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PHYLLANTHUS RETICULATUS POIR. – AN IMPORTANT MEDICINAL PLANT: A REVIEW OF ITS PHYTOCHEMISTRY, TRADITIONAL USES AND PHARMACOLOGICAL PROPERTIES

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Keywords:

Phyllanthus reticulatus, Traditional, Fruit, Leaf

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ABSTRACT: The medicinal plants are widely used by traditional medical practitioners for curing various diseases in their day to day life. In traditional system of medicine different parts of *Phyllanthus reticulatus* are used for curing various ailments. Bark is used as astringent and diuretic. Leaves are antidiarrheal and roots are used for asthma. Fruit of the plant is used in inflammation. *Phyllanthus reticulatus* has been proved to show antidiabetic, antiviral, anticancer, antiplasmodial, hepatoprotective, antibacterial and anti-inflammatory activities. The plant contains tannic acid, terpenoids, flavonoids, phenolic compounds and steroids as main chemical constituents. This article aims to provide a comprehensive review on the phytochemical and pharmacological aspects of this plant. The innumerable medicinal properties and therapeutic uses of *Phyllanthus reticulatus* prove its importance as a valuable medicinal plant.

INTRODUCTION: In traditional culture medicinal plants are used all over the world and they are becoming increasingly popular in modern society as natural alternatives to synthetic chemicals [1]. *Phyllanthus reticulatus* (Family – Euphorbiaceae) commonly known as pancoli or karineli, (Synonym: *Kirganelia reticulata* Poir.) is a large glabrous or pubescent shrub with smooth or lanticellate branches growing from 8-10 ft in height. The plant is widely present in Tropical Africa, Srilanka, South East Asia, China, Malaysia and throughout India, mostly in hedges or waste places. Fruiting and flowering season of plant is from July to March. Leaves of the plant contain tannic acid and gum. Fruit of the plant becomes purplish black when ripe.

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The leaves are used as diabetic and cooling medicine. It is reported to be used as diuretic, alternative, attenuant, astringent and as antidiarrhoel [2-5].

Taxonomy:

Domain :	Eukaryota
Kingdom:	Plantae
Claudus :	Angiosperm
Order :	Malpighiales
Family :	Euphorbiaceae
Tribe :	Phyllantheae
Genus :	Phyllanthus
Species :	*P.reticulatus*

Plant morphology: A large, branched and scandent shrub with branches smooth or tuberculate and somewhat angled. Leaves have alternate arrangement, lanceolate, simple and variable in size. The apex of the leaves is acute, ventral side is dark green in colour while dorsal side is light-green.

It is having bitter taste and pungent odour. Leaves are 2.5-5 cm long and 0.7-1.5 cm broad, oblong and elliptic in shape. The margins of the leaves are emarginated to undulate. Flowers are axillary on slender branches. Fruits are coriaceous or fleshy and 8-16 seeded. Seeds are irregularly trigonous [6-7]. Plant is shown in **figure 1(a, b)**.

(a)

(b)

FIG. 1: *PHYLLANTHUS RETICULATUS* FLOWER AND FRUIT

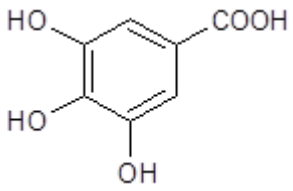
Common names:

Sanskrit:	Pulika, Krishna-kamboji
Bengali:	Panjulil
Gujarati:	Datwan
Hindi:	Panjuli
Kannada:	Pulaveri, Anamsule
Malayalam:	Niruri, Nireli
Marathi:	Pavana
Oriya:	Jandaki
Tamil:	Abaranji, Karunelli, Kattukilanelli
Telugu:	Nallapurugudu, pulaguwa, Phulsar

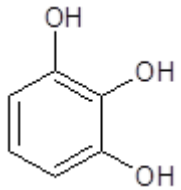
Chemical constituents: Three compounds (lupeol, lupeol acetate, and stigmasterol) were isolated and identified by phytochemical study conducted on the leaves of *Phyllanthus reticulatus* [8].

Scopoletin was isolated from the chloroform soluble fraction of a methanol extract.

