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## A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF *PHYLLANTHUS AMARUS* SCHUM. AND THONN.

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**ABSTRACT:** *Phyllanthus amarus* Schum and Thonn herb is in traditional medicine for more than 3000 years. It belongs to a family of Euphorbiaceae and commonly known by the name of carry me seed, stone breaker, gala of wind, etc. It is a branching annual herb of 30 - 60 cm height widely spread throughout tropics and sub-tropics as a weed. *Phyllanthus amarus* is gaining momentum for its hepatoprotective, anti-carcinogenic, anti-bacterial, anti-viral, anti-inflammatory and more activities as it contains different combinations of secondary metabolites, which render them medicinal properties. The major class of bioactive compounds like alkaloids, flavonoids, lignans, sterols, tannins, triterpenes and volatile oils has been isolated. Lignans like phyllanthin and hypophyllanthin, flavonoids like quercetin were isolated from the leaves of *P. amarus*. This review is an effort to represent the phytochemicals and their pharmacological properties which constantly addresses a challenge because of a large number of compounds present as a mixture in the extract with trace amounts.

**INTRODUCTION:** The genus *Phyllanthus* is one of the most important groups of plants traded as a raw herbal drug in India<sup>1</sup>. The genus *Phyllanthus* of family Euphorbiaceae, consists of approx. 1000 species, spread over tropical and sub-tropical continents like America, Africa, Australia and Asia<sup>2, 3</sup>. In India, *Phyllanthus amarus* is widely distributed as a weed in cultivated and waste lands<sup>4</sup>. All three major habits i.e., trees, shrubs and herbs are seen amongst the *Phyllanthus* species. Ravikant et al., have also described southern India to be the genetic hotspot of *Phyllanthus* species<sup>5</sup>. *Phyllanthus amarus* Schum. and Thonn. has a long history of usage by people, because of its rich medicinal values.

Commonly known by the name of Bhumi amla, belongs to a large family of upright or prostrate herbs or shrubs, often with milky acrid juice<sup>6</sup>. In Unani literature, it is described by the name of 'Bhuti' which means Bhum Amlak - Amla of Land<sup>7</sup>. It plays important role in the development of green medicines which are safer to use and more dependable than costly synthetic drugs with no adverse effects. *P. amarus* has been described in Ayurveda by the Sanskrit name - Bhoomy-aamlakee, Taamalakee and Bhoodha tree<sup>8</sup>. *P. amarus* uses are gaining momentum because of their novel antiviral activity against hepatitis B virus and for several other biological activities such as kidney and gallbladder stones, for cold, flu, tuberculosis, liver diseases, etc<sup>9</sup>.

**Vernacular Names:** The plant is known by different vernacular names in the different areas by the local people (Table 1). It is commonly called carry me seed, stone breaker, wind breaker, leaf flower or gale of wind<sup>10</sup>. *Phyllanthus* means leaf and flower because of its appearance, where flower, fruit and leaf appear to be fused<sup>11</sup>.

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**TABLE 1: NAMES USED WORLDWIDE OF *P. AMARUS* ARE AS FOLLOWS**<sup>8, 12</sup>

S. no.	Language	Vernacular Names
1	Hindi	Bhumi amla, Jangli amla
2	English	Black catnip, Carry me seed, Child pick-a-back, Gale of wind, Gulf leaf flower, Hurricane weed, Shatterstone, Stone breaker
3	Tamil	Keelanelli (Keezhanelli)
4	Bengali	Bhui amla
5	Rajasthani	Gugario
6	Oriya	Bhuiola
7	Telugu	Nela urika
8	Kannada	Nela-nelli, Kirunelli
9	Malayalam	Kilanelli
10	Sanskrit	Bhoomyaamlakee, Bhoodhatree, Tamalakee
11	French	Poudre de plomb (ivory coast)
12	America	Yerba de la nina <sup>10</sup> , Chanca piedra <sup>13</sup> , Hurricane weed
13	Spanish	Yerba magica

