract significantly decreased formation of granuloma tissue in chronic inflammation model.[38]

3.8 Anidiabetic: The effect of the aqueous leaf and seed extracts of *P. amarus* at oral dose of 150, 300 and 600 mg/kg was investigated for their antidiabetic and anti-lipidemic potentials. The extract produced a dose-dependent decrease in the fasting plasma glucose and cholesterol, and reduction in weights in treated mice. The results suggest that the extract could be enhancing peripheral utilization of glucose but the mechanisms on how this works remain unclear. [39] Extraction and fractionation of *P. amarus* hexane extract led to the isolation of dotriacontanyl docosanoate, triacontanol and a mixture of oleanolic acid and ursolic acid. Dotriacontanyl docosanoate and the mixture of oleanolic acid and ursolic acid are reported from this plant species for the first time. All compounds were tested in the α-amylase inhibition assay and the results revealed that the oleanolic acid and ursolic acid (2:1) mixture was a potent α-amylase inhibitor with IC_{50} = 2.01 μg/ml (4.41 μM) and that it contributes significantly to the α-amylase inhibition activity of the extract. Three pure pentacyclic triterpenoids, oleanolic acid, ursolic acid and lupeol were shown to inhibit α-amylase.[40] The use of aqueous extract of *P. amarus* and *Vitex doniana* stem bark on blood glucose of Streptozotocin induced diabetes rats produce a significant ($p<0.05$) antidiabetic and hepatoprotective effect at a dose of, 100 mg/kg body weight.[41]

3.9 Anti diarrhoeal: The anti-diarrhoeal and gastro-intestinal protective potentials of aqueous extract of leaves of *P. amarus* were investigated in mice. Graded doses of the aqueous extract (100-800 mg/kg) administered orally produced a dose-related inhibition of gut meal travel distance in normal mice. The highest intestinal transit inhibition of 31.65% was

obtained with 400 mg/kg. In castor oil induced diarrhoea in mice, *P. amarus* extract (400 mg/kg) delayed the onset of diarrhoea, reduced frequency of defecation and reduced gut meal travel distance significantly resulting in intestinal transit inhibition of 79.94% compared to 86.92% produced by morphine (100 mg/kg). [42]

3.10 Antimalarial: *Tridax procumbens* (TP) and *P. amarus* (PA) have antiplasmodial activities. The aqueous and ethanolic extracts of PA were the most active, yielding EC50 values of 34.9µg/ml and 31.2µg/ml, respectively in the tetrazolium-based assay. The TP and PA produced and IC50 values of 24.8µg/ml and 11.7µg/ml, respectively in the hypoxanthine assay. Protection of human RBCs against P. falciparum damage by the extracts highly correlated with their antiplasmodial activities. None of the extracts, within the concentration range (1.9–500µg/ml) studied produced any overt toxicity to human RBCs.[43]**.** Among 42 extracts, prepared from 14 medicinal plants used in Vietnamese traditional medicine to treat malaria, 24 were found to have antiplasmodial activity by inhibiting the growth of the chloroquine resistant *Plasmodium falciparum* strain FCR-3 with EC50 values less than 10µg/ml.[44]

3.11 Antinociceptive: The hydroalcoholic extract (HE) of the four new species of Phyllanthus, given intraperitoneally, produced significant inhibition of acetic acid-induced abdominal constrictions, with mean ID(50) values of 0.3, 1.8, 7.4 and 26.5 mg/kg for *Phyllanthus amarus, Phyllanthus orbiculatus, Phyllanthus fraternus and Phyllanthus stipulatus,* respectively. In the formalin test, the four species of Phyllanthus, also produced graded inhibition against both phases of formalin-induced licking, being more active in relation of the late phase. The HE of the Phyllanthus species elicited significant inhibition of the capsaicin-induced neurogenic pain, with mean ID(50) values of 8.9, 6.7, >30 and approximately 30 mg/kg *for P. amarus, P. fraternus, P. stipulatus and P. orbiculatus*, respectively. Given orally all HE of the Phyllanthus species were less potent and efficacious than when given by intraperitoneally.[45]