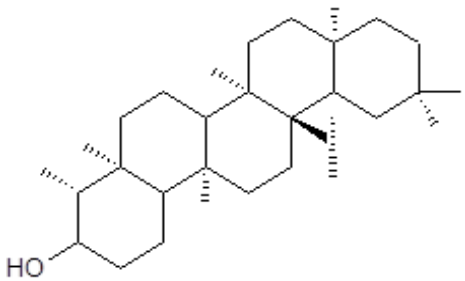
Other isolated compounds are tannic acid, friedelin, epifriedelinol, betulin, taraxerone, beta-sitosterol, glochidonol, octacosanol, taraxeryl acetate and 21-alpha-hydroxyfriedelan-3-one, betulinic acid. Coumarin was isolated from stem bark [9, 6]. Eight compounds (β- sitosterol-3-O-β- glucoside, stigmasterol- 3- O- β- glucoside, methyl gallate, ellagic acid, corilagin, methyl brevifolin carboxylate, kaempferol, astragalin, including two flavonoid glycoside rutin (quercetin- 3- rutinoside) and quercetin-3-O- β- D glucopyranoside (isoquercitrin) were isolated from the butanol soluble fraction of the methanolic extract of the leaves of *phyllanthus reticulatus* by conventional methods [10]. Rutin was also quantitated from the methanolic leaf extract by thin layer high performance chromatography [11]. Ellagic acid was found as the chemical constituent for the inhibition of rheumatoid arthritis [12]. The structures of chemical constituents have been shown in **figure 2**.



