Recent Advances in Pharmacological and Phytochemistry Studies on *Phyllanthus amarus*

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**Abstract**

The use of medicinal plants for the treatment of various diseases has been increased due to minimum side effect compared to synthetic drug. Further the herbal products are considered as safe drugs. *Phyllanthus amarus* claimed tribal people for remedy of different diseases namely diarrhoea, dysentery, dropsy, jaundice, intermittent fevers, kidney problems, urinary bladder disturbances, pain, gonorrhoea, diabetes, urogenital disorders, chronic dysentery, skin ulcers, sores, swelling, itchiness, tubercular ulcers, ringworm, scabies and wounds. *Phyllanthus amarus* contains isobubbialine, epibubbialine, securinine, nor-securinine, dihydrosceurinine, geranin, corilagin, 1,6-digalloyglucopyranoside rutin, quercetin 3-O-galloyl rutin, rutin, amarulone, niranthin, nirtetraline, phyllanthin, hypophyllanthin, phyllanthin, hypo-phyllanthin, demethylene dioxy-niranthin, kaempferol, astragalin, etc chemical constituents in its different parts. The extract of *Phyllanthus amarus* retains multiple pharmacological activities such as Anticarcinogenic, Antiproliferative, Gastroprotective, Cardioprotective, Antileptospiral, Antibacterial, Antidiabetic, Antiviral, Antivenom, Antiinflammatory etc. We planned to illustrate the recent studies appeared in Phytochemistry and Pharmacological activities of *Phyllanthus amarus* in order to highlight its multi-activity properties.

**Keywords:** *Phyllanthus amarus*, Pharmacological, Phytochemistry

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1 Introduction

Medicinal plants may be defined as those plants that are commonly used in treating and preventing specific ailments and that are generally considered to be harmful to humans. From thousands of years, plants have been an important source of medicine and plays a key role in world health. It is estimated that approximately one quarter of prescribed drugs are plant extracts or active ingredients obtained from plant sources. World Health Organization estimates that about 80% of these people rely almost exclusively on traditional medicine for their primary healthcare needs. Medicinal plants are the “backbone” of traditional medicine, which means more than 3.3 billion people in the less developed countries utilize medicinal plants on a regular basis.

Medicinal plants not used only for the treatment of diseases but also as potential material for maintaining good health and conditions. The reasons for this is because of their better cultural acceptability, better compatibility and adaptability with the human body and pose lesser side effects. Medicinal plant contains chemical compounds that dictate their therapeutic potency. Researchers have shown that different plants contain different bioactive components at different concentrations. The higher the amount of the important phytochemical in medicinal plants, the greater therapeutic potency or medicinal importance of the plants.

*Phyllanthus* is one of the ancient medicinal plants cultivated for its highly priced fruits and other parts. The genus *Phyllanthus* belongs to family Euphorbiaceae, is one of the largest genera of flowering plants consists of about 800 species which are distributed in a wide range of habitats exhibiting relatively wider range of habits such as annual or biennial herbs, shrubs and trees throughout the tropical and subtropical regions of both the hemispheres.
The name ‘Phyllanthus’ means “leaf and flower” and named so because of its appearance where flower, fruit and leaf appears fused. Different species of Phyllanthus are considered to be very effective and rich in biochemical compounds used in health care, food and cosmetic industry. Numerous phytochemical and bioactivity studies have been carried out on Phyllanthus species, resulting in the isolation and identification of various compounds (alkaloids, coumarins, flavonoids, lignans, and terpenes). The major lignans of the genus namely, phyllanthin and hypophyllanthin, have been shown to be antihypertotopic against carbon tetrachloride and galactosamine induced hepatotoxicity.

*Phyllanthus amarus* commonly known as Bhumi amla, is upright or prostrate herbs or shrubs, often with milky acid juice. In Unani literature, it is described by the name of “Bhuti” which means Bhum Amlak - Amla of Land. *Phyllanthus amarus* has been 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.

In India, it is widely distributed as a weed in cultivated and waste lands. It is an annual herb grows to a height 6 inches to15 inches. Stem is angular with numerous distichous, elliptic oblong leaves. Flowers are yellowish, whitish or greenish, auxillary, males flowers 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.