**Botanical Characteristics:** *Phyllanthus amarus* is a branching annual glabrous herb which is 30 - 60 cm high and has slender leaf bearing branchlets, distichous subsessile leaves with elliptic-oblong, obtuse, rounded base (**Fig. 1**). Flowers are axillary and yellowish, whitish or greenish. Male flowers are in groups of 1 - 3 whereas females are solitary. Fruits are depressed-globose like smooth capsules

present underneath the branches and seeds are trigonous, pale brown with longitudinal parallel ribs on the back<sup>14</sup>. Capsules on stalks are 1 - 2 mm long, round, smooth, 2 mm wide six seeds. The plant has explosive seed capsules that propel the seeds some distance from the plant. Seeds are triangular, light brown, 1 mm long with 5 - 6 ribs on the back<sup>10, 15</sup>.

**FIG. 1: PHYLLANTHUS AMARUS FOUND IN RAJASTHAN IN ITS HABITAT**

**Distribution:** *P. amarus* is a common pantropical weed that grows well in moist, shady and sunny places. It is widely spread throughout tropics and subtropics<sup>11, 16</sup>. The taxonomic revision of genus *Phyllanthus* by Webster included closely-related genera *P. amarus*, under the sub-section Swartziani of the section *Phyllanthus*. The nomenclature, taxonomic distinctness and close relatives of *P. amarus* were addressed in detail based on morphology and geographical distribution<sup>17 - 19</sup>. It

is said to be related to *P. abnormis*, which is endemic to sandy areas in Texas and Florida of southern USA.

It is, therefore, most likely that *Phyllanthus amarus* originated in the Caribbean area as a vicarious species of *P. abnormis* of the southern United States and has spread around the tropics by trading vessels<sup>17</sup>. Among approx. 1000 species of genus *Phyllanthus*, 53 species are found in India, of which

23 species are endemic. These are distributed throughout the Indian subcontinent, with higher densities in the southern region. Among 53 species of *Phyllanthus*, 37 are shrubs, 13 are herbs and 3 are trees<sup>20</sup>.

Jain et al., 2003 assessed the molecular diversity of *P. amarus* across India using RAPD (random amplified polymorphic DNA) markers. The genetic variability was assessed across 33 locations covering the states of Tamil Nadu, Karnataka, Maharashtra, Gujarat, Assam, West Bengal, Tripura, Uttar Pradesh, Punjab and Haryana. Intra population variation was larger in accessions from southern India compared to other parts of the country. *P. amarus* grows wildy in all drier parts of Rajasthan<sup>21</sup>.

**Phytochemical Properties:** Phytochemistry is regarded as the heart of herbal therapy and the phytochemical research plays an important role in the development of green medicines, which are safer to use (**Table 2**). The major class of bioactive

compounds like alkaloids, flavonoids, lignans, phenols, tannins, terpenes and volatile oils has been isolated. These bioactive compounds further include their respective phytoconstituents. Alkaloids possess securinine, nor-securinine, epibubbialine, isobubbialine, dihydrosecurinine<sup>22, 23</sup>. Flavonoids contain Quercetin, kaempferol, astragalín, quercetin-3-O-glucoside, quercitrin<sup>10, 13, 24-26</sup>. Likewise, Tannins include Amarulone, geraniin, amariin, furosin, corilagin, melatonin, phyllanthusin D<sup>13, 24, 25</sup>. Lignans contains important pharmacological activities because of its phytoconstituents such as Phyllanthin, hypo-phyllanthin, 5-dimethoxy-niranthin, nirtetralin, phyltetralin, hinokinin, 4-(3,4-dimethoxy-phenyl)-1-(7-methoxybenzo[1,3]dioxol-5-yl)-2,3-bismethoxymethyl-but - -an-1-ol<sup>10, 23, 27, 28, 29, 30, 31, 32</sup>. Sterols include Amarosterol A, amarosterol B<sup>33</sup>. Triterpenes like Phenazine and phenazine derivatives, 2Z, 6Z, 10Z, 14E, 18E, 22E-farnesyl farnesol<sup>24, 30</sup> and volatile oils such as Linalool, Phytol<sup>34</sup>.