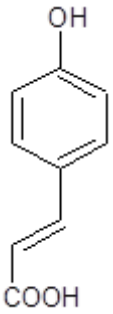
GALLIC ACID



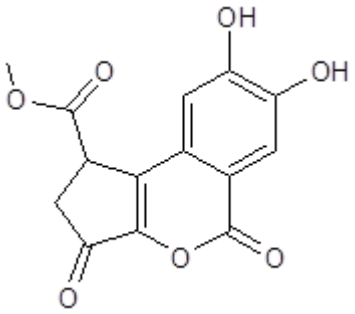
PYROGALLIC ACID



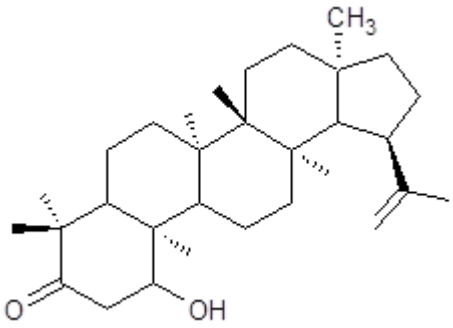
EPI-FRIEDELANOL



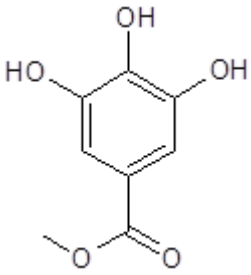
p- COUMARIC ACID



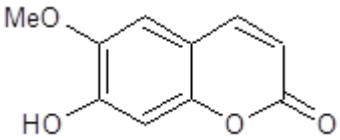
METHYL BREVIFOLIN



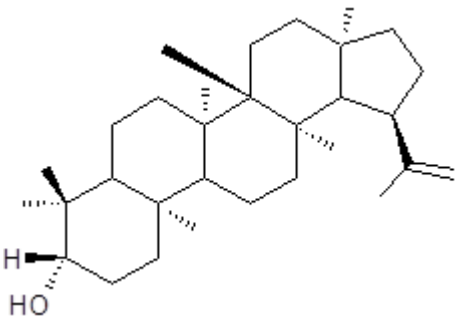
GLOCHIDONOL



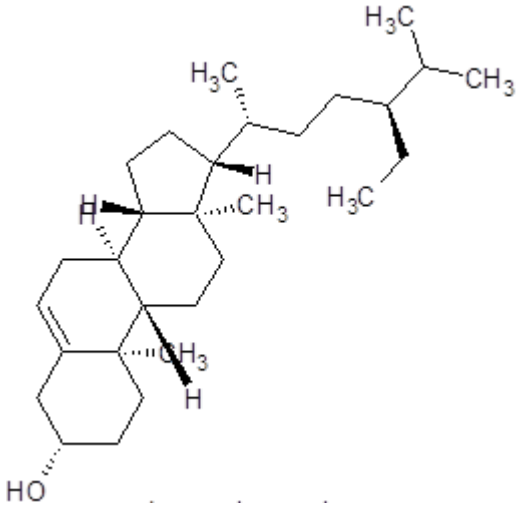
METHYL GALLATE



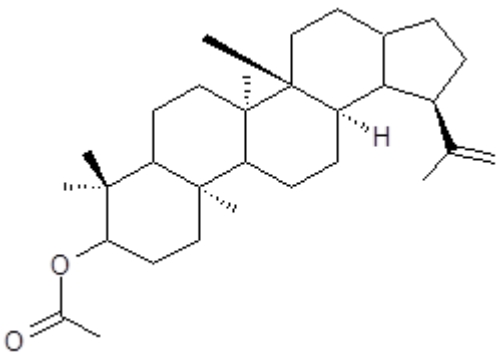
SCOPOLETIN



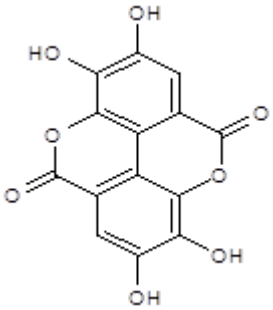
LUPEOL



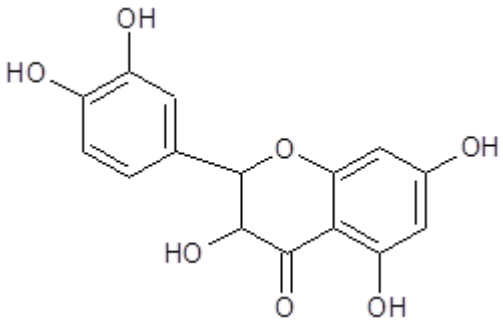
β-SITOSTEROL



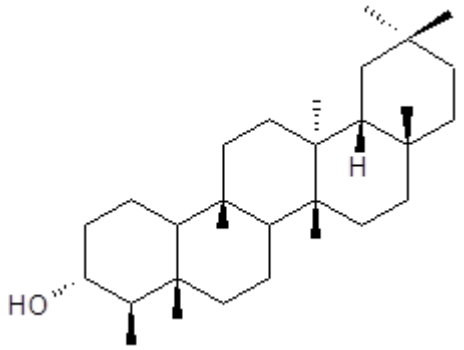
LUPEOL ACETATE



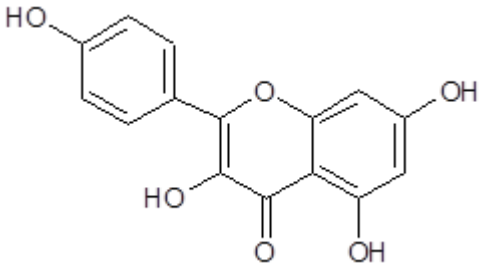
ELLAGIC ACID



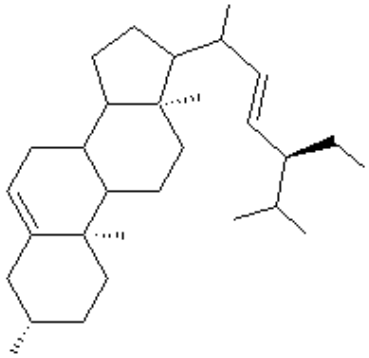
QUERCETIN



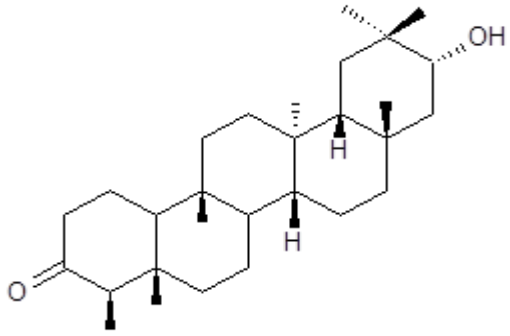
FRIEDELANOL



KAEMPFEROL



STIGMASTEROL



21 α- HYDROXYFRIENDELIN

FIGURE 2: STRUCTURES OF PHYTOCONSTITUENTS

Polyherbal formulation: 'Diabet' is the polyherbal formulation that has anti-diabetic activity. 500mg/kg dose of 'Diabet' showed anti-diabetic activity in alloxan induced diabetic rats using glibenclamide as standard drug. 'Diabet' also alters SOD, CAT, GPx and GSH enzymes to reduce oxidative stress [13-16].

Use as natural indicator in acid base titration: The pulp of the fruit is pH sensitive and thus showed pink colour in acidic conditions and yellow color in basic conditions. The fruit extract was used as indicator in acid-base titrations. The equivalence point was matched with the equivalence point obtained by standard indicators (Methyl red, Phenolphthalein, methylorange: bromocresolgreen (0.1:0.2) [17].

Traditional use of *Phyllanthus reticulatus* in different countries

West Africa: Wood is used for threshing sticks and roof binders. Ashanti people use interchangeably with *P. floribundus* for post-partum treatment using leaves boiled with palm fruit, juice of the stem is used for sore eyes and twigs are as chew sticks.

South Africa: Powder of leaves is applied locally to sores, burns, suppurations and chafed areas; twig is used as chew stick.

East Africa: Fruits are used as famine food. Roots and bark are used as red to black dye. Juice is blown into eyes for soreness. Root infusion is for gonorrhea and root decoction is used as a purgative and for hookworm.

