ETHNOMEDICINAL, TRADITIONAL AND PHARMACOLOGICAL ASPECTS OF *Plumbago zeylanica* Linn.

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Summary

Plumbago zeylanica Linn.is distributed as a weed throughout the tropical and subtropical countries of the world. The herb has been used for hundreds of years as a traditional system of medicine. It possesses important activities like analgesic, antibacterial, antifungal, memory-inducing, anti-cancer, anti-inflammatory, hepatoprotective, larvicidal, anti-diabetic, anti-fertility, and immunosuppressive properties. The roots of *P. zeylanica* are also used as expectorant, anti-rheumatic, anti-scabies, appetite stimulant, anti-diarrhoeal, anti-periodic, anti-malarial and for the treatment of leprosy. Besides these the antioxidant value of this herbal plant has also been reported. These reports are very encouraging and indicate that herb should be studied more extensively for its therapeutic benefits.

Keywords: Plumbago zeylanica, pharmacological activities, IgG, ELISA, DPPH, NBT

Introduction

From the most ancient times, human beings have had a primal belief that plants contain healing powers[(1)].Herbs have proved themselves effective in treating every conceivable type of health problem in tens of millions of patients. Herbs are still the main system of health care for 80% of the world's population[(2)]. The rest 20% also depend substantially on plant based medicines[(3)].Medicinal plants are important to the global economy. In 1980, WHO estimated the world trade at US$500 million[(4)].The new patent policy under 'GATT', which came into force by the year 2005, has encouraged the herbal market.Traditional medicine is an important part of African culture. More than 80% of Africans rely on plant-based medicine. Latin Americans also relic on traditional medicines for their health care needs[(5)].

India is one of the richest countries of the world as regards genetic resources of medicinal plants. It has about 1500 species of flowering plants out of which about 17% are considered to be of medicinal value[(6)]. About 2500 plants have been reported to be used in ethno-medicine[(7)]. The Ayurvedic Drug Formulary prepared by Department of Indian System of Medicine lists 387 plants[(8)]. The Unani system of medicine describes 440 plants, out of which 360 are common to other systems practiced in the country[(9)].Plants are used medicinally indifferent countries and are a source of many potent andpowerful drugs[(4)].

The plant species *Plumbago zeylanica* (Plumbaginaceae), known vernacularly as Chitraka and popularly as Ceylon Leadwort, is distributed as a weed throughout the tropical and subtropical countries of the world. The genus *Plumbago* includes 3 species viz., *Plumbago indica* L.(P. *rosea* L.), *P.capensis* L., and *P. zeylanica* L., which are distributed in several parts of India[(10)].

This review article would be able to determine the proximate pharmacological activities of the whole plant of *P. zeylanica* Linn.

Plumbago zeylanica Linn. : The plant

Plumbago zeylanica Linn., commonly known as *Ceylon Leadwort* or *Doctorbush*[11]is a herb that grows wild in India and has been used by rural and tribal people since hundreds of years as a traditional system of medicine. It is native to SE Asia. It is much branched, evergreen shrub that reaches about 6 feet (2 meters) in height[12].The word comes from two Latin words*plumbum* (lead) and *agere* (to resemble), a 'leadlike ore', alluding to historical use as a cure for lead poisoning[13].

Botanical classification[14]

Domain : Eukaryota

Kingdom: Plantae

Subkingdom : Viridaeplantae

Phylum : Tracheophyta

Subphylum: Euphyllophytina

Infraphylum : Radiatopses

Divison : Magnoliophyta

Class: Magnoliopsida

Subclass: Caryophyllidae

Superorder : Plumbaginanae

Order : Plumbaginales

Plumbago zeylanica (flowers); Location: Kahoolawe, Uprange

Family : Plumbaginaceae

Subfamily : Plumbaginoideae

Tribe : Theeae

Genus: *Plumbago*

Species : *zeylanica*

Botanical name : Plumbago zeylanica

Synonyms[15, 16]