**TABLE 2: PHYTOCHEMICALS PRESENT IN *P. AMARUS***

S. no.	Secondary Metabolite	Structural Definition	Some Important Phytochemicals	References
1.	Alkaloids	Alkaloids are a group of naturally occurring nitrogenous organic compounds of plant origin.	Securinine, nor-securinine, epibubbialine, isobubbialine, dihydrosecurinine.	22, 23
2.	Flavonoids	Flavonoids are polyphenolic molecules containing 15 carbon atoms and are soluble in water.	Quercetin, kaempferol, astragalín, quercetin-3-O-glucoside, quercitrin.	10, 13, 24-26
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.	13, 24, 25
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-diethoxy-phenyl)-1-(7-methoxybenzo[1,3]dioxol-5-yl)-2,3-bismethoxy methyl-butan-1-ol	10, 23, 27-32
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.	33
6.	Triterpenes	Triterpenes are a class of chemical compounds having three terpene units with the molecular formula C <sub>30</sub> H <sub>48</sub> or consists of six isoprene units.	Phenazine and phenazine derivatives, 2Z, 6Z, 10Z, 14E, 18E, 22E-farnesyl farnesol.	24, 30
7.	Volatile Oils	A volatile oil is a concentrated hydrophobic liquid containing volatile aroma compounds from plants.	Linalool, Phytol.	34

**Ethno-pharmacological Uses:** If the selection of plants is made on the grounds of their traditional use, the chance of research success is greater<sup>35</sup>. This herb is in traditional medicine for more than 3000 years<sup>36</sup>.

- *Phyllanthus amarus* herb has found its traditional uses in several health problems because of its efficacy in the field of gastrointestinal disorders<sup>37</sup>.
- It is used in several female problems such as in leucorrhoea, menorrhagia and mammary abscess and can act as galactagogue<sup>38</sup>.
- Fresh leaf paste has the capacity to cure white spots on skin, diabetes, and jaundice<sup>39-42</sup>.
- Whole plant extract is used in urinary problems, liver disease, dyspepsia, anorexia, constipation and dysentery<sup>43,44</sup>.
- Gonorrhoea and syphilis can be treated by a decoction of leaves, sugar and cumin seeds<sup>45</sup>.
- Treatment of malaria has been successful by *P. amarus* whole plant extract<sup>46</sup>.

It is an ingredient of the most popular formulations of Ayurveda- Chyawanprash, which is consumed at large scale not only in India but also throughout the world because of its anti-inflammatory activity<sup>47</sup>.

**Pharmacological Activities:** Plants as a source of new drugs are still poorly explored of all plant species. Only a small percentage has been investigated phytochemically and even a smaller percentage has been properly studied in terms of their pharmacological properties<sup>48</sup>.

**Antioxidant Activity:** Methanolic extract of *P. amarus* was found to have potential antioxidant activity as it could inhibit lipid peroxidation and scavenge hydroxyl and superoxide radicals *in-vitro*. The amount required for 50% inhibition of lipid peroxide formation was 104 µg/ml and the concentrations needed to scavenge hydroxyl and superoxide radicals were 117 and 19 mg/ml respectively<sup>49</sup>. Different drying treatments led to a 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, the breakdown of cellular constituents as well as hydrolysis of tannins<sup>50</sup>.

The antioxidant activity of some of the principal constituents, namely amariin, 1-galloyl-2,3-dehydrohexahydroxydiphenyl (DHHD)-glucose, repandusinic acid, geraniin, corilagin, phyllanthusiin D, rutin and quercetin 3-O-glucoside were examined for their ability to scavenge free radicals in a range of systems including DPPH, 2,2-azobis-3-ethylbenzthiazoline-6-sulfonic acid (ABTS)/ferrylmyoglobin, ferric reducing antioxidant power (FRAP) and pulse radiolysis.

The compounds showed significant antioxidant activities with differing efficacy depending on the assays employed. Amariin, repandusinic acid and phyllanthusiin D showed higher antioxidant activity among the ellagitannins and were comparable to the flavonoids, rutin and quercetin 3-O-glucoside<sup>26</sup>. *P. amarus* extracts appear to act as an *in vivo* natural antioxidant and an effective gastro-protective agent that is as effective as cimetidine. *Phyllanthus amarus* may also offer protection against toxic effects of alcohol to the liver<sup>51</sup>. Phyllanthin, one of the active lignin present in *P. amarus* was isolated from the aerial parts, by silica gel column chromatography employing gradient elution with hexane-ethyl acetate solvent mixture.