Sudan: As diuretic, refrigerant.

Kenya: Bark is used as dye for tanning fishing lines.

Tanzania: Root decoction is used for dysmenorrhea. Whole plant is used in gonorrhea. Dried bark, leaves, aerial parts are used as diuretic, for intestinal hemorrhage and anemia. Fresh leaf juice is used for muscle spasms. Dried bark is used for dysmenorrhea, diarrhea with anal bleeding. Dried root bark is used for promoting fertility.

India: Dried bark and leaves decoction are as a diuretic, alterative and for cooling effect and also used for smallpox.

Sri Lanka: Bark decoction is used as an astringent and diuretic. Fruit is as astringent and also used for bowel inflammation.

Indochina: Used for smallpox, syphilis, bleeding gums.

Malay Peninsula: Stem and leaves are rubbed on chest for asthma, leaves decoction drunk for sore throat.

Philippines: Leaves and bark infusion as a diuretic, alterative, depurative, refrigerant, and odontalgic, applied to the abdomen for pinworms, fruit as an astringent to bowels and used against inflammations and blood diseases [18].

Pharmacological review of *Phyllanthus reticulatus*

1. **Antidiabetic activity:** Petroleum ether and ethanolic extracts of leaves of the *Phyllanthus reticulatus* was found to have antidiabetic activity in tribal area. The extracts were orally tested at 500 and 1000 mg/kg for hypoglycemic effect in alloxan treated mice. The extract showed antidiabetic activity at the dose of 1000 mg/kg [19].

2. **Antiplasmodial activity:** The leaves of *Phyllanthus reticulatus* were reported to have invitro antiplasmodial activity against chloroquine sensitive (K67) and chloroquine-resistant (ENT36) stains of plasmodium falciparum with IC50 ≤ 10 micrograms/ml [20].

3. **Hypocholesterolemic activity:** The aqueous extract of aerial parts of *Phyllanthus reticulatus* was shown to have hypocholesterolemic activity. Feeding of atherogenic diet increased serum cholesterol, triglyceride, LDL-cholesterol and HDL-cholesterol level, VLDL-cholesterol and protein carbonyl level when compared to normal group at over a period of 45 days.

   Administration of aqueous extract of *P. reticulatus* at 250 and 500 mg/kg showed statistically significant decrease in total cholesterol ($P<0.05$), VLDL-cholesterol ($P<0.001$), triglyceride ($P<0.001$), LDL-cholesterol ($P<0.05$), and protein carbonyl level ($P<0.05$) while increase in HDL-cholesterol level ($P<0.05$) as compared to hypercholesterolemic rats.

   The aqueous extract treated animals showed decrease in atherogenic index and increased percentage of protection at both the doses, i.e. 250 and 500 mg/kg [21].

4. **Antimicrobial activity:** The methanolic extract of stem bark of *P. reticulatus* was found to have antimicrobial activity. The antimicrobial activity was determined by disc diffusion method. The samples were dissolved separately in chloroform and applied to sterile filter paper discs at a concentration of 400 microgram/disc. Kanamycin disc (30 microgram/disc) was used as standard. The zone of inhibition produced by the pet ether, carbon tetrachloride and chloroform soluble fractions of methanolic extract ranged from 14-19mm, 14-20mm and 10-18mm, respectively [22].

5. **Cytotoxic activity:** Methanolic extract of stem bark of *P. reticulatus* was reported to have cytotoxic activity. DMSO solutions of the plant extracts were assayed for cytotoxicity against *Artemia salina* in a 1-day in vivo assay. The concentrations were obtained by serial dilution technique. The lethality of the pet ether, carbon tetrachloride and chloroform soluble fractions of the methanolic extract to brine shrimp was determined on *A. salina*.

   The LC_{50} obtained from the best-fit line slope were found to be 2.34, 3.89, and 1.99 microgram/ml for pet ether, carbon tetrachloride and chloroform respectively. In comparison with the positive contol (vincristine sulphate), the cytotoxicity exhibited by the pet ether and chloroform soluble fractions of methanolic extract was significant [23].

6. **Hepatoprotective activity:** Hepatoprotective activity of *Phyllanthus reticulatus* was evaluated using ethanolic extract of aerial parts of the plant. Two partially purified organic fractions designated by PR1 and PR2 of the fat free ethanol extract of aerial parts were tested for the hepatoprotective activity in rats against CCL_4 - induced liver damage.

