

***Phyllanthus niruri*: Magical Ayurvedic herb for liver disease**

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ABSTRACT

Phyllanthus niruri is a common tropical herb of ayurveda that is used to treat various diseases since ancient times. However, it is primarily used to treat liver specifically liver cancer, hepatitis and kidney problems. In case of liver cancer, it can be used against proliferative nature of cancerous cells. It has anti-proliferative property that promotes caspase 3 induction and subsequently it triggers death of cancerous cells in liver. Similarly, it can be used in Hepatitis that is caused by the hepatitis viral infection primarily. It also consists antiviral property due to the presence of gallic acid and ellagic acid that inhibit DNA polymerase activity and inhibit virus proliferation. It is also known as stone breaker. Additionally, it can be used against inflammation, skin disorders, hyperglycemia, hypertension, malaria, hemolytic diseases and various bacterial diseases. Present review paper is an attempt to summarize the reported role of this magical herb in various diseases specifically liver and kidney related diseases.

Figure : 01

References : 19

Table : 01

KEY WORDS : Antiproliferative, Hepatitis, Hepatoprotective, Phyllanthin, Phytochemical

Introduction

Phytochemicals are chemical compounds synthesized by plants to resist them against fungi, bacterial and viral infections. Phytochemicals also provide several health benefits to human health as it can act as a substrate for various biochemical reactions, absorbents to eliminate undesirable constituents from body, ligands to antagonize the cell receptors and most importantly scavengers of toxic free radicals generated in the body due to metabolic activities. It is a multipurpose herbal plant with several health benefits including nutritional and medicinal advantages. *P. niruri* is typically found in tropical climate with common names as stone breaker, gale of the wind and seed under leaf etc. The *Phyllanthus* genus consists of approximately 1000 species and many of them are utilized in the treatment

of various disorders. Firstly, it was described by Linnaeus in 1737 and present mainly in Asia, Africa, and America region. In India, it is primarily present in Jharkhand, Rajasthan, Bihar and Chhattisgarh where it grows in the month of June. Fruiting starts by mid-July or August till the end of the rainy season. It grows naturally by the sides of roads, on street corners and in construction material dumps. In the hotter areas, it typically grows as a winter weed. In tropical and subtropical climate, *Phyllanthus* genus consists of more than 600 species of annual herbs, shrubs and trees¹⁵. *Phyllanthus niruri*, *urinaria*, *maderaspatensis*, *virgatus* etc. are some important species in this genus. Taxonomically, it is classified as a member of the phylum Tracheaophyta and family Phyllanthaceae. It is an annual herb where leaves are elliptic, oblong and obtuse shapes. *Phyllanthus niruri* consists of extremely acute stipules

TABLE-1: Phytochemicals of *Phyllanthus niruri* and their beneficial uses

Flavanoids
<ul style="list-style-type: none"> • Rutin ;prevents hypertension, antioxidant • Quercetin; anti-fungal,anti-oxidant. • Astragalin; incresed immunity • Catechin; antiproliferative (liver)
Terpenes
<ul style="list-style-type: none"> • Limonene; anti-carcinogenic (liver cells) , skin infections • p-Cymene; antioxidant , anti-microbial, anti-cancerous (mammary cells) • Lupeol; antioxidant aganinst cadmium toxicity in liver
Coumarins
<ul style="list-style-type: none"> • Ellagic acid; inhibits carcinogens binding to DNA, inhibits mutation • Methyl brevifolincarboxylate; prevents hypertension and hyperglycemia,
Lignans
<ul style="list-style-type: none"> • Phyllanthin; prevents CCl4 toxicity (organ failure), antiviral (HIV and Hepatitis B) • Niranthin and Phyltetralin; anti-inflammatory
Tannin
<ul style="list-style-type: none"> • Repundusinic acid; inhibits human immunodeficiency virus type-1 • Geraniin; antinociceptive(analgesic) , prevents hypertension • Corilagin; thrombolytic, antifungal (<i>Candida glabrata</i>)
Alkaloids
<ul style="list-style-type: none"> • Norsecurinine; anti-malarian, anti-bacterial, (gamma-aminobutyric acid)

and axillary flowers. In this species, male flowers can be one to three in number while female flowers are solitary² (Fig.1).