Arabia Shitaraj, Ensain, Enkin

Assamese Agiyachit, Agnachit, Boga agechita

Bengali Chita, Safaid-chitarak

Burma Kanchopphiju, Kinkhenphiu

Chinese Pai Hua T'eng

English White flowered leadwort, Ceylon leadwort

French Dentalaire

German Bleiwurz, Zahnkraut

Gujarati Chitrakmula

Hindi Chira, Chitrak

Indonesia Ceraka (Sumatra), Poksor (Jawa), Kareka (Madura), Oporie (Timor)

Kannada Chitramula, Chitramulika, Vahni, Bilichitramoola

Kashmiri Chitra, Shatranja

Malayalam Vellakoduveli, Thumpokkoduveli

Manipuri Telhidak angouba

Marathi Chitraka, Chitramula

Nepal Chitu

Oriya Chitamula, Chitoparu, Ogni

Punjabi Chitra

Phillipine Sagdikit (Tagalog), Talankaw (Iloc)

Sanskrit Chitraka,Agni, Vahni, Jvalanaakhya, Krishanu, Hutaasa, Dahana, Hutabhuk, Shikhi

Swahili Sanza

Tamil Chitramoolam, Kodiveli, Kanilam, Sittragam

Tswana Mosikomabe

Telugu Chitramulamu, Agnimata

Urdu Sheetraj Hindi, Cheetah, Chitalakhri

Macroscopy[17, 18]

Roots: Long; tuberous; 30 cm or more in length; 6 mm or more in diameter; outer surface smooth; including root stocks; reddish to deep brown; scars of rootlets present; disagreeable odour and acrid taste.

Powder (root): Light yellow; agreeable smell and bitter taste; rough texture.

Stem: Glabrous; climbing, prostate, or erect.

Bark: Thin; brown; internal structure striated; disagreeable odour; acrid taste.

Leaf: Simple; alternate; petiolate or sessile; ovate, lance-elliptic, spatulate or ovate-oblong blades; apex acute, acuminate or obtuse with entire or wavy margin; attenuate base; 7 cm in length, 3.8 cm in diameter; glabrous.

Flower: White to pale bluish white; arranged in terminal spikes; calyx is tubular, 12.5-28 mm in length; glandular-hairy; corolla tube is slender,17-33 mm in diameter, limb rotate and 5-lobed; stamens are 5 on a disc; style is slender with 5 stigmatic branches.

Fruit: Membranous capsule enclosed within the persistent calyx; 7.5-8 mm long; pale-yellow brown; with glue on the soft spines.

Seed: Reddish brown to dark-brown; apex acute.

Microscopy[19, 20, 21]

Roots:

Cork: T.S. of root showed outermost layer cork with 5-7 rows of light brown cells; cubical to rectangular in shape.

Secondary Cortex:2-3 rows of thin walled rectangular secondary cortex; light brown cells.

Cortex: Simple or compound cortex cells round with intercellular spaces; filled with starch grains.

Phloem: Small, polygonal and thin-walled; well-developed with phloem fibers; lignified with pointed ends and narrow lumen; yellow contents absent.

Cambium: Single-layered; tangentially elongated.

Xylem: Light yellow to whitish; xylem vessels arranged in single or radial rows with a length of 190.87µm,width 67.09µm, and wall thickness 5.6µm; fibers had a length of 318.71µm, width of 30.09µm and wall thickness 4.32µm; tracheids are also filled with starch grains; medullary rays are narrow.

Medullary ray: Single to multilayered loaded with simple to compound starch grains, radially elongated, stone cells absent.

Powder (root): Fragments of thin walled parenchyma cells with simple starch grains; spiral to helical elongated xylem vessels; phloem fibers; simple to compound starch grains; cork cells.

Leaves: Dicotyledonous organization; irregular in shape.
*Lamina:*One palisade layer; two to three spongy layers.
Vascular bundles: Horizontal.
Mesophyll: Idioblast cells were occasionally found in intercellular spaces containinglesser amount of tannins than *P. indica*.
Trichomes: Not found; an exception to that of *P. indica* which contains non-glandular trichomes in the outermost layer of stem.