Characterization of Phyllanthin was done by mass spectrophotometry, UV-visible spectrophotometry, elemental analysis, FTIR, HNMR, CNMR and mass spectral analysis. Free radical scavenging activity of *P. amarus* extract and phyllanthin was also examined using DPPH assay. The CCl<sub>4</sub> treatment caused a significant decrease in cell viability. It was observed that phyllanthin effectively alleviated the changes induced by CCl<sub>4</sub> in a concentration-dependent manner, with much smaller strengths as compared to *Phyllanthus amarus* extract<sup>52</sup>.

To study the improved antioxidant status and reduction in the risk of oxidative stress, rats were treated with *P. amarus* aqueous extract (PAAEt) at a dose of 200 mg/kg body wt/day for 8 weeks along with the assay of lipid peroxidation (LPO), Vitamin C, uric acid and reduced glutathione (GSH) and

antioxidant enzymes: Glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD). 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<sup>53</sup>.

Using DPPH (1,1-diphenyl-2-picrylhydrazyl) method, free radical scavenging activity was evaluated using *in-vitro* callus which showed that the methanol extract of *P. amarus*., contains the highest amount of phenolic compounds and exhibits the greatest antioxidant activity in comparison to other extracts and even more as compared to *in-vivo* plant extraction<sup>54</sup>.

**Anti-diabetic Activity:** The methanolic extract of *P. amarus* was found to reduce the blood sugar in alloxan diabetic rats by 6% at a dose level of 200 mg/kg body weight and 18.7% reduction in blood sugar<sup>49</sup>. Anti-diabetic effect of an aqueous and hydroalcoholic extract of *P. amarus* used in Togo for treating diabetes and many other diseases. Two doses (500 and 1000 mg/kg) of the both extracts were administered orally to diabetic rats. Consequently, aqueous and hydroalcoholic extract of *P. amarus* decreases significantly blood glucose level after 15 days of administration<sup>55</sup>. A study by Shetti, oral administration of ethanolic leaf extract (400 mg/kg body weight) for 45 days resulted in significant decline in blood glucose and increase in the activity of glucokinase in the liver of diabetic mice<sup>56</sup>.

**Antimicrobial Activity:** Antimicrobials of plant origin have an extremely large therapeutical potential. They are effective in the treatment of infectious diseases, while simultaneously alleviating many of the side effects that are often connected with synthetic antimicrobials<sup>57</sup>. The effect of nor-securinine, an alkaloid isolated from *Phyllanthus amarus* was studied against spore germination of some fungi (*Alternaria brassicae*, *Alternaria solani*, *Curvularia penniseti*, *Curvularia* sp., *Erysiphe pisi*, *Helminthosporium frumentacei*) as well as pea powdery mildew (*E. pisi*) under glasshouse conditions. The sensitivity of fungi to nor-securinine varied considerably. Nor-securinine was effective against most of the fungi. Pre-inoculation treatment showed greater efficacy than post-inoculation in inhibiting powdery mildew

development on pea plants in a glasshouse. Maximum inhibition occurred at 2000 µg/mL<sup>58</sup>.

Six intestinal organisms were isolated and identified: *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, *E. coli*, *P. mirabilis* and *E. faecalis*. Both agar diffusion and broth dilution methods were used to assay antimicrobial activity against the organisms. *Phyllanthus amarus* showed bacteriostatic action at this concentration because sub-culture yielded growth except on plate of *K. pneumoniae*. Alcoholic extract of *P. amarus* showed the maximum zone of inhibition and minimum inhibitory concentration against all the microorganisms. The minimum zone of inhibition and comparatively greater inhibitory concentration were determined in petroleum ether, and the aqueous extract of *P. amarus* showed less antimicrobial activity against all the experimental strains<sup>59</sup>. The antimicrobial analysis was carried out using disc diffusion method as described by Boer et al.,<sup>15</sup>.

