

# Pharmacological activities and phytochemical constituents of *Phyllanthus reticulatus* Poir. – A review

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**Abstract**—*Phyllanthus reticulatus* Poir. (Phyllanthaceae) is a shrub distributed in Australia, Asia, and Africa. Various parts of this plant species are employed to cure a variety of illnesses in ethnomedicines such as urine infection, malaria, headache, dysmenorrhea, abscess, anemia, asthma, diarrhea, smallpox, syphilis, inflammation, rheumatism, sores, and envenomation. So far, there is no systematic comprehensive review has been published to analyze, summarize, and document the scientific finding of phytochemistry and pharmacological activities of this plant species. Hence, this work aims to present a comprehensive review to offer a base and encourage to carry out further phytochemical and pharmacological researches of *P. reticulatus*. The Web of Science was utilized to identify the appropriate published articles from 1900 to September 2020. Compounds including astragaloside, corilagin, isoquercitrin, taraxerone, pinoselin, friedelin, reticulate side A, and sitosterol been identified in this plant species. So far, only *in vitro* and *in vivo* scientific evidence are available for the pharmacological activities of various parts of *P. reticulatus* and more investigations involved *in vitro* bioassays. Researches show that *P. reticulatus* contains analgesic, antibacterial, antidiabetic, antifungal, anti-human immunodeficiency virus-1, antihypercholesterolemic, anti-inflammatory, antioxidant, antiplasmodial, and hepatoprotective activities. Further, none of the pharmacologically active compound has been recognized in this plant species. Hence, additional pharmacological activities and phytochemical analysis studies should be performed to deliver more scientific evidence for ethnomedicinal uses of this plant species. This work summarized the available phytochemical and pharmacological activities findings of *P. reticulatus* and also delivers a foundation for additional phytochemical and pharmacological activities investigations of *P. reticulatus*.

**Keywords** – *Phyllanthus reticulatus*, Phyllanthaceae, Sri Lanka, Siddha Medicine, Ayurveda

## I. INTRODUCTION

*Phyllanthus reticulatus* Poir. is a shrub that belongs to the family Phyllanthaceae. This plant species is found in Australia, Asia, and Africa (Conservatoire et Jardin botaniques & South African National Biodiversity Institute, 2012). Also, it is called (Neerppoola) in Tamil. *P. reticulatus* is used for many purposes including food, medicine, and others. Fruits are consumed as food in Sierra Leone and East Africa (Lewis, 1986). Various parts of this plant species are used to treat various disorders in traditional medicines like urine infection, bleeding gums, genital ulcer, burns, suppuration, malaria, muscle spasms, hookworm, headache, dysmenorrhea, abscess, sore eyes, anemia, gastrointestinal bleeding, asthma, diarrhea, blood disorders, smallpox, syphilis, inflammation, rheumatism, constipation, colic, fever, sores, chafes, envenomation, and venereal sores in Africa and Asia (Chhabra *et al.*, 1984; Hedberg *et al.*, 1983; Ilham *et al.*, 1995; Jayaweera, 1982; Lewis, 1986; Panthong *et al.*, 1986; Selvanayagam *et al.*, 1995; The Institute of Ayurveda and Alternative Medicine, 2020). Notably, its bark and tender leaf are used to treat diabetes in Sri Lankan Siddha Medicine (Sathasivampillai *et al.*, 2017).

*P. reticulatus* has many applications to heal several diseases in traditional medicines as mentioned above. Anyway, only some of the traditional medicinal uses have been proved by scientific studies. Also, no systematic comprehensive review has been published to analyze, summarize, and document the scientific finding of phytochemistry and pharmacological

activities of this plant species. Hence, this work aims to present a comprehensive review to offer a base and encourage to carry out further phytochemical and pharmacological researches of *P. reticulatus*.

A literature review was performed using the Web of Science to find the appropriate published articles of *P. reticulatus* from 1900 to September 2020. *Phyllanthus reticulatus* was used as a search term and only phytochemical and pharmacological activities related to published articles were considered in this study.