3.12 Antioxidant: The total phenolic content (TPC) and antioxidant activity of fresh and dried *P. amarus* plant materials were evaluated using the Folin-Ciocalteau method, 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging activity and ferric reducing antioxidant power (FRAP) assays. Different drying treatments led to significant reduction (P<0.05) in antioxidant properties of *P. amarus* methanolic extracts, with microwave drying causing the highest decrease in TPC and antioxidant activity exhibited by the reduction in both radical scavenging activity and FRAP. On the other hand, boiling water extracts appeared to exhibit significantly stronger antioxidant potentials (P<0.05) even in dried plant materials due to greater solubility of compounds, breakdown of cellular constituents as well as hydrolysis of tannins. Its strong free radical scavenging activity suggests that it has great potential in the food industry as functional food ingredient. [46] *P. amarus* aqueous extract (PAAEt) treated rats showed a significant decrease in plasma LPO and a significant increase in plasma vitamin C, uric acid, GSH levels and GPx, CAT and SOD activities. single cell gel electrophoresis experiment reveals that PAAEt was devoid of genotoxicity and had a significant protective effect against H2O2, STZ and nitric oxide (NO) induced lymphocyte DNA damage. [47]

3.13 Diuretic: Diuretic, hypotensive and hypoglycaemic effects of *Phyllanthus amarus (*syn. *Phyllanthus niruri)* on human subjects were assessed. Nine mild hypertensives (four of them also suffering from diabetes mellitus) were treated with a preparation of the whole plant of *P. amarus* for 10 days. Suitable parameters were studied in the blood and urine samples of the subjects, along with physiological profile and dietary pattern before and after the treatment period. Significant increase in 24 hr urine volume, urine and serum Na levels was observed.[48] A number of species and genuses reporting diuretic effects. Of these, the most promising, at the present time, are the species *Foeniculum vulgare*, *Fraxinus excelsior*, *Hibiscus sabdariffa*, *Petroselinum sativum* and *Spergularia purpurea*, and species from the genuses *Cucumis* (*Cucumis melo* and *Cucumis trigonus*), *Equisetum* (*Equisetum bogotense*, *Equisetum fluviatile*, *Equisetum giganteum*, *Equisetum hiemale* var. *affine* and *Equisetum myriochaetum*), *Lepidium* (*Lepidium latifolium* and *Lepidium sativum*), *Phyllanthus* (*Phyllanthus amarus*, *Phyllanthus corcovadensis* and *Phyllanthus sellowianus*) and *Sambucus* (*Sambucus mexicana* and *Sambucus nigra*). However, there the number of studies is limited and we recommend that further studies be conducted to confirm reported effects. [49]

3.14 Hypotensive: The effect of the aqueous extract of the leaves of *P. amarus* on blood pressure was evaluated in normotensive male rabbits. Intravenously administered aqueous doses (5 mg to 80 mg/kg) of the extract to anaesthesized normotensive male rabbits produced a significant fall in mean diastolic, systolic and mean arterial pressures in a graded dose response manner. The dose of 5 mg/kg produced the least hypotensive effect, causing a fall in mean diastolic, systolic, and mean arterial pressure of 13.3 ± 3.1, 19.7 ± 5.4, and14.3 ± 3.4 mmHg, respectively, while the dose of 80 mg/kg produced the greatest fall in mean diastolic, systolic, and mean arterial pressure of 49.7 ± 7.9, 45.5 ± 9.5, and 48.00 ± 6.5 mmHg, respectively. [50]

3.15 Hypolipidemic: Hydro-alcoholic extract of leaves of *Phyllanthus amarus* Schumach (HAEPAS) was studied for its *in-vivo* anti-hyperlipidemic potential using cholesterol diet induced hyperlipidemia model in rats. The result of study indicated that HAEPAS possess significant hypolipidemic activity at doses 300 and 500 mg/kg. [51] Four hundred Type 2 diabetics were selected randomly from 828 patients. Ten experimental and ten control groups were formed each group comprising 20 patients. Aqueous extract of a particular plant was given to a particular experimental group for two months maintaining homogeneity in other variables to allow statistical analysis. Blood samples were collected at monthly intervals and biochemical parameters were analyzed. Fasting blood sugar level was lowered by *Mangifera indica* (136±14 to 130±12 mg/dl, $p<0.02$), *Murraya koenigii* (134±9 to 129±10 mg/dl, $p<0.03$) and *Azadirachta indica* (125±12 to 120±9 mg/dl, $p<0.03$). *Ocimum sanctum*s not only lower total cholesterol (TC) (142±14 to 137±15 mg/dl, $p<0.03$) and LDL (91±14 to 85±19 mg/dl, $p<0.03$) level but also increase HDL (25±3 to 27±4 mg/dl, $p<0.03$) level. In addition, *Allium cepa*, *Mangifera indica, Murraya koenigii* and *Phyllathus amarus* showed significant ($p<0.03$) reduction in triglycerides (TG), TC, and very low density lipoproteins (VLDL) levels. *Mangifera indica, Murraya koenigii, Ocimum santum, Phyllanthus amarus, Allium cep* and *Azadirachta indica* exhibited anti-diabetic as well as hypolipidemic effects in Type 2 diabetic patients. [52]