The crude extract and fractions were tested against the *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* for their antimicrobial and antifungal activities. The results showed that the dichloromethane fraction had activity against all the test organisms with MIC at 100 µg/ml while the hexane, ethyl acetate and aqueous methanol fractions showed no activity against the organisms. The results of the antifungal study showed that the fractions have activity against the organism *Candida albicans* as the plates did not show growth of any organism after incubation at 37°C for 21 days<sup>60</sup>. This suggests that the fraction is active against the fungus, *Candida albicans*. This is in agreement with a previous report by Foo and Wong, 1992<sup>13</sup>.

The significant antibacterial activity of ethanolic extracts of the *P. amarus* and *P. niruri* against *E. coli* is an indication of their therapeutic potential in the management of UTI. Results obtained in this work agree with the findings of previous authors on the anti-microbial status of *P. amarus*<sup>61-63</sup>. The inhibitory activities of *P. amarus* and *P. niruri* extracts were the same against four of the five *E. coli* isolates. It could be suggested that a decoction or an infusion of either of the two herbs could help in the treatment of UTI<sup>64</sup>.

**Anti-viral Activity:** Study on 25 compounds isolated from *P. amarus*, *P. multiflorus*, *P. tenellus* and *P. virgatus* found that niranthin, nirtetralin, hinokinin and geraniin at the non-cytotoxic concentration of 50  $\mu\text{m}$ , suppressed effectively both HBsAg and hepatitis B effective antigen (HbeAg) expression, of these, niranthin showed the best anti-HBsAg activity, while the most potent anti-HBeAg activity was observed with hinokinin<sup>65</sup>. *In-vitro* culture of hairy roots of *P. amarus* induced by *Agrobacterium rhizogenes* was shown to possess 85% inhibition (in contrast to 15% in the control) in binding of Hepatitis B Surface Antigen (HBsAg) to its antibody (anti-HBs) after 24 h of incubation with HbsAg-positive sera *in-vitro* at 37 °C<sup>66</sup>. The aqueous extract of *P. amarus* showed partial antiviral activity against white spot syndrome virus in shrimp at the concentration of 150 mg/kg of animal body weight for 30 days<sup>67</sup>. Effect on viral RNA replication was investigated by using Taq Man Real time RT-PCR. *P. amarus* root extract showed significant inhibition of HCV-NS3 protease enzyme; whereas *P. amarus* leaves extract showed considerable inhibition of NS5B in the *in-vitro* assays. Results suggested the possible molecular basis of the inhibitory activity of *P. amarus* extract against HCV which would help in optimization and subsequent development of specific antiviral agent using *P. amarus* as a potent natural source<sup>68</sup>.

**Anti-cancer Activity:** The methanolic extract of *P. amarus* hairy roots revealed potent antiproliferative activity in the MCF-7 cells through induction of apoptosis mediated by increased intracellular reactive oxygen species (ROS) in conjunction with decreased mitochondrial membrane potential<sup>69</sup>. The effects of aqueous extract of the whole plant of *P. amarus* against Cr (VI)-induced oxidative toxicity *in-vitro* in MDA-MB-435S human breast carcinoma cells revealed a distinct decline in Cr(VI)-induced cytotoxicity was noticed in MDA-MB-435S cells with an increase in extract dosage. Its phenolic constituents simultaneously may inhibit Cr (VI)-induced oxidative toxicity to MDA-MB-435S cells<sup>70</sup>.

*Phyllanthus amarus* was shown to be capable of inducing apoptosis in conjunction with its antimetastatic action, with more than 3-fold increase of caspases-3 and -7, the presence of

DNA-fragmentation and terminal deoxynucleotidyl transferase mediated dUTP nick end labeling assay (TUNEL)-positive cells. The ability of *Phyllanthus amarus* to exert antimetastatic activities is mostly associated to the presence of polyphenol compounds in its extracts<sup>71</sup>.

**Anti-venom Activity:** *Phyllanthus amarus* and *Andrographis paniculata* plant extracts when combined possess potent snake venom neutralizing capacity and could potentially be used for therapeutic purposes in case of snakebite envenomation. Di-herbal plant extracts effectively neutralized the cobra venom induced lethal activity. About 0.24 mg of di-herbal plant extract is able to completely neutralize the lethal activity of 2 LD<sub>50</sub> of *N. naja* venom<sup>72</sup>.

