Review Article

Indian Journal of Biology
Volume 1 Number 2, July - December 2014

Phyllanthus Amarus a Traditional Herb with Pharmacological Properties: A Brief Review

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Abstract

Phyllanthus amarus is a traditional medicinal herb of India and belongs to the family Euphorbiaceae. The roots, leaves and stem contain several bioactive compounds which have therapeutic potentials. During last two decades there has been a surge of scientific validation of medicinal property of *P. amarus*. The present review summarizes information concerning the morphology, ecology, ethnopharmacology, phytochemistry, biological activities, and clinical applications 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

Keywords: *Phyllanthus amarus;* Antioxidant; Phyllanthin; Pharmacological.

Introduction

The use of natural products derived from animal, plants and microorganisms have been used for centuries. Later on these were recorded, documented thus leading to the development of a branch of science known as pharmacognosy. Plant derived drugs have gained wide acceptance and currently there is a renewed interest in pharmacologically active natural compounds. Herbal medicine is an integral part of Complementary and Alternative Medicine (CAM) which includes many other forms such as healing arts, traditional Chinese medicine, ancupunctureetc.[1-2] CAM is also gaining wide acceptance from scientific community worldwide and this is reflected in an increasing number of natural products entering orthodox medicine.[3] *Phyllanthus amarus* belongs to the family Euphorbiaceae, has long been used in traditional medicine system not only in India but in many Asian and African countries. The plant is highly praised for its therapeutic potential in Indian phytotherapy and traditional medicine viz. in treatment of diabetes, bladder problems, dropsy, diabetes, jaundice, asthma and bronchial infections and it has been shown to possess anti-hepatitis-B virus surface antigen activity.[4]

The plant is a small, erect annual herb whose stem has a green smooth capsule, and grows up to 10–60 cm in height. The flowers have 5 white sepals and an apical acute anther and the leaves are elliptic and obstuse. The fruit has a green capsule, smooth and fruiting pedicels measuring 1–2 mm and which are dilated at the apex. Few available vernacular names has been listed in table 1. This review is intended to give a view mainly on the biological activities of *Phyllanthus amarus*, the compounds isolated, their pharmacological properties, clinical and laboratory

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investigation and their safety evaluation.

Phytochemical studies

Several active compounds have been identified in *P. amarus* extracts. Most common among them are lignans like phyllanthin and hypo-phyllanthin, flavonoids like quercetin, astragalin, ellagitannins like amarinic acid, amarin and phyllanthisiin D. Lignan, phyllanthin is the bitter constituent while hypophyllanthin is the non-bitter constituent, both are present in high amounts in leaves while their presence in stems is somewhat low. In addition, presence of other lignans is low such as lintetralin, isolintetralin, etralin, 5-demethoxyniranthin etc. also repandusinic acid and niruriside have been isolated by various other groups. It has also been reported that the plant contains bioflavonoids such as quercetin.[5-11]

Pharmacological studies

Antioxidant activity

It was reported that methanolic extracts of *P. amarus* showed high antioxidant activities and has potent free radical scavenging activity and could scavenge superoxides and hydroxyl radicals andcan inhibit lipid peroxides.[12-13] Lim *et al* 2007 reported the different antioxidant properties of *P. amarus* extracts obtained by various drying methods. They found that boiling water extracts has stronger antioxidant potentials due to greater solubility of compounds [14]. Furthermore, it was found that various doses of *P. amarus* decreases ethanol induced oxidative stress by increasing antioxidant status in male Wister rats.[15] Using single cell gel electrophoresis (SCGE) experiment it was revealed that aqueous extract of *P. amarus* did not have any genotoxicity and offered a significant protective effect against H_2O_2, STZ and nitric oxide (NO) induced lymphocyte DNA damage.[16]

Antiviral activity

Phyllanthus amarus is traditionally involved in hepatitis treatment.[17] Further it was found to possess antiviral activity against hepatitis B virus (HBV) which is due to its ability to inhibit DNA polymerase activity and suppression of mRNA transcription, translation and also replication.[18-19] It also has been found to inhibit HIV replication, its reverse transcriptase and also it does not allow HIV-1 attachment to cellular receptor for CD4.[20]