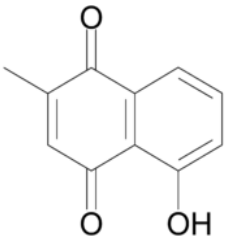
Phytochemistry

Constituents:

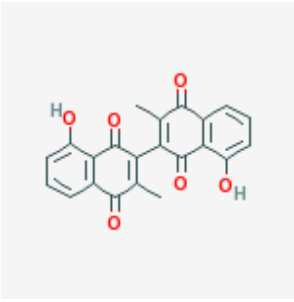
A raw phytochemical overview with thin layer chromatography of crude extracts showed the presence of alkaloids, phenols and flavonoids.

Roots:

Naphthoquinones—

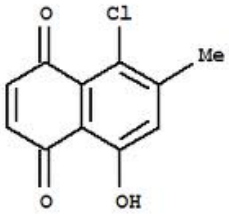


Plumbagin

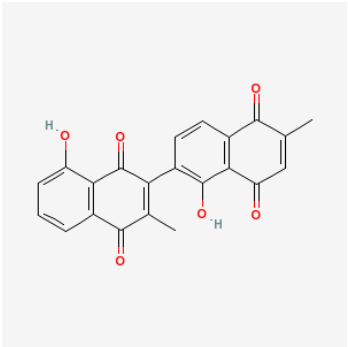


Biplumbagin

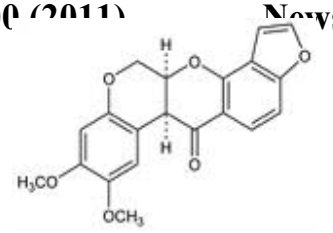
3-



Chloroplumbagin

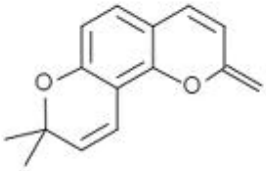


Chitranone

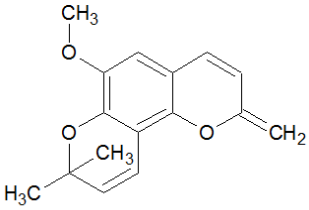


Elliptone

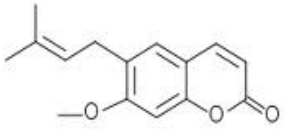
Coumarins—



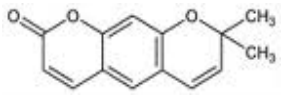
Seselin



5-methoxyseselin

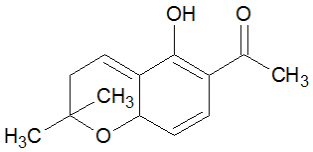


Suberosin

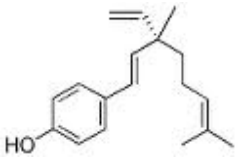


Xanthyletin

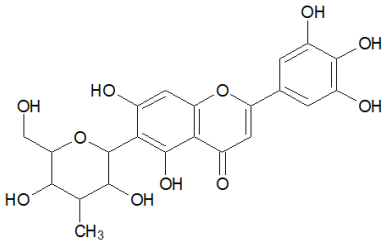
Other compounds—



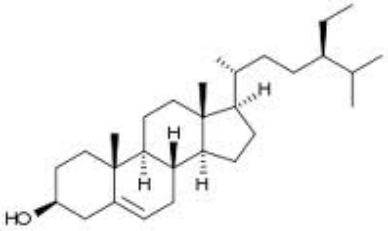
2,2-dimethyl-5-hydroxy-6-acetylchromene



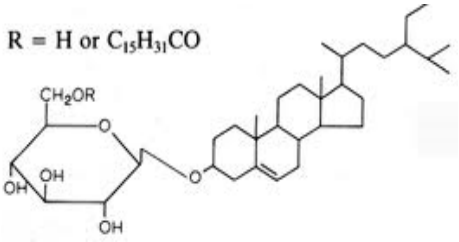
Bakuchiol



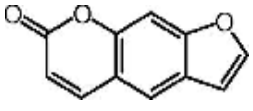
Isoaffinetin



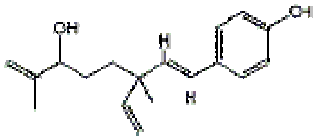
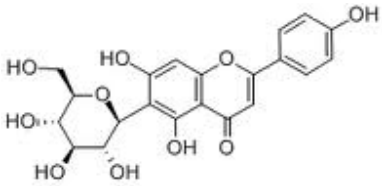
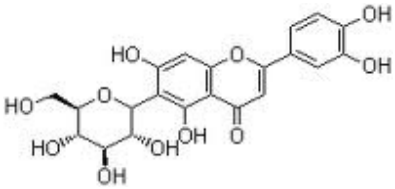
β-sitosterol