#### **Fertility Effect:**

**Fertility in Male:** There is a claim on the use of aerial parts of *Phyllanthus amarus* to improve the fertility in men, by traditional practitioners. *Phyllanthus amarus* leaf extract causes an increase in the level of Testosterone but has little or no effect on the levels of Leutinizing Hormone (LH) and Follicle Stimulating Hormone (FSH)<sup>73</sup>. This increase may be responsible for the enhancement of fertility because the optimum level of Testosterone is required for normal sex drive in adult male and increase in spermatozoa, hence an increase in male fertility<sup>74</sup>.

**Anti-fertility in Female:** It was investigated in cyclic adult female mice at a dose of 100 mg/kg body weight for 30 days orally of an alcoholic extract of the whole plant of *P. amarus*. The results revealed no significant change in absolute body and organ weights and even in general metabolic status. Cohabited females with normal male mice were unable to become pregnant as their cyclicity was affected<sup>75</sup>. On the other side in the female it has resulted in the abortion of some pregnant female mice. Experiments were designed to test the effect of aqueous extract of *P. amarus* (AEPA) leaves on implantation and pregnancy. AEPA reduced the time frame for implantation in the treated rats and caused abortion of pregnant rats. Although the aqueous extract of *Phyllanthus amarus* reduces the time frame for implantation, its abortifacient effect does not support the traditional claim that it can treat sterility<sup>76</sup>.

**Anti-inflammatory Activity:** *Phyllanthus amarus* ethanol, aqueous and hexane extracts showed an inhibition of LPS-induced production of NO and PGE2. The extracts also attenuated the LPS-induced secretion of Tumor necrosis factor (TNF). Both extracts reduced expression of iNOS and COX-2 and inhibited activation of NF- $\kappa$ B, but not of AP-1. *P. amarus* inhibited induction of interleukin (IL)-1 $\beta$ , IL-10, and interferon- $\gamma$  in human whole blood and reduced TNF- $\alpha$  production *in-vivo*<sup>77</sup>. 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. The methanol extract of *Phyllanthus amarus* significantly inhibited carrageenan, bradykinin, serotonin and prostaglandin E1-induced paw edema, but failed to inhibit the histamine-induced paw edema. The extract significantly decreased the formation of granuloma tissue in chronic inflammation model<sup>78</sup>.