## II. PHYTOCHEMICAL CONSTITUENTS

More information like part used, extract, identified compound, and reference is listed in Table 1. Compounds have been identified in leaf, root, stem, and whole plant of this plant species. However, the greatest number of compounds have been discovered in the whole plant. Compounds including astragaloside, corilagin, ellagic acid, isoquercitrin, and kaempferol 3-rutinoside have been isolated from leaves (Lam *et al.*, 2007; Neves and Neves, 1966; Pojchaijongdee *et al.*, 2010). Also, taraxerone is found in the root (Joshi *et al.*, 1981) and pinoselin, betulinic acid, 3,4,3'-tri-O-methylellagic acid, 21 $\alpha$ -hydroxyfriedelin-3-one have been identified in the stem (Hui *et al.*, 1976; Pojchaijongdee *et al.*, 2010; Sangkasila, 1998). However, friedelin and sitosterol, etc. have been isolated from both stem and leaves (Hui *et al.*, 1976). Compounds like hovetrichoside A, isotachioside, mananthoside I, phyllanthusmin C, and reticulatol have

been identified in the whole plant (Lan *et al.*, 2010; Ma *et al.*, 2012). Ethanol extracts contain the majority of the compounds. More phytochemical studies should be conducted to isolate more natural compounds from various parts of this plant species which might be novel and have many pharmacological activities.

## I. PHARMACOLOGICAL ACTIVITIES

Hitherto, only *in vitro* and *in vivo* scientific evidence are available for the pharmacological activities of various parts of *P. reticulatus*. Anyhow, more researches have been conducted using *in vitro* bioassays. More information including the level of scientific evidence, pharmacological activity, part used, extract, bioassay/model, dose/concentration, duration, and reference are listed in Table 2. Leaf, aerial, root, and stem have exhibited a variety of pharmacological activities like analgesic (Saha *et al.*, 2007), antibacterial (Direkbusarakom *et al.*, 1998; Eldeen *et al.*, 2011), antidiabetic (Kumar *et al.*, 2008), antifungal (Chellappandian *et al.*, 2018), anti-human immunodeficiency virus-1 (HIV-1) (Eldeen *et al.*, 2011; Tai *et al.*, 2011), antihypercholesterolemic (Maruthappan and Shree, 2010), anti-inflammatory (Saha *et al.*, 2007), antioxidant (Chellappandian *et al.*, 2018; Eldeen *et al.*, 2011), antiplasmodial (Omulokoli *et al.*, 1997), and hepatoprotective (Das *et al.*, 2008) activities. The antifungal activity has a larger number of investigations and leaves have been used in a greater number of pharmacological studies.

Leaves possess antibacterial, antidiabetic, antifungal, anti-Human immunodeficiency virus-1, antioxidant, and antiplasmodial activities. Furthermore, methanol extract was utilized in the majority of the studies and it exhibited pharmacological activities including antibacterial, anti-human immunodeficiency virus-1, anti-inflammatory, antioxidant, and antiplasmodial activities. On the other hand, none of the pharmacologically active compound has been identified in this plant species. Hence, further pharmacological activities and phytochemical analysis correlated investigations should be performed to identify the active compounds. It seems that the ethnomedicinal applications to treat diseases like malaria, inflammation, rheumatism, muscle spasms, diabetes, and abscess have been evidenced by reported analgesic, antibacterial, antidiabetic, antifungal, anti-inflammatory, and antiplasmodial activities. Anyhow, there is no existing scientific evidence for healing including hookworm, headache, smallpox, syphilis, and asthma. Thus, future researches should be carried out to provide more scientific evidence for ethnomedicinal uses of this plant species.