β-sitosteryl-glucoside



Psoralen

12-hydroxyisobakuchiol Saponaretin Isoorientin

Amongst all these compounds plumbagin is the major ingredient (5-hydroxy-2-methyl-1,4-naphthoquinone ($C_{11}H_8O_3$), with 1% in the whole plant, but with higher percentages in the root, crystallizing as slender orange coloured needles, soluble in organic solvents, less soluble in water, volatile with steam[22].

Ethnomedicinal / traditional uses

Traditionally *P. zeylanica* Linn. have several medicinal uses. The roots either in the form of paste, decoction or powders are used in filariasis, depigmentation of the skin, relieving constipation, treating non-bleeding piles, and in cleansing the uterus (abortifacient). The roots are also used as expectorant, anti-rheumatic, anti-scabies, appetite stimulant, anti-diarrhoeal, anti-leprotic, anti-periodic, anti-bacterial, anti-viral, anti-malarial, anti-oxidant[23].

Gastrointestinal diseases:

The Chinese believes that *P. zeylanica* has the ability to increase digestive heat with fire-like power. In Nepal, it is being used to treat dyspepsia, diarrhoea and haemorrhoids. In Ayurveda, the plant is recommended for removing worms, stimulating appetite, absorbing excess fluidsfrom the intestines, destroyingtoxins and as a digestive. In Mauritius and Rodrigues Islands, the inhabitants recognized theroots asa remedyfor diarhhoea and dyspepsia. Amongst theworms that succumb to it is the hookworm. In Ghana, the roots are applied as an enema for the treatment of haemorrhoids[24, 25, 27, 30, 32, 33, 35, 37, 38].

Respiratory diseases:

The Ayurvedic practitioners sometimes use the plant to treat cough and breathing difficulties. In Zimbabwe, an infusion of the roots is used for shortness of breath[25, 27].

Gynaecological and obstetrical diseases:

The Malays provide decoction of the plant on the third day postpartum. The leaves are eaten as a vegetable as a measure of delaying menstruation. Illicit induction of abortion is done by giving a decoction of the roots; a practice which should be frowned upon by the society. In Africa, the pulped roots or aerial parts are inserted into the vagina to induce abortion; an dangerous practice which could result in death[26, 27, 28, 29, 32, 36].

Genito-urinary diseases:

In Indonesia, the leaves are applied over the pubic region to help ease dysuria. The barks, roots or leaves are used to treat gonorrhea and syphilis[27, 30].

Inflammatory diseases:

In Ethiopia, the powdered bark, root or leaf is used to treat gonorrhea, syphilis, and tuberculosis. The Zambians make use of the roots boiled in milk as a remedy for inflammation of the mouth, throat and chest. In Himachal Pradesh, the natives use a paste of the roots to induce drainage of abscesses. In Indonesia, it is used as an anti-rheumatic remedy by local application over the affected site. However, it has to be used with great caution because of its vesicant effects on the skin[27, 30, 31, 33].

Skin diseases:

Decoction ofthe rootsis usedfor scabies. It is widelyused to treatvarious skindiseases including leprosy, ringworms, dermatitis, acne, sores and ulcers. Most of the time the roots are the part that is being used for skin problems. However, care must be taken as it can also cause skin irritation and vesicular eruptions. Dried and pulverized root is a remedy for parasitic

skin infestation. Paste of the root in vinegar, milk and water is used to treat influenza and blackwater fever in Africa[27, 29, 30, 33, 38, 39].

Other uses:

Extract of the roots is used to treat hypertension in a Malay community. A paste of the roots is applied behind the ear to help relieve headache. Another way of relieving headache is by applying the root paste in the palate. Tincture of the root bark is an antiperiodic and a sudorific. The root cooked with meat in a soup is considered an aphrodisiac amongst the Zimbabwe people[26, 27, 28, 30, 33, 34].