*Phyllanthus amarus* herb has a number of traditional uses such as diarrhoea, dysentery, dropsy, jaundice, intermittent fevers, kidney problems, urinary bladder disturbances, pain, gonorrhoea, diabetes, urogenital disorders, chronic dysentery, skin ulcers, sores, swelling, itchiness, tubercular ulcers, ringworm, scabies and wounds. It is also used in cough, asthma, other bronchial infections, kidney related problems, appendix inflammation and prostate problems. Because of its efficacy in the field of gastrointestinal disorders it is used in the treatment of disorders like dyspepsia, colic, constipation and dysentery. The herb has found to be effective in several female problems such as in leucorrhoea, menorrhagia and mammary abscess and can act as galactagogue.

Hence it will be worthy to review on *Phyllanthus amarus* and produce data mainly on the pharmacological activities and chemical constituents of the plant to the scientists.

### 2 Phytochemistry of *Phyllanthus amarus*

Phyllanthus amarus have numerous phytochemical constituents such as alkaloids, phenols, tannins, and flavonoids, terpenoids, steroids, saponins, carbohydrates etc displayed in table 1 & Fig 1.

<table>
<thead>
<tr>
<th>Bioactive compounds</th>
<th>Phytochemicals</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloids</td>
<td>Isobubialine, Epibubialine, Securine, nor-securine, dihydrosecurine</td>
<td>10 Houghton et al.; 11 Kassuya et al.</td>
</tr>
<tr>
<td>Tannins</td>
<td>Geraniin, corilagin, 1,6-digalloylglucopyranoside rutin, quercetin-3-O-glucopyranoside, Amarulone, Phyllanthusiin D &amp; Amarin, Furosin, corilagin, melatonin, phyllanthus D (ellagitannin)</td>
<td>12 Foo et al.</td>
</tr>
<tr>
<td>Lignans</td>
<td>Niranthin, Nirtetalrin, Phytetralin, Hypophyllanthin, Phyllanthin, hypo-phyllanthin, dimethylenedioxy-niranthin, 5-demethoxy-niranthin, Isolintetralin, hinokinin, 4-(3,4-dimethoxy-phenyl)-1-(7-methoxy benzol[1,3]dioxol-5-yl)-2,3-bismethoxymethyl-butano-1-ol, nippyllin (3',5,9,9'pentamethoxy-4-hydroxy4', 5'-methylenedioxyxylignan) and phyllinurin (3,4-methylenedioxy-5'-methoxy-9'-hydroxy-4',7'-epoxy-8,3'-neolignan), cubebin dimethyl ether and urinatetralin</td>
<td>13 Leite et al.; 14 Maciel et al.; 15 Singh B et al.; 16 Elfahmi et al.</td>
</tr>
<tr>
<td>Ellagitannins</td>
<td>Amarin, 1-galloyl-2,3-dehydroxxyhydroxydiphenyl (DHHDP) glucose, Repandusinic acid, Geraniin, Corilagin, Phyllanthusiin D, and flavonoids namely rutin, and quercetin 3-O-glucoside, 1-Galloyl-2,4-dehydroxyhydroxynpyrrolyl glucopyranose elaeocarpusin, repandusinic acid A and geraniinic acid</td>
<td>17 Londhe et al.</td>
</tr>
<tr>
<td>Volatile oil</td>
<td>Linalool and Phytol</td>
<td>18 Moronkola et al.</td>
</tr>
<tr>
<td>Triterpenes</td>
<td>Phenazine and phenazine derivatives, 2Z, 6Z, 10Z, 14E 18E, 22E-farnesil farnesol</td>
<td>14 Maciel et al.; 15 Foo et al.</td>
</tr>
<tr>
<td>Sterols</td>
<td>Amarosterol A, amarosterol B</td>
<td>20 Ahmad et al.</td>
</tr>
<tr>
<td>Flavonoid</td>
<td>Quercetin, kaempferol, astragalin, quercetin-3-O-glucoside, quercitrin, gallic acid, (-)-epicatechin, (+)-gallocatechin, (-)-epigallocatechin, (-)-epicatechin 3-O-gallate and (-)-epigallocatechin 3-O-gallate</td>
<td>19 Foo et al.; 21 Foo et al.; 30 Ishimaru et al.</td>
</tr>
</tbody>
</table>
Also mineral elements such as iron manganese, magnesium, zinc, calcium, potassium, phosphorus, copper and chromium were found in appreciable amount, with calcium present in the highest concentration.