Modulation of genetic damage

Gowrishankar and Vivekanandan (1994) investigated the relative efficacy of crude extract of P.*amarus* in preventing genetic damage in root meristem of *Vicia faba* induced by tannery wastes.[21] Treatment with aqueous extract of *Phyllanthus* species offered protection against cytotoxicity induced by lead, aluminium salts and also favorably modulated Ni induced clastogenecity in mice.[22,23]

Hepatoprotective ability

The hepatoprotective activity of ethanolic extract of *Phyllanthus amarus* were reported by several workers. They opined that phytochemicals present acts as hepatoprotective agents and protect hepatocytes against CCl_4 and galactosamine induced cytotoxicity in rats.[24] It was found that *P. amarus* extract administration increases life span of animals with hepatocellular carcinoma [25]. In fine it may be concluded that lignans such as phyllanthin and hypophyllanthin present in the extracts of *P. amarus* accounts for its hepatoprotective ability

Antisterile activity

The effect of an insecticide carbofuran was studied on estrous and follicular growth in

virgin female rats. Treatment with lignans viz. phyllanthin and hypophyllanthin at a dose of 100mg/kg body weight of rats was found to augment estrous cycle in rats. Further, orally feeding of cyclic female mice with alcoholic extract of the whole plant of *P. amarus* at a dose of 100 mg/kg bodyweightfor 30 days revealed nosignificant change in absolute body and organ weights nor there was any alteration in general metabolic status. However when these females were kept with normal male mice they were unable to become pregnant as their cycle was affected.[26]

Anti-inflammatory activity

Some investigators investigated the anti-leison and anti-inflammatory activity of *P.amarus* extract in adult male Wister rats. The same group investigated anti-inflammatory activity by carrageenan induced mice pawedema method. Both water and methanolic extract of *P. amarus* at a dose of 100,200 and 500mg/kg produced an inhibition of inflammation which may be due to phyllanthin and hypophyllanthin.[27] Extracts of *P. amarus* inhibited NO, PGE_2 and TNFá formation. It was evident from their investigation that *P. amarus* significantly reduces the induction of pro-inflammatory enzymes, i-NOS and COX 2 and they in turn stops production of cytokines.[28]

Antifungal activity

It was reported that the chloroform fraction of the aerial part of *P. amarus* showed significant inhibitory activity on *M. gypseum* which is a dermatophytic fungi.[29] Nor-securinine inhibited germination of spores of many fungi. However there were few contradictory reports that root extract of *P. amarus* did not show any inhibitory activity.

Anticancer activity

Crude alcoholic extract of aerial parts of *P. amarus* was found to inhibit cytochrome P450 enzymes both*in vivo* as well as *in vitro*. *P. amarus* at concentrations of 100 and 200µg/mL has shown toinduce DNA-fragmentation.[30] Oral administration of methanolic extract of stem and leaves of *P. amarus* was found to enhance the life span of leukemia harboring animals and decrease the incidence of anemia. MNNG induced stomach cancer in male Wistar rats was significantly reduced by the administration of methanolic extract of aerial parts of *P. amarus* at a dose of 150 and 750 mg/kg body weight. The frequency of gastric neoplasms was reduced considerably. The elevatedenzymes level in the stomach was also found to be reduced by *P. amarus* treatment.[31] *P. amarus* administration was found to decrease the activity of phase I enzyme and also increased the cellular glutathione(GSH) and glutathione-S-transferase (GST), thereby decreasing theeffect of toxic metabolites of cyclophosphamide on the cells. Administration of *P. amarus* did not reduce the tumor reducingactivity of cyclophosphamide. However, administration of *P. amarus* can significantly reduce the toxic sideeffects of cyclophosphamide without interfering with the antitumor efficiencyof cyclophosphamide. When the aqueous extract of *P. amarus* was administered to cancer bearing mice, it lowered the tumor incidence, and also lowered the level ofcarcinogen-metabolizing enzymes of liver cancer markersin a dose dependent manner.[32] It might be due to structural chemistry of lignans and their antioxidant properties. Aqueous extract of *P. amarus* was reported to be a potent inhibitor of the hepatocarcinogenesis induced by NDEA in rats. The biomarkers of toxicity viz. g-glutamyl transpeptidase, glutamyl-S-transferase, reduced glutathione and the aniline-4-hydroxylase,cytochrome P450 enzyme were elevated in NDEA-treated animals, whereas they were favorably modulated in animals treated with the carcinogenplus *P. amarus* extract. Few scientist suggested that nirtetralin, niranthin, phyllanthin and hypophyllanthin as probable candidates for the anticancer efficacy of *P. amarus*. Alcoholic extract of *P. amarus* was investigated for its potential in vivo and in vitro

