



# A Review Of Its Medicinal Uses, Pharmacology, Phytochemistry And Toxicology Of *Plumbago Indica*

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## Abstract

The biggest genus of flowering plants in the Plumbaginaceae family is called *