**TABLE 3: PHARMACOLOGICAL ACTIVITIES REPORTED IN *P. AMARUS* BY VARIOUS AUTHORS**

S. no.	Pharmacological Activity	Work Done	Place	Ref.
1	Anti-oxidant Activity	Hypoglycemic effect of methanol extract of <i>Phyllanthus amarus</i> Schum and Thonn on alloxan induced diabetes mellitus in rats and its relation to antioxidant potential.	Thrissur (India)	49
		Anti-oxidant properties of <i>Phyllanthus amarus</i> extracts as affected by different drying methods.	Malaysia	50
		Antioxidant activity of some polyphenol constituents of the medicinal plant <i>Phyllanthus amarus</i> Linn.	Pune, Mumbai (India), New Zealand	26
		Gastroprotective and antioxidant activities of <i>Phyllanthus amarus</i> extracts on an absolute ethanol-induced ulcer in albino rats.	Nigeria	51
		Isolation, Characterization and Anti-oxidative effect of Phyllanthin against CCl <sub>4</sub> -induced toxicity in HepG2 cell line.	Ahmedabad, Chennai (India)	52
		The anti-oxidant potential of aqueous extract of <i>P. amarus</i> in rats.	Anantapur (India)	53
2	Anti-diabetic Activity	Determined the free radical scavenging properties for different <i>in-vivo</i> and <i>in-vitro</i> plant extraction of <i>P. amarus</i> .	Jaipur (India)	54
		Hypoglycemic effect of methanol extract of <i>Phyllanthus amarus</i> Schum and Thonn on alloxan induced diabetes mellitus in rats and its relation to antioxidant potential.	Thrissur (India)	49
		Antidiabetic activity of <i>Phyllanthus amarus</i> Schum and Thonn on alloxan induced diabetes in male wistar rats.	Togo, France	55
3	Antimicrobial Activity	Antidiabetic effect of ethanolic leaf extract of <i>Phyllanthus amarus</i> in alloxan induced diabetic mice.	Dharwad (India)	56
		Antifungal activity of nor-securinine against some phytopathogenic fungi.	Varanasi (India)	58
		Determination of antimicrobial potentialities of different solvent extracts of the medicinal plant: <i>Phyllanthus amarus</i> Schum. and Thonn.	Jaipur (India)	59
		Biological and Chemical Evaluation of the Extracts of the Leaf of <i>Phyllanthus amarus</i> Schum.	Nigeria	60
4	Anti-viral Activity	Antibacterial attributes of extracts of <i>Phyllanthus amarus</i> and <i>Phyllanthus niruri</i> on <i>Escherichia coli</i> the causal organism of urinary tract infection.	Nigeria	64
		Screening of 25 compounds isolated from <i>Phyllanthus</i> Species for anti-human hepatitis B virus <i>in-vitro</i> .	Taiwan	65
		Development of a potent <i>in vitro</i> source of <i>Phyllanthus amarus</i> roots with pronounced activity against the surface antigen of the hepatitis B virus.	Kolkata (India)	66
		Screening the antiviral activity of Indian medicinal plants against White spot syndrome virus in shrimp.	Vellore (India)	67
		Inhibition of hepatitis C virus replication by herbal extract: <i>Phyllanthus amarus</i> as potent natural source.	Bangalore (India)	68
5	Anti-cancer Activity	Hairy root extract of <i>Phyllanthus amarus</i> induces apoptotic cell death in human breast cancer cells.	Mumbai (India)	69
		Aqueous extract of <i>Phyllanthus amarus</i> inhibits chromium (VI)-induced toxicity in MDA-MB-435S cells	Vellore (India)	70
		Anti-metastatic effects of <i>Phyllanthus</i> on human lung (A549) and breast (MCF-7) cancer cell lines. PLoS ONE 6, e20994.	Malaysia	71
6	Anti-venom Activity	Isolation, purification, and characterization of active compound from <i>Andrographis paniculata</i> Linn. and <i>Phyllanthus amarus</i> L. and testing the anti-venom activity of the di-herbal extract by <i>in-vitro</i> and <i>in-vivo</i> studies.	Chennai (India)	72
7	Fertility Effect			
7a	Fertility in male	The Phytochemical constituents and the effects of methanol extracts of	Nigeria	73

<i>Phyllanthus amarus</i> leaves (kidney stone plant) on the hormonal parameters of male guinea pigs.				
7b	Anti-fertility in female	Contraceptive effects of <i>Phyllanthus amarus</i> in female mice.	Ahmedabad(India)	75
		Effect of aqueous extract of <i>Phyllanthus amarus</i> leaves on implantation and pregnancy in rats.	Nigeria	76
8	Anti-inflammatory Activity	<i>Phyllanthus amarus</i> has anti-inflammatory potential by inhibition of iNOS, COX-2, and cytokines via the NF-κB pathway.	Germany	77
		Evaluation of anti-inflammatory activity of methanol extract of <i>Phyllanthus amarus</i> in experimental animal models	Mumbai	78

**CONCLUSION:** *P. amarus* is attracting many researchers since many decades because of its potent pharmacological uses, which is discussed above like jaundice, diabetes, syphilis, dysentery, fever, gonorrhoea, etc. Every country has their own traditional use of *P. amarus* but the way of curing disease is almost common everywhere. The extracts of the plant possess various activities like anti-viral, anti-diabetic, anti-hepatotoxic, antibacterial, antifungal and anti-inflammatory. This can be of great use for identifying more alternatives to cure different diseases. As this plant grows in tropical and sub-tropical areas, consequently in countries like India, Nigeria and Malaysia, more research work is continued. The aim of this review was to gather the research work undertaken till date in order to provide enough baseline for future works.

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