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Review Article

PLEIOTROPIC POTENTIALS OF *PHYLLANTHUS AMARUS*: AN OVERVIEW

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ABSTRACT

Phyllanthus amarus, is an herb used widely in traditional medicinal systems of India. It has been noted hepatoprotective, anti-inflammatory, analgesic, antipyretic, antiviral, ant diabetic and antimicrobials activity of *Phyllanthus amarus* in this review. In Ayurvedic system, the herb is well known for its antispasmodic, antianemic properties and is used in urinary as well as hemorrhage disorders. *Phyllanthus amarus* is known to contain a varied range of phytoconstituents including tannins, alkaloids, flavanoids and other chemicals of medicinal value. This herb has been useful in traditional system as appetizer, stomachic and gastro-protective. *Phyllanthus amarus* has been studied widely for their anticonvulsant activity. Moreover, the *Phyllanthus amarus* is known to be a cardioprotective agent who act as a hypotensive agent and maintain the cholesterol level of body. This review enlightens the pharmacological potentials of *Phyllanthus amarus*.

Key Words: Hepatoprotective, Gastroprotective, Flavonoids.

INTRODUCTION

Phyllanthus amarus, (PA) a plant belonging to family Euphorbiaceae is an herb used widely in traditional medicinal systems of India, Nigeria, China, Cuba and many other countries[1,2]. In Ayurvedic system, the herb is well known for its antispasmodic, antianemic properties and is used in urinary as well as hemorrhage disorders[1,2,3]. Various preparation of PA are used as stomachic, hepatoprotective, in antiwound, anti-malarial, and treatment of STD[1,2,3]. PA is known to contain a varied range of phytoconstituents including tannins, alkaloids, flavonoids and other chemicals of medicinal value[1,3].As a part of traditional medicinal system for over 3000 years the plant found its use in curing and preventing various medical ailments[4]. The PA is well known for female problems like menorrhagia, galactogogue, and also mammary abscess[5]. The paste of PA's leaves is reported to cure jaundice[5]. PA is found to be anti-cancer agent [5]. Moreover PA is reported to possess anti-diabetic action[1,5]. Furthermore it has shown protective hypolipidimic, anti-inflammatory effect and antidote effect in snake bite [1,5] The present review explored the pleotropic pharmacological potentials of *Phyllanthus amarus*.

Traditional Presence

Since the plant is present around for about 3000 years in our traditional systems, either Ayurvedic or Chinese system possess a load amount of literature on its use in maintaining physiological balance in human body thus maintaining the health of an individual[4]. PA is reported as analgesic, anti-inflammatory, anti-diabetic, cytotoxic, diuretic, purgative, anti-pyretic, vermifuge, emmenagogue, chologogue, aphrodisiac, anti-dysenteric, stomachic, hepatoprotective and nephroprotective agent[1]. Moreover, it is also being widely used in treatment of kidney stones, vaginitis, menstrual problems, urinary tract infections, venereal diseases, conjunctivitis, tuberculosis, ulcers, gallstones, bronchitis[1,4]. The extract of the aerial parts of herb is known to be good blood purifier in light malaria fever and root extract is known to show positive effects in jaundice[3]. Such a wide range of uses of PA mark its great importance in traditional medicinal treatment[3]. The plants aerial parts have been widely used in form of various traditional dosage forms including pastes, decoction, and infusions[1].

Morphology and Phytoconstituents

PA is an annual small erect herb of Phyllanthus genus belonging to family Euphorbiaceae[1,2]. The word Phyllanthus means 'leaf and flower' which owe to fused appearance of flower, leaf and fruit of the plant[4]. The herb is monoecious herb that usually attains a height of 30-60cm on its full maturity[4]. The plant is normally found in tropical as well as sub-tropical habitats and grows as a weed with other main crops and is indigenous to rainforests of Amazon, Southern India, China and other tropical regions of World[5]. The plant owns leaf bearing branchlets having sub sessile and elliptically oblong leaves with rounded base[6,7, 8,15]. The flowers are whitish or greenish in color and are present in group of 1-3 (males) while the female flowers are found solitary[5]. The fruits of plant normally occur in smooth capsules, found under the branches and possess depressed globose shape[8].

The herb is well known for its varied range of medicinal importance all due to presence of lots of phytoconstituents responsible for its pharmacological actions[8] .Alkaloids like Isobubbialine and Epibubbialine along with tannins like Geraniin, Amarulone and lignans like phyllanthin, hydrophyllanthin, nirurin forms the main active constituent of plant[8].The aqueous extract of plant is found to contain phenolic constituents as confirmed by its HPLC[8].Volatile oils like linalool, phytol along with triterpenes like ursolic acid, oleanolic acid, lupeol were also confirmed to be present as part of phytoconstituents[3]. PA also contain hydrolysable tannins and condensed tannins which are confirmed to possess anti-microbial activity along with phenolic constituents of plant[8].