Table 1: Compounds identified in *P. reticulatus*

Part used	Extract	Identified compound	Reference
Leaf	Methanol	(5R*,6R*)-4,6-Dimethoxycarbonyl-5-[2',3',4'-trihydroxy-6'-(methoxycarbonyl) phenyl]-5,6-dihydro-2H-pyran-2-one, 2,7-di-O-methylellagic acid, astragalol, corilagin, ellagic acid, isoquercitrin, kaempferol 3-rutinoside, methyl gallate, methylbrevifolincarboxylate, quercitrin, rutin, stigmasterol-3-O- $\beta$ -glucoside, $\beta$ -Sitosterol-3-O- $\beta$ -glucoside, 3,4,3'-tri-O-methylellagic acid	Lam <i>et al.</i> (2007); Neves and Neves (1966); Pojchaijongdee <i>et al.</i> (2010)
Leaf	Petroleum ether	Friedelin, sitosterol	Hui <i>et al.</i> (1976)
Root	NS	Taraxerone	Joshi <i>et al.</i> (1981)
Stem	Ethanol	Betulinic acid	Hui <i>et al.</i> (1976)
Stem	Methanol	3,4,3'-tri-O-methylellagic acid	Pojchaijongdee <i>et al.</i> (2010); Sangkasila (1998)
Stem	Petroleum ether	Friedelin, friedelan-3 $\beta$ ol, glochidonol, sitosterol, 21 $\alpha$ -hydroxyfriedel-4(23)-en-3-one, 21 $\alpha$ -hydroxyfriedelan-3-one	Hui <i>et al.</i> (1976)
Stem	NS	Pinoresinol	Sangkasila (1998)
Whole plant	Ethanol	(-)-epigallocatechin, 19-hydroxyspruceanol 19-O- $\beta$ -d-glucopyranoside, 3-(3-methylbut-2-en-1-yl) isoguanine, 3,4-dihydroxyphenylpropanol 3-O- $\beta$ -d-glucopyranoside, carthamoside B <sub>5</sub> , hovetrichoside A, isotachioside, mananthoside I, turpenionosides A, turpenionosides B	Lan <i>et al.</i> (2010)
Whole plant	Ethanol (95%)	(+)-lyoniresinol, (3S,5R,6S,9R)-megastigman-3,9-diol 3-O- $\alpha$ -L-arabinofuranosyl-(1->6)- $\beta$ -D-glucopyranoside, 7-megastigmen-3-ol-9-one 3-O- $\alpha$ -L-arabinofuranosyl-(1->6)- $\beta$ -D-glucopyranoside, cleistanthol, phyllanthusmin B, phyllanthusmin C, reticulatuside A, reticulatuside B, spruceanol, syringaresinol	Ma <i>et al.</i> (2012)
NS	NS	Epi-friedelanol, p-coumaric acid, pyrogallol acid	Chandler and Hooper (1979); Neves and Neves (1966)

Abbreviation - NS: Not stated

Table 3: Pharmacological activities of *P. reticulatus*

Level of scientific evidence	Pharmacological activity	Part used	Extract	Bioassay / model	Dose / concentration	Duration	Reference
<i>In vitro</i>	Antibacterial	NS	Ethanol	<i>Aeromonas hydrophila</i> assay	2.5 mg/ml (MIC)	NA	Direkbusarakom <i>et al.</i> (1998)
		NS	Ethanol	<i>Vibrio harveyi</i> assay, <i>Vibrio parahaemolyticus</i> assay	5 mg/ml (MIC)	NA	
<i>In vitro</i>	Antibacterial	Leaf	Methanol (80%)	<i>Bacillus licheniformis</i> assay	164 µg/ml	NA	Eldeen <i>et al.</i> (2011)
		Leaf	Methanol (80%)	<i>Pseudomonas stutzeri</i> assay	180 µg/ml	NA	
		Leaf	Methanol (80%)	<i>Escherichia coli</i> assay, <i>Klebsiella pneumoniae</i> assay	312 µg/ml	NA	
		Leaf	Methanol (80%)	<i>Staphylococcus aureus</i> assay	79 µg/ml	NA	
		Leaf	Methanol (80%)	<i>Bacillus spizizenii</i> assay	84 µg/ml	NA	
		Leaf	Methanol (80%)	<i>Bacillus spizizenii</i> assay	84 µg/ml	NA	
<i>In vitro</i>	Antifungal	Leaf	Ethanol	<i>Trichophyton simii</i> assay	1000 µg/ml (MFC)	NA	Chellappandian <i>et al.</i> (2018)
		Leaf	Ethanol	<i>Trichophyton rubrum</i> (CI-1) assay, <i>Trichophyton rubrum</i> (CI-2) assay, <i>Trichophyton mentagrophytes</i> (CI-1) assay, <i>Microsporum gypseum</i> assay	125 µg/ml (MIC)	NA	
		Leaf	Ethanol	<i>Trichophyton tonsurans</i> assay, <i>Trichophyton simii</i> assay, <i>Trichophyton mentagrophytes</i> (CI-2) assay	250 µg/ml (MFC)	NA	
		Leaf	Ethanol	<i>Trichophyton rubrum</i> (CI-1) assay, <i>Trichophyton rubrum</i> (CI-2) assay, <i>Trichophyton mentagrophytes</i> (CI-1) assay, <i>Microsporum gypseum</i> assay	500 µg/ml (MFC)	NA	