Table 1: Some vernacular names of Phyllanthusamarus

Sr. No.	Vernacular names	Language
1.	Bhuiaola, badianala	Oriya
2.	Bihari,	Muikoa, Kantara
3.	Nelauirika, Nelavusari	Telugu
4.	Kirunelli	Kannada
5.	Kizhkkayinelli, Kilanelli	Malayalam
6.	Gugario	Rajasthani
7.	Black catnip	English
8.	Bhumyaamlaki, Bhoodhatree	Sanskrit
9.	Bhuiamala, Sadahazurmani	Bengali
10.	Jangliamla	Hindi
11.	Weisse Blattblume	German

inhibition of CYP1A1, CYP1A2,CYP2B1/2, CYP2E1, CYP1A, CYP2A, CYP2B, CYP2D, and CYP3A isoforms. It was found that all the CYP450 enzymes were significantly inhibited by the *P. amarus* extract in a concentration-dependent manner.[33]

Effect on endocrine system

Methanolic extracts of *P. amarus* caused a significant change in hormonal parameters in guinea pigs. There was an increase in levels of testosterone at 7^{th}, 14^{th} and 21^{st} day of treatment with methanolic extracts at dose of 50-800mg/kg body weight. The levels of LH were significantly reducedon treatment with extracts of *P. amarus*.[34]

Hypoglycaemic and hypocholesterolemic activity

Adeneye *et al* 2006 investigated the antidiabetic and antilepidemic effect of the aqueous leaf and seed extracts of *P. amarus* at a dose of 150, 300 and 600mg/kg. The aqueous extract produced a dose dependent decrease in the fasting plasma glucose and cholesterol which may be due to increase in circulating insulin level. Treatment of human subjects with aqueous extracts of *P. amarus* increased urine volume, increased levels of Na levels in urine and blood and simultaneously it reduced systolic pressure in hypertensive human subjects.[36]

Other effects

The extracts of *P. amarus* has ability to reduce forces of smooth muscle contraction, this study was conducted on guinea pig ileum.[37] Rutin, quercetin and ellagitannins present in the extracts of *P. amarus* has been found to be radioprotective. Further these compounds also have the ability to protect single stranded DNA breaks in plasmid pBR322.[38] The extracts of this plant has protective potentials against gentamycin induced nephrotoxicity in adult male rats, further the extracts also maintained the status of blood urea nitrogen and serum creatinine levels at near normal.

Conclusions

Although extracts from various parts of *P. amarus* have medicinal application from ancient period, modern medicines can be developed after exhaustive research of its bioactive compounds, mechanisms of action, toxicity and proper randomized clinical trials. It would be prudent to investigate its constituents singly and in combination. Further, time of collection of plant materials, nature of soil, extraction procedures and storage affects quality of bioactive compounds. As global scenario is changing towards use of non-toxic plant products as alternative form of medicine, development of modern drugs

from *P. amarus* should be emphasized for treatment of various diseases. Extensive research work should be undertaken on its bioactive products for better therapeutic potentials.

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