It consists of unique properties that makes it highly valuable in ayurvedic medicine. There has been growing interest in this plant due to its hepatoprotective properties. It is known as for its ability to heal liver damage since ancient times. Liver damage can be caused by various chemicals, drugs and numerous infections⁴. It

can lead to metabolic dysfunction and fatal complications such as CCL4-induced acute liver injury. The pathogenesis of the damage involves the release of free radicals leading to lipid peroxidation and subsequently destruction of cellular membrane occurs. It is further followed by increased inflammatory response of the body. Alcohol consumption also can cause multiple disorders in liver but primarily it occurs due to hepatitis virus infection that contributes to an estimated 8,20,000



Fig. 1 : Adaxial surface of *P. niruri* flowers, fruits and reproductive structure present on the abaxial surface of *P. niruri* herb.

deaths every year. *P. niruri* can be used as an effective ayurvedic medicine to address such problem with dosages of upto 1000 mg per day¹².

During hepatitis infection, the viral enzymes NS5B RNA dependent RNA polymerase and NS3 protease are essential for the growth and replication of virus¹⁶. The phytochemicals of *P. niruri* inhibit virus growth by inhibiting DNA polymerase and RNA polymerase in virus⁶. Additionally, antiproliferative activity is also reported against human liver carcinoma cells (Huh-7 and HepG2) and human breast cancer cells (MCF-7). Mechanistic insight shows the induction of caspase-3 that trigger the death of apoptotic cell through extrinsic and intrinsic signaling. Phyllanthin is a major bioactive lignan in *Phyllanthus* species that exhibited time dependent and dose dependent growth inhibition of HepG3 cells⁷. It protects from hepatic damage by reducing aspartate amino transferase (AST) and alanine amino transferase (ALT). Moreover, *P. niruri* is a remedy for various ailments, including diuretics, vaginitis, hyperglycemia, jaundice, dyspepsia and kidney stone removal¹.

P. niruri acts as immuno modulator. It can modulate immune system and protect body against various diseases through inhibiting glycoprotein (6LZG) and protease (5R74). Recently, it was also reported in corona virus (COVID -19) pathology where severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection transmit through nasal route specifically. *P. niruri* increases the non-specific immune responses including phagocytosis, chemotaxis and cytotoxicity. In cellular immunity, it increases the T-lymphocytes proliferation through heightened secretion of interleukin-4, interferon-

G and decreased secretion of interleukin-2 and 10⁸.

Phytochemicals in P. niruri

Phytochemicals are nothing but the chemicals that are synthesized by the plants for their survival and protection under stress conditions. These are mainly termed as secondary metabolites. In case of plants, the environment with high carbon dioxide, water, light intensity, pathogen attack, grazing and similarly limited amount of carbon dioxide, water, etc can cause stress condition to the plant. However, plants adapt themselves according to the situation by the production of secondary metabolites. For example, *Azadirachta indica* (neem) has bitter taste due to the presence of limonoid as secondary metabolite that protect it from herbivores. The secondary metabolites present in this plant mentioned in Table 1 and can be beneficial to us also. They provide protection against viruses, bacteria, reactive oxygen species produced during stress in humans and plants both⁹.

The phytochemicals in *P. niruri* include flavonoids and sub types that provide protection from hypertension, liver diseases and reactive oxygen species produced during stress, fungal infection and hence increase overall immunity. Others are terpenes and sub types that are anti cancerous and relieve cytotoxicity produced in liver due to excess alcohol consumption. Coumarins and sub types have distinct function of inhibiting mutation in DNA induced by any morphogen. Lignans and sub types can be a source of medication for hepatitis patients. Alkaloids have anti-malarial property and enhance other benefits of the plant.

Medicinal value of P. niruri

Ayurvedic medications have no harmful side effects as

it completely heals the problem slowly instead of instant pain relieve with further complications. *P. niruri* is a great example of positive effects of ayurvedic plants with no harmful effects. It is a medicinal plant which can be used to treat numerous health problems such as liver cancer, hepatitis, diarrhea, constipation, fever, skin infections, hypertension, cytotoxicity, bacterial, fungal infections, malaria, diabetes, kidney and liver stones.

Hepatoprotective property

It is experimentally proved that the plant is effective against carbon tetrachloride (CCl_4) and alcohol toxicity in CCl_4 induced rat through reduction in superoxide peroxidase, alanine and aminotransferase. When CCl_4 enters the body, it gets breakdown into trichloromethyl (CCl_3) and a free radical of calcium ion. The CCl_3 inhibits apoptosis through binding to specific protein of the pathway that can cause permanent loss of regular cell death process in the cell where the protein is present. Hence making the cells immortal commonly termed as cancerous cells form by the transformation of normal cells. The CCl_3 plays a major role in invasion and metastasis of malignant tumors and thus promoting the development of malignant tumor cells. It may activate proliferation of cancerous cells by TRAF6/NF- κ B pathway¹¹. It serves as a macrophage inflammatory protein, capable of being expressed on the surfaces of numerous cells as epithelial, macrophages, and lymphocytes.