Level of scientific evidence	Pharmacological activity	Part used	Extract	Bioassay / model	Dose / concentration	Duration	Reference
		Leaf	Ethanol	<i>Trichophyton mentagrophytes</i> (CI-2) assay, <i>Trichophyton tonsurans</i> assay	62.5 µg/ml (MIC)	NA	
<i>In vitro</i>	Anti-Human immunodeficiency virus-1	Leaf, Stem	Methanol	Ribonuclease H inhibitory assay	50 µg/ml	NA	Tai <i>et al.</i> (2011)
		Leaf	Methanol	Human immunodeficiency virus-1 cytopathic assay	5.6 µg/ml (EC <sub>50</sub> )	NA	
		Stem	Methanol	Human immunodeficiency virus-1 cytopathic assay	20.8 µg/ml (IC <sub>50</sub> )	NA	
		Leaf	Methanol	Human immunodeficiency virus-1 cytopathic assay	6.3 µg/ml (IC <sub>50</sub> )	NA	
<i>In vitro</i>	Anti-Human immunodeficiency virus-1 reverse transcriptase	Leaf	Methanol (80%)	Human immunodeficiency virus-1 reverse transcriptase assay	131 µg/ml (IC <sub>50</sub> )	NA	Eldeen <i>et al.</i> (2011)
<i>In vitro</i>	Antioxidant	Leaf	Ethanol	2, 2-diphenyl-1-picrylhydrazil free radical scavenging assay	NS	NA	Chellappandian <i>et al.</i> (2018)
<i>In vitro</i>	Antioxidant	Leaf	Methanol (80%)	2, 2-diphenyl-1-picrylhydrazil free radical scavenging assay	10.8 µg/ml (IC <sub>50</sub> )	NA	Eldeen <i>et al.</i> (2011)

Level of scientific evidence	Pharmacological activity	Part used	Extract	Bioassay / model	Dose / concentration	Duration	Reference
<i>In vitro</i>	Antiplasmodial	Leaf	Methanol	Chloroquine-sensitive (K67) <i>Plasmodium falciparum</i> assay	1.7 µg/ml (IC <sub>50</sub> )	NA	Omulokoli <i>et al.</i> (1997)
		Leaf	Methanol	Chloroquine-resistant (ENT36) <i>Plasmodium falciparum</i> assay	10 µg/ml (IC <sub>50</sub> )	NA	
		Root	Methanol	Chloroquine-resistant (ENT36) <i>Plasmodium falciparum</i> assay	159.8 µg/ml (IC <sub>50</sub> )	NA	
		Root	Methanol	Chloroquine-sensitive (K67) <i>Plasmodium falciparum</i> assay	165.1 µg/ml (IC <sub>50</sub> )	NA	
		Stem	Methanol	Chloroquine-resistant (ENT36) <i>Plasmodium falciparum</i> assay	23.9 µg/ml (IC <sub>50</sub> )	NA	
		Stem	Methanol	Chloroquine-sensitive (K67) <i>Plasmodium falciparum</i> assay	7.7 µg/ml (IC <sub>50</sub> )	NA	
<i>In vivo</i>	Analgesic	Aerial	Ethyl acetate, Methanol	Radiant heat tail-flick method	300 mg/kg	1 h	Saha <i>et al.</i> (2007)
		Aerial	Ethyl acetate	acetic acid-induced writhing inhibition method	150 mg/kg	10 min	