Phyllanthin

Hypophyllanthin

Phyllanthus D (ellagitannin)

Methyl brevifolin carboxylate

Niranthin

Phyltetralin

Niruriside

Corilagin

Isolintetralin

Epicatechin
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Fig 1: Chemical Structure of some active constituents presents in Phyllanthus amarus

3 Pharmacological activities of Phyllanthus amarus antibacterial and anti-inflammation activities and antioxidant effects24 (Table 2).

The Phyllanthus amarus has pharmacological activities such as anti-diabetic, antitumor, immunomodulation, antifungal.

Table 2: Pharmacological activities of various parts of Phyllanthus amarus

<table>
<thead>
<tr>
<th>Part used</th>
<th>Pharmacological activity</th>
<th>Findings of effectiveness</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaves</td>
<td>Anticarcinogenic &amp; anti-tumour activity</td>
<td>Inhibition of metabolic activation of carcinogen as well as the inhibition of cell cycle regulators responsible for cancerous growth and DNA repair</td>
<td>25 Rajeshkumar et al.</td>
</tr>
<tr>
<td>Roots</td>
<td>Antiproliferative activity</td>
<td>Induction of apoptosis mediated by increased intracellular reactive oxygen species in conjunction with decreased mitochondrial membrane potential in the MCF-7 cells through</td>
<td>26 Abhyankar et al.</td>
</tr>
<tr>
<td>Whole plant</td>
<td>Anti-cancer Activity</td>
<td>Decline Cr(VI)-induced cytotoxicity in MDA-MB-435 human breast carcinoma cells with an increase in extract dosage</td>
<td>27 Guha et al.</td>
</tr>
<tr>
<td>Whole plant</td>
<td>Antimetastatic effects</td>
<td>Inducing apoptosis in conjunction, 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</td>
<td>28 Lee et al.</td>
</tr>
<tr>
<td>Aerial parts</td>
<td>Anti-oxidant activity</td>
<td>Different drying treatments led to a significant reduction in antioxidant properties of P. amarus methanol extracts</td>
<td>29 Lim et al.</td>
</tr>
<tr>
<td>Aerial parts</td>
<td>Gastroprotective, &amp; antioxidant activities</td>
<td>Effective gastro-protective agent that is as effective as cimetidine against toxic effects of alcohol on an absolute ethanol-induced ulcer in albino rats</td>
<td>30 Shokunbi et al.</td>
</tr>
<tr>
<td>Leaves</td>
<td>Anti-oxidant activity</td>
<td>Phyllanthin effectively alleviated the changes induced by CCl4-induced toxicity in HepG2 cell line in a concentration-dependent manner by reducing oxidative stress</td>
<td>31 Krithika et al.</td>
</tr>
<tr>
<td>Callus</td>
<td>Anti-oxidant activity</td>
<td>Methanol extract of Phyllanthus amarus contains the highest amount of phenolic compounds and exhibits the greatest antioxidant activity in comparison to other extracts</td>
<td>32 Sen et al.</td>
</tr>
<tr>
<td>Whole plant</td>
<td>Cardioprotective effect</td>
<td>Showed protection from HF-diet induced increase in stress markers (LPO and PO), decreased non-enzymatic (GSH and Vit-C) and enzymatic (GR, GPx, GST, SOD, and CAT) antioxidants in</td>
<td>33 Putakala et al.</td>
</tr>
<tr>
<td>Plant Part</td>
<td>Activity Type</td>
<td>Activity Description</td>
<td>Reference</td>
</tr>
<tr>
<td>------------</td>
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</tr>
<tr>
<td>Whole plant</td>
<td>Antileptospiral activity</td>
<td>Showed inhibitory action of methanol and aqueous extract against leptospira</td>
<td>34 Chandan et al.</td>
</tr>
<tr>
<td>Leaves</td>
<td>Antibacterial &amp; antidiabetic activities</td>
<td>In vitro antidiabetic evaluation showed a concentration dependent activity</td>
<td>35 Ukwubile et al.</td>
</tr>
<tr>
<td>Leaves</td>
<td>Anti-diabetic Activity</td>
<td>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.</td>
<td>36 Raphael et al.</td>
</tr>
<tr>
<td>Leaves</td>
<td>Anti-diabetic Activity</td>
<td>Oral administration of ethanolic leaves extract for 45 days resulted in significant decline in blood glucose and increase in the activity of glucokinase in the liver of diabetic mice</td>
<td>37 Shetti et al.</td>
</tr>
<tr>
<td>Whole plant</td>
<td>Antifungal activity</td>
<td>Nor-securinine, an alkaloid isolated from Phyllanthus amarus was effective against most of the fungi</td>
<td>38 Sahni et al.</td>
</tr>
<tr>
<td>Leaves</td>
<td>Antimicrobial &amp; antifungal activities</td>
<td>The dichloromethane fraction had activity against all the test organisms with MIC at 100 μg/ml</td>
<td>39 Okwute et al.</td>
</tr>
<tr>
<td>Aerial parts</td>
<td>Antibacterial &amp; antioxidant</td>
<td>Showed inhibitory activities against four of the five E. coli isolates due to antioxidant property</td>
<td>40 Eldeen et al.</td>
</tr>
<tr>
<td>Roots</td>
<td>Anti-viral Activity</td>
<td>Possess 85% inhibition 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.</td>
<td>41 Bhattacharyya et al.</td>
</tr>
<tr>
<td>Aerial parts</td>
<td>Anti-viral Activity</td>
<td>Aqueous extract 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</td>
<td>42 Balasubramaniam et al.</td>
</tr>
<tr>
<td>Roots and Leaves</td>
<td>Anti-viral Activity</td>
<td>Root extract showed significant inhibition of HCV-NS3 protease enzyme; whereas leaves extract showed considerable inhibition of NS5B in the in-vitro assays against HCV</td>
<td>43 Ravikumar et al.</td>
</tr>
<tr>
<td>Aerial parts</td>
<td>Antivenom activity</td>
<td>Di-herbal plant extracts (P. amarus &amp; A. paniculata) effectively neutralized the cobra venom induced lethal activity</td>
<td>44 Somakumar et al.</td>
</tr>
<tr>
<td>Leaves</td>
<td>Fertility Effect</td>
<td>Causes an increase in the level of testosterone but has little or no effect on the levels of luteinizing hormone and follicle stimulating hormone</td>
<td>45 Obianime et al.</td>
</tr>
<tr>
<td>Whole plant</td>
<td>Contraceptive effects</td>
<td>The results revealed no significant change in absolute body and organ weights and even in general metabolic status</td>
<td>46 Rao et al.</td>
</tr>
<tr>
<td>Whole plants</td>
<td>Anti-inflammatory Activity</td>
<td>Significantly inhibited the production of pro-inflammatory mediators (TNF-α, IL-1β, PGE2) and COX-2 protein expression in LPS-induced U937 human macrophages</td>
<td>47 Hemavathy et al.</td>
</tr>
<tr>
<td>Whole plant</td>
<td>Anti-inflammatory Activity</td>
<td>Extract also down regulated the expression of upstream signaling molecules, TLR4 and MyD88, which play major role in activation of NF-κB, MAPK and PI3K-Akt signaling pathways.</td>
<td>48 Kiemer et al.</td>
</tr>
</tbody>
</table>
It also attenuated the LPS-induced secretion of Tumor necrosis factor (TNF) and reduced expression of iNOS and COX-2 and inhibited activation of NF-κB