Pharmacological Potentials

Hepatoprotective Property

It's been since ages that PA is been used as hepatoprotective agent for which the lignans phyllanthin and hydrophyllanthin are mainly responsible[10,11]. It's been considered that plant own its hepatoprotective activity to the anti-oxidant nature of its phyto-chemicals which inhibits the action of reactive oxygen species (ROS) and oxidative stress. Nimesulide is an anti-inflammatory drug which leads to significant decrease in enzyme superoxide dismutase (SOD), glutathione disulphide reductase (GSH) and CAT thus leading to increase in oxidative stress on liver and hence causing hepatic damage[9,11]. PA is found to be prevention of Nimesulide induced hepatotoxicity[13,14]. Also the leaf extract is reported to show action in acetaminophen induced hepatic damage while seeds reported to show their activity in Chloroform induced hepatic injury[9]. Some studies have been carried out for isolating the main active constituent responsible of hepatoprotective property. The maximum yield of hepatoprotective principle was obtained by immobilization of cells of PA with silver nitrate[10]. The herb is well known to execute liver protecting action but still studies are going on for isolating basic principles to understand the mechanism of action of herb[9].

Anticancer Activity

Leaves of PA in form of aqueous extract are known to possess potent cytotoxic activity. The extract is known to act against 20-metylcholanthrene (20MC) induced sarcoma development. The inhibition of DNA topoisomerase II of mutant cell culture along with inhibition of cell cycle regulatory enzyme cdc 25 tryosine phosphatase of saccharomyces cerevisae is considered to be responsible for anti-tumour and cytotoxic action of herb[5,9].

The ethanolic extract of leaves of herb is found to be useful in treating Azaserine induced pancreatic cancer in albino mice thus evidencing the cytotoxic activity of the herb occurring due to inhibition of cell cycle regulators[16].

Anti-Diabetic Activity

The extract of herb PA is known to show significant reduction in blood glucose level. It has been also reported to lower postprandial blood glucose level after a heavy glucose diet. It's been considered that PA owe it's anti-diabetic effect and hypoglycemic action to phyllanthin, hydrophyllanthin, nirulin, flavonoids, terpenes, tannins and other constituents which synergistically enhance the activity of glycolytic and gluconeogenic enzymes[17,18,19]. The extract has also cause significant decrease in cholesterol levels thus evidencing better metabolism of lipids in diabetic patients hence saving them from complications[16]. It has also been considered that *Phyllanthus amarus* tend to affect the activity of Acid and Alkaline Phosphatase enzyme which further get reflected on glucose metabolism in the body thus affecting blood glucose levels[17]. Even knowing the significant action of *Phyllanthus amarus* against diabetes, the mechanism of action and active principle responsible for the effect are yet to be discovered.

Anti-Inflammatory Activity

Phyllanthus amarus in form of aqueous extract is been reported to show anti-inflammatory effects. It has shown considerable relief in paw edema in albino mice induced by serotonin and prostaglandin E1. The extract has been found to sufficiently inhibit action of inflammatory cells including bradykinins, prostaglandin and serotonin. However the anti-inflammatory effect was not that significant in histamine induced paw edema[20,21]. The herb extract (alcoholic) was found to inhibit tumour necrosis factor (TNFα), interleukin-(IL) 1β, and interleukin (IL)-10 in whole human blood thus relieving inflammation[21,22,23].

All the studies related to anti-inflammatory activity of PA indicates that it acts as a strong and potent agent in case of curing inflammation.

Analgesic and Anti-Pyretic Activity

The aqueous as well as ethanolic extract of PA is reported to produce analgesia better than many available standard drugs. It also indicated better anti-pyretic action than pre-existing formulations. At glance the herb is well fitted for treating infection induced fever, thus a well evident research is required for the drug, so as to use it in treatment of pyrexia[24,25].

Anti-Microbial Activity

The methanolic extract of herb is known to show anti-microbial activity against various strains of bacteria's like Pseudomonas aeruginosa, Staphylococcus aureus and Candila albicans etc. It showed active action against bacterial growth inhibition and thus preventing microbial infections. However, the rate of inhibition of microbial growth is found to be significantly lower as compared to conventional drugs including ciprofloxin and ofloxacin[1].