Pharmacological activities

Plumbago zeylanica plant is analgesic, anti-bacterial, anti-fungal, memory-inducing, anti-cancer, anti-inflammatory, hepatoprotective, larvicidal, anti-diabetic, anti-fertility, and immunosuppressive. The roots of the plant is used as an anti-oxidant.

Analgesic activity:

The ethanolic callus extract and root extract at dose 100, 200 and 400mg/kg were evaluated for peripheral and central analgesic activity by glacial acetic acid induced writhing. Root extract ($P < 0.01$) can reduce the writhing count at 200mg/kg whereas callus extract alters the pain threshold at 400mg/kg. Light creamish brown and granular callus formed with MS medium supplemented with naphthalene acetic acid (1.5 ppm) and kinetin (0.25 ppm) possessed peripheral analgesic activity[40].

Antibacterial activity:

The chloroform extract of *Plumbago zeylanica* L. root showed antibacterial activity against *Eschirichiacoli*(16.7±0.14 mm), *Salmonella typhi*(14.3±0.04 mm) and *Staphylococcus aureus* (12.0±0.54 mm). Moderate inhibition shown against *Klebsiellapneumonia* (9.2±0.73

mm), *Serratia marcescens*(8.6±0.07 mm) and *Bacillus subtilis*(8.0±0.61 mm), and lower against *Proteus vulgaris* (5.9±0.55 mm) and *Pseudomonas aeruginosa*(4.8±0.87mm). The methanolic extract exhibited moderate activity while aqueous extract has been found weak against the bacterial strains[41].

Antifungal activity:

Plumbagin, the chief constituent found in the plant, at the concentration of 100µg inhibits the growth of fungal pathogens *viz*., *Cladosporium cladosporioides*(28.2 cm^2), *Alternaria tunis*(12.5 cm^2), *Botrydiplodia theobromae*(12.5 cm^2), *Aspergillusniger*(12.5 cm^2), *Fusariumoxysporum*(7.1 cm^2), *Colletotrichum gloeosporioides*(5.4 cm^2) and *Cercospora nicotinae*(5.3 cm^2)[42].

Memory-inducing activity:

The effect of *P. zeylanica* roots was employed on scopolamine induced amnesia for learning and memory of mice. The chloroform extract of plant at dose 200 mg/kg has shown promising memory enhancing effect in mice. The extract significantly reversed the amnesia induced by scopolamine (0.4 mg/kg i.p.)[43].

Anticancer activity:

Anticancer evaluation of *Plumbago zeylanica* L. leaves against Ehrlich Ascites Carcinoma was done in animal model. Administration of the ethanolic extract of the leaves at concentration 200mg/kg reduced the tumour volume (3.42±0.082), packed cell volume (1.05±0.092) and viable tumour cell count % 10^7 cells/ml (4.85±0.23) in a dose dependent manner[44].

Anti-inflammatory activity:

The methanolic extract of *P. zeylanica* roots tested for its anti-inflammatory effects at 300 and 500 mg/kg concentrations produced 31.03% and 60.30% ($P \leq 0.01$) inhibition of acute inflammation. The test carried out in carrageenan (1 in 0.5% CMC) induced rat paw oedema

proved that methanolic extract of root is effective against acute inflammation (0.41±0.061 ml and 0.23±0.083 ml,respectively)[45].

Hepatoprotective activity:

Triterpenes and sterols found in *P. zeylanica* is effective against paracetamol-induced hepatic toxicity. The blood samples taken from animals treated with petroleum ether root extract of the plant at the dose 300 mg/kg body weight has a significant protection against paracetamol-induced hepatocellular injury[46].

Larvicidal activity:

The methanolic extract of *P. zeylanica* roots possesses larvicidal activity against two mosquito species, *Aedes aegypti* and *Anopheles stephensi*. The LC_{50} concentration against fourth instar larvae of *Aedesaegypti* and *Anopheles stephensi* was found to be 169.61±7.99mg/lit and 222.34±8.65 mg/lit, respectively[47].