3.16 Immunomodulatory: Thirty two male Wistar rats of average body weight of 85.5 ± 4.55 g were grouped into four (A-D). Group A received distilled water (control), while doses of 250, 500 and 1000 mg/kg body weight of extract were orally administered once daily for 84 days to animals in groups B, C and D respectively. The extract reduced the body weights of rats ($p<0.05$) with increasing doses and significant lowering of blood glucose ($p<0.05$) was shown in an almost similar manner. Serum interleukin-2 concentration increased ($p<0.05$), while serum interleukin-6 and tumour necrosis factor-α concentrations reduced ($p<0.05$). The total white blood cell (WBC) and lymphocytes (L) count were increased ($p<0.05$) and reductions ($p<0.05$) were presented in the neutrophil counts at 500 and 1000 mg/kg body weight. The total cholesterol, triacylglycerol, very low density lipoprotein cholesterol and low density lipoprotein cholesterol concentrations were reduced ($p<0.05$) in an almost dose dependent manner. High density lipoprotein cholesterol concentration increased ($p<0.05$) and the atherogenic index were reduced significantly ($p<0.05$) at the doses. Uric acid concentrations were reduced ($p<0.05$) in an almost dose dependent manner. Significant increases ($p<0.05$) were recorded in reduced glutathione concentrations in the liver, while liver malondialdehyde concentration was decreased significantly at 250 mg/kg body weight of extract ($p>0.05$). The result of the study established scientifically the folklore use of the aqueous leaf extract of *P. amarus* as blood tonic for the prevention and/ or cure of infective and degenerative diseases. [53]

3.17 Nephropathy: The *Hibiscus sabdariffa* group showed significantly decreased serum oxalate and glycolate, and higher oxalate urinary excretion. The *P. amarus* group showed significantly increased urinary citrate vs the untreated group. Histological examination revealed less CaOx crystal deposition in the kidneys of *Hibiscus sabdariffa and P. amarus* treated rats than in untreated rats. Those rats also had significantly lower renal tissue calcium content than untreated rats. All parameters in the *Orthosiphon grandiflorus* treated group were comparable to those in the untreated group.[54]

3.18 Mennorahagia: Phytochemical studies have shown the presence of many valuable compounds such as lignans, flavonoids, hydrolysable tannins (ellagitannins), polyphenols, triterpenes, sterols and alkaloids. The extracts and the compounds isolated from P. amarus show a wide spectrum of pharmacological activities including antiviral, antibacterial, antiplasmodial, anti-inflammatory, antimalarial, antimicrobial, anticancer, antidiabetic, hypolipidemic, antioxidant, hepatoprotective nephroprotective and diurectic properties. [55]

3.19 Antiamnesic: *Phyllanthus amarus* (PAs) 50, 100 and 200 mg/kg produced a dose- dependent improvement in memory scores of young and older mice. PAs also reversed successfully the amnesia induced by scopolamine (0.4 mg/kg, i.p.) and diazepam (1 mg/kg, i.p.). The, brain cholinesterase activity was also reduced. The underlying mechanism of action for the observed nootropic effect may be attributed to pro-cholinergic activity exhibited by Pas.[56]

3.20 Ameliorative: The hydroalcoholic extract of *Phyllanthus amarus* effectively mitigated the toxic effects of carbon tetrachloride in a dose-dependent manner and offered significant protection to the liver thus proving its Ameliorative potential. [57]

3.21 Toxicological assessment: There was no mortality among the animals and they did not show any toxicity or behavioral changes at the dose level of 2000 mg/kg. These findings suggest that *Phyllanthus amarus* was safe and non-toxic to rats upto 2000 mg/kg.[58]

4. Conclusion

Phytochemical studies have shown the presence of many valuable compounds such as lignans, flavonoids,

hydrolysable tannins (ellagitannins), polyphenols, triterpenes, sterols and alkaloids. The extracts and the compounds isolated from *P. amarus* show a wide spectrum of pharmacological activities including antiviral, antibacterial, antiplasmodial, anti-inflammatory, antimalarial, antimicrobial, anticancer, antidiabetic, hypolipidemic, antioxidant, hepatoprotective nephroprotective and diurectic properties. The present review summarizes information concerning the morphology, ecology, ethnopharmacology, phytochemistry, biological activities, clinical applications and toxicological reports of *P. amarus*. This review aims at gathering the research work undertaken till date on this plant in order to provide sufficient baseline information for future works and commercial exploitation.

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