The CCl_3 and free radical can mediate lipid peroxidation in the cell membrane that subsequently destroy the cell membrane. It leads to passive diffusion of calcium, sodium, water, increase cell size and finally disrupt cell potential leading to cell death⁹.

Other than CCl_4 toxicity, the plant may treat many liver damages as alcoholic hepatitis caused by high alcohol consumption for longer period, steatohepatitis (non-alcoholic fatty liver disease) caused by excess fat storage in the liver. Both alcoholic and non-alcoholic hepatitis lead to liver fibrosis, occur due to high accumulation of fibrous tissue forming scars in the liver. Scars formation in the liver is the stage prior to liver failure (cirrhosis) and in severe cases it can cause multiple organ failure if not treated timely¹⁷.

Anti-viral property

Several *Phyllanthus* plants were reported to consist of strong anti-viral property due to the presence of some important phenols, flavanoids, alkaloids and tannins. Lignans also have anti-viral property. *P. niruri* is effective against hepatitis-C virus (HCV), human immunodeficiency virus (HIV) and hepatitis-B virus (HBV) as it inhibits DNA polymerase and RNase-H activity essential for virus replication inside the host cell. It was

reported that it acts as a co-receptor for HIV-1 and suppress its activity¹³. Phyllanthin present in the plant extract binds to surface antigen of HBV and HIV-1 reverse transcriptase thus inhibiting the viral antigens. Repandusinic acid present in the plant inhibits the template primer during reverse transcription. Nirtetralin A and B present in the plant extract had inhibitory effect on HBV antigens and low cytotoxicity on the host cell. An aqueous extract of the plant also inhibits endogenous DNA polymerase especially of HBV and HCV virus¹⁰.

Anti-bacterial property

P. niruri extracts perform inhibition of gram-positive bacteria due to the presence of phenolic compounds. Inhibition is more potent against Gram-positive microbes. Biochemical analysis of extract revealed that the presence of ellagitannins specifically geraniin and corilagin inhibit growth of broad-spectrum bacterial species such as *Pseudomonas*, *Helicobacter pylori*, *Escherichia coli*, *Listeria*¹⁹. In one report, *P. niruri* extract was responsible for higher concentration of neutrophils, WBC and decreased lymphocytes in blood when it was administered to mice³. It also can be used over wounds to prevent bacterial infection. It may cure disorders like anemia, jaundice, cystitis, prostatitis, urinary tract infections and venereal diseases which are caused by the bacterial infections⁵.

Stone breaker property

Common name of *P. niruri* explains itself being known as "stone breaker" or "shatter stone" due to its inhibitory effect against calcium oxalate (CaOx) aggregation, cause stone in human urine. Renal epithelial cell become the attachment site for CaOx crystal formation. It reduces calcium in hypercalciuric patients and extract intake increases urinary excretion of magnesium and potassium. It eliminates the gall stones and kidney stones². It was reported that the plant has anti-lithiasic activity due to the presence of flavonoids, catechin, epicatechin. It can not only dissolve CaOx crystals but modify and alter their size also. Recent studies revealed that *P. niruri* extract promotes calculi removal as well as calcium normalization in humans. Therefore, it acts in prevention and dissolution of calculi due to the presence of high glycosaminoglycans (GAGS) content in plant extract of *P. niruri*¹⁴.

Conclusion

In conclusion, *Phyllanthus niruri* is an excellent medicinal herb, mainly found in tropical countries including India. It can be used by anyone as a medication against several health problems due to its pharmaceutical properties including hepatoprotective, antiviral, antibacterial, antidiabetic, stone breaker,

inflammation and much more. The phytochemicals present in the plant makes it effective against the various health problems. It can be used as drug to treat viral induced liver disorders and viruses. It supports better digestion, protection against fatty liver diseases,

jaundice, powerful liver cleanser that detoxifies all harmful agents from the body thus providing clear skin and protects it from sun damage also. Therefore, it as a multifunction natural drug without any side effects when consumed under guidance.

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