Antidiabetic activity:

Oral administration of ethanolic root extract of *P. zeylanica*(100 mg, 200 mg/kg/p.o), tolbutamide (250 mg/kg/p.o) increased the activity of hexokinase and decreased the activity ofglucose-6-phosphatase ($P < 0.001$) in streptozotocin treated diabetic rats[48].

Antifertility activity:

The acetone and ethanolic extracts of the leaves of *P. zeylanica* were most effective in interrupting the estrous cycle of the rats ($P < 0.05$) at dose levels 200 and 400 mg/kg. The animals exhibited prolonged diestrous stage of the estrous cycle corresponding to a temporary inhibition of ovulation. The anti-ovulatory activity was reversible on discontinuation of treatment[49].

Immunosuppressive activity:

The aqueous root extract of *P. zeylanica*(1 mg) with ovalbumin (10 µg i.p.) exhibited the significant suppression of ovalbumin-specific IgG antibody response (0.025 O.D at 4 nm) in BALB/c mice determined by enzyme-linked immunosorbent assay (ELISA) with dilution factor 1:400 for 56 days ($P < 0.05$). The extract (2 mg) with ovalbumin (10 µg i.p.) also suppressed the anti-ovalbumin antibody response in dose-dependent manner (0.3 O.D at 490 nm)[(50)].

Antioxidant activity:

The isolation and spectral data for new flavonoid 2-(2,4-Dihydroxy-phenyl)-3,6,8 trihydroxy chromen-4-one from the roots of *P. zeylanica* were determined and the antioxidant activity was studied by free radical scavenging and superoxide radical scavenging methods. The antioxidant activity by DPPH was found to be 96µg/ml and by NBT as 4.6µg/ml which were greater than that of standard (quercetin) 45µg/ml by DPPH and 10 µg/ml by NBT assay[(51)].

Blood coagulation profile activity:

The structure of active principle of the plant is similar to that of vitamin K. The plant extract (2 mg/kg body weight) and napthoquinone (2 mg/kg body weight) given to individual groups were screened for its effect on bleeding time, clotting time, prothrombin time, platelet count and platelet adhesion in albino rats after 1-day, 15-day and 31-day treatment. the platelet adhesion was significantly decreased after plant extract and napthaquinone-treated animals in both with and without blood volume reduction after 15th as well as 31st day. Even at a lower dosage level (2 mg/kg body weight), the chronic P. zeylanica administration prolongs the bleeding time by altering platelet adhesiveness and the coagulation[(52)].

Antiallergic activity:

70% ethanol extract of *P. zeylanica* stems show ability to inhibit mast cell-dependent immediate allergic reaction. This is evidenced by the fact that the extract could inhibit systemic anaphylactic shock induced by compound 48/80 in mice, reduce homologous passive cutaneous anaphylaxis and skin reactions induced by histamine or serotonin in rats. In vitro, the extract

could reduce histamine release from rat peritoneal mast cells caused by compound 48/80 and antigen. It also markedly increased intracellular cAMP content of rat mast cells[53].

Abortifacient activity:

Treatment with powdered root of P. zeylanica during the first 7 days of pregnancy resulted in per implantationary loss together with loss of uterine proteins of 13,000; 19,000 and 26,000 and 75,000 Da molecular weights. For those given the root from day 6 to day 17 of pregnancy proteins of molecular weights 55,000 and 65,000 Da were absent. This shows that proteins of 13,000; 19,000; 26,000 and 75,000 Da influence implantations while those of 55,000 and 65,000 Da are required for maintenance of pregnancy[54].

Lipid metabolism activity:

Plumbagin was reported to reduce serum cholesterol and LDL-cholesterol by 53% - 86% and 61% - 91 % respectively; lower cholesterol/ phospholipid ration by 45.8%; elevates decreased HDL-cholesterol significantly in rabbits. It was also observed that plumbagin could prevent accumulation of cholesterol and triglycerides in liver and aorta and regressed atheroma plaques of thoracic and abdominal aorta. The treated rabbits excreted more faecal cholesterol and phospholipids[55].

Conclusion

This article briefly reviews the traditional knowledge, ethnomedicinal, pharmacological and therapeutic applications of the plant *Plumbago zeylanica* Linn. This is an attempt to compile and document information on different aspects of *P. zeylanica* and highlight the need for research and development.

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