Gastro-Protective AND Anti-Ulcer Activity

The herb has been in use since ages in traditional system as appetizer, stomachic and gastro-protective[26]. The drug is well known to be used as gastro-protective agent. The possible mechanism suggests the increase contraction of gastric mucosa and inhibition of inflammatory cells thus reducing ulceration of stomach, inhibition of edema, and removal of leukocytes from sub-mucosal layers and also improving appetite[26]. The increase in gastric contraction suggests increase in surface area and decrease in volume per unit area of inflammatory agent, thus leading to protection of gastric mucosa proving the evident role of herb in traditional medicinal system as stomachic.

Anti-Viral Activity

The herb extract is reported to inhibit Hepatitis C virus, Dengue virus 2, Chikunguniya mosquito vector [27,28]. The herb extract is known to execute a very good inhibitory effect on dermatophytic fungi, Microsporum gypseum[28]. PA inhibit the replication of HCV monocistronic RNA replicon and HCV H77S viral RNA in Hepatitis C cell culture which accordingly lead to inhibition of viral activity of Hepatitis C[1]. The herb also possesses activity against the development stage of mosquito. It has been considered that PA act as respiratory toxicant in mosquito leading to blockage of impulse flow causing mosquito death and preventing the spread of Chikunguniya virus by acting as an excellent mosquitocidal herb[29]. PA also significantly alter protein structure mediating spread of dengue virus. By altering the protein structure the herb successfully inhibit viral action of dengue virus[28,29].

Anticonvulsant Activity

Phyllanthus amarus has been studied widely for their anticonvulsant activity. For this evaluation it has been tested on albino mice which have already been given a dose of pentylenetetrazole (PTZ) or been treated with maximal electroshock induced seizures (MES) for causing convulsions[30]. The aqueous as well as ethanolic extract of stem and leaves were found considerably effective in reducing hind limb extension caused by MES. Also they caused significant reduction in seizures caused by PTZ[30].

Wound Healing Activity

As we know that *Phyllanthus amarus* has anti-oxidant activity, this character of herb also contributes to wound healing in a

person[31]. The herb extract was applied to wounded laboratory rats and effect on wound healing was studied. The extract was found to enhance the wound healing process. It also reduces the size of scar formed and enhances the healing process by enhancing recovery of peripheral nerves after injury[31,32]. The wound healing potential of herb is attributed to the anti-oxidant nature of herb. It's been reported that plant extract inhibits the microbial and fungal growth at the site of injury. It also boosts angiogenesis resulting in formation of fibroblasts and hence leads to improved wound healing time[32,33].

Antiamnesic Activity

The effect of herb extract was studied for its nootropic effect and anticholinestrase activity in Swiss albino mice. Scopolamine and Diazepam was used as standard drug for inducing amnesia. The herb extract was found to enhance memory of young and older mice and diminishing the amnesic effect of standard drugs[34]. Though the phytoconstituent namely phyllanthin is considered responsible for anti amnesic action but still the exact mechanism of action of drug need to be studied and understood[34].

Hypotensive or Antiatherosclerotic Activity

Phyllanthus amarus is known to produce cardiovascular effects by acting as a hypotensive agent[35]. The extract of herb is known to lower the cholesterol level in body and also enhance lipid metabolism thus preventing the vasculature from blockage resulting due to accumulation of lipids in lumen[35,36,37].

The effect of herb extract in lowering blood pressure in rabbit was studied. The drug causes significant decrease in blood pressure and this effect was inhibited by dose of atropine. The hypotensive action of drug was dose dependent[36].

Miscellaneous Activity

The herb extract either aqueous or alcoholic is reported to show aphrodisiac activity, diuretic activity, and contraceptive activity but the actual mechanism of action and active principle involved leading to these activities of herb is still under research[37]. The extract is also known to show immunomodulatory activity, increasing the number of WBC's in body[37].

CONCLUSION

PA is an ancient herb with utmost medicinal value. The herb has been proved to be of importance in hepato-toxicity, hyperglycemia and in microbial infections. The herb is also known to possess excellent potential for wound healing due to anti-oxidant nature of its phyto-constituents. Despite being having so much useful pharmacologic effects the herb has not been part of traditional or modern medical systems due to lack of knowledge of the mechanism of action of active principle known as well as difficulty in isolating the active principles that are unknown. Even being present in traditional literature for about centuries the exact potential of herb is yet to be understood. Phyllanthus amarus is shown hepatoprotective, anticancer, anti-inflammatory, ant diabetic, antipyretic, antiviral etc in this review article moreover it is brief describing the pleiotropic effects of Phyllanthus amarus.

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