Level of scientific evidence	Pharmacological activity	Part used	Extract	Bioassay / model	Dose / concentration	Duration	Reference
<i>In vivo</i>	Antidiabetic	Leaf	Ethanol, Petroleum ether	Alloxan-induced diabetic mouse	500 mg/kg	21 d	Kumar <i>et al.</i> (2008)
<i>In vivo</i>	Antihypercholesterolemic	Aerial	Aqueous	Atherogenic diet-induced hypercholesterolemic rat	250 mg/kg	45 d	Maruthappan and Shree (2010)
<i>In vivo</i>	Anti-inflammatory	Aerial	Ethyl acetate, Methanol	Carrageenan-induced rat hind paw edema model	150 mg/kg	1 h	Saha <i>et al.</i> (2007)
<i>In vivo</i>	Hepatoprotective	Aerial	Ethanol (95%)	Carbon tetrachloride-induced liver damaged rat	200 mg/kg	15 d	Das <i>et al.</i> (2008)

## Abbreviations

HIV: Human Immunodeficiency Virus, EC<sub>50</sub>: Half maximal effective concentration, IC<sub>50</sub>: Half maximal inhibitory concentration, MFC: Minimal Fungicidal Concentrations, MIC: minimum inhibitory concentration, NA: Not Applicable, NS: Not Stated

### A. *In vitro* studies

Antibacterial (Direkbusarakom *et al.*, 1998; Eldeen *et al.*, 2011), antifungal (Chellappandian *et al.*, 2018), anti-human immunodeficiency virus-1 (Eldeen *et al.*, 2011; Tai *et al.*, 2011), antioxidant (Chellappandian *et al.*, 2018; Eldeen *et al.*, 2011), and antiplasmodial (Omulokoli *et al.*, 1997) activities possess *in vitro* level of scientific evidence of *P. reticulatus*. The majority of the studies have been carried out to study the antifungal activity. The most efficient (based on the lowest extract concentration used) *in vitro* investigation was conducted by Omulokoli *et al.* (1997). In this study, leaf methanol extract (IC<sub>50</sub> 1.7 µg/ml) revealed antiplasmodial activity in chloroquine-sensitive (K67) *Plasmodium falciparum* assay. Thus, it is recommended that conducting further *in vivo* and clinical trial researches for the studies exposed more efficient consequences in *in vitro* bioassays.

### B. *In vivo* studies

Until now, analgesic (Saha *et al.*, 2007), antidiabetic (Kumar *et al.*, 2008), antihypercholesterolemic (Maruthappan and Shree, 2010), anti-inflammatory (Saha *et al.*, 2007), and hepatoprotective (Das *et al.*, 2008) activities have been reported in *in vivo* evidence. The majority of the *in vivo* evidence is available for analgesic activity. A study implemented by Saha *et al.* (2007) seems the best study (based on the lowest dose and duration of the study) among the reported *in vivo* studies. Aerial ethyl acetate extract (150 mg/kg) orally administered to acetic acid-induced writhing rat model exhibited the analgesic activity after 10 minutes. Henceforth, it is suggested that to carry out clinical trials for the reported *in vivo* studies.

## II. CONCLUSION

Several compounds have been identified in *P. reticulatus* and this plant species contains several pharmacological activities. Also, it has a wide range of ethnomedical uses. Hence, further phytochemical studies should be conducted to identify the pharmacologically active compound in *P. reticulatus*. Moreover, further *in vitro*, *in vivo*, and clinical trial investigations should be performed for various extracts and discovered compounds in *P. reticulatus* to provide more scientific evidence for its ethnopharmacological applications. This work summarized the available phytochemical and pharmacological activities findings of *P. reticulatus*. This work also delivers a foundation for additional phytochemical and pharmacological activities investigations of *P. reticulatus*.

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