   The rats showed promising hepatoprotective activity by significant changes of pentobarbital – induced sleeping time, changes in serum levels of sGPT, sGOT, sALP and bilirubin. Both the fractions (PR1 and PR2) were found to decrease the sleeping time elevated by CCl_4 due to the decrease of liver functionality. The action was more prominent in case of PR1 fraction [24, 30].

7. **Antibacterial activity:** The leaf extracts of *phyllanthus reticulatus* were investigated for Antibacterial activity. The methanol, chloroform, and hexane extract showed potential in vitro antibacterial activity. The extracts were studied for their susceptibility to gram-positive (*Staphylococcus aureus*) and gram-negative organisms (*Escherichia coli, Pseudomonas aeruginosa, and Salmonella typhi*).

   Antibacterial activity was determined by using agar well diffusion and broth dilution methods. The extract showed minimum inhibitory concentration and minimum bactericidal concentration at concentration of 100 to 6.25 mg/ml. Extracts showed zone of inhibition ranging from 9.07-30.18mm, 8.17-24.57 mm and 5.60-14.67 mm for methanol, chloroform and hexane extract respectively. Organisms were found to be more sensitive to methanolic extract [25].

8. **Antinociceptive and Anti-hyperglycemic activity:** Methanolic extract of leaves of *Phyllanthus reticulatus* have been reported to have antinociceptive and anti- hyperglycemic effect in mice. The methanol extract of leaves of *Phyllanthus reticulatus* showed significant antinociceptive activity when administered to mice in acetic acid-induced gastric pain writhing tests. Maximum inhibition of writhing (39.1%) was observed at an extract dose of 200 mg/kg body weight. The standard drug, aspirin, when administered at a dose of 200 mg/kg body weight inhibited writhings by 50.4%.

   The methanol extract of *Phyllanthus reticulatus* leaves exhibited dose-dependent and significant anti-hyperglycemic activity in glucose-induced hyperglycemic mice. Even at the lowest dose of the extract tested (100 mg/kg body weight) serum glucose levels were lowered by 18.4%. The maximum serum glucose lowering effect was found with the dose of 400 mg extract/kg body weight (35.0%) [26].

9. **Analgesic and Anti-inflammatory activity:** The extract of leaves of *Phyllanthus reticulatus* have been reported to have analgesic and anti-inflammatory activity. The petroleum ether, ethyl acetate, and methanol extracts were chosen for pharmacological screening.

   In the acetic acid-induced writhing test, the ethyl acetate extract at doses of 150 and 300 mg/kg showed 51.23 and 65.12% inhibition of writhing, respectively. A significant elongation of tail-flick time was evident both in the ethyl acetate and the methanol extracts (42.38 and 60.49%) only at the 300 mg/kg dose level. In carrageenan-induced rat paw oedema model, the methanol extract at the 300 mg/kg dose level showed 40.03% inhibition of oedema at the end of 4 h [27].

10. **Antioxidant activity:** The methanolic and ethanolic extract of entire plant has been proved to have antioxidant activity. Methanolic extract possessed higher activity as compared to ethanolic extract. The extract showed antioxidant activity by different invitro antioxidant assays, including 2, 2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging, β-carotene bleaching, superoxide anion radical scavenging, reducing power and metal chelating assay at different concentration (100, 200, 400mg/kg). Entire plant powder showed 90% antioxidant activity when compared with standard Butylated hydroxyl toluene (BHT) (85%) at a concentration of 400µg/ml [28].

11. **Anti-hepatitis B viral activity:** Two fractions (PR1 and PR2) of ethanolic extract at concentration of (20mg/ml and 40mg/ml) showed Anti-hepatitis B virus surface antigen (anti-HBsAg) activity by in vitro system using reverse passive haemagglutination method. Both the fractions were found to show anti- hepatitis B virus surface antigen (anti-HBsAg) activity. The activity was due to binding of the agents with the antibody binding sites present on HBsAg [29].

CONCLUSION: Necessity is the mother of invention. This dictum fully applies to the rural or primitive societies, which have to discover solutions to almost all their needs and problems from the natural resources around them. In recent years ethnomedicinal studies received much attention as this brings to light the numerous little known and unknown medicinal virtues especially of plant origin. In the present article, we have reviewed the relevant literatures to congregate the botanical, ethnobotanical, phytochemical and pharmacological information on *Phyllanthus reticulatus.*

A survey of literature revealed that the plant is having promising pharmacological activities. The analysis of literature also pin points the fact that although the number of diseases for which *Phyllanthus reticulatus* finds used as medicine is fairly large yet its therapeutic efficacy has been assessed only in few cases. In view of the wide range of medicinal uses of the plant, it is imperative that more clinical and pharmacological studies should be conducted to investigate unexploited potential of this plant.

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