Extract inhibited induction of interleukin (IL)-1β, IL-10, and interferon-γ in human whole blood and reduced TNF-α production in-vivo

Methanol extract significantly inhibited carrageenan, bradykinin, serotonin and prostaglandin E1-induced paw edema, but failed to inhibit the histamine-induced paw edema

Whole plant Anti-inflammatory Activity

Leaves and stem Anticonvulsant activity

Whole plant Diuretic effect

4 Conclusion

Presently the use of medicinal plants increased considerably globally due to lesser side effects. The studies explored Phyllanthus amarus is one of the utmost needed medicinal plants for the treatment of different diseases.

Phyllanthus amarus are rich in secondary metabolite and are the key factors for various pharmacological activities. The present information concerning Phyllanthus amarus may serve as the baseline data to impose to do widespread studies for the innovative of novel active compounds and promote evaluation for their pharmacological activities.

5 Conflict of interests

None

6 Author’s contributions

MG and JSV collected the data and drafted the manuscript. Both authors have read and approved the final manuscript.

7 References


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44. Sornakumar RSA, Kunthavai PC, Gnaniash S. Isolation, purification and characterization of active compound from Andrographis paniculata and Phyllanthus amarus Linn. and testing the antivenom activity of the di-herbal extract by in-vitro and in-vivo studies. International Research journal of Pharmacy 2014; 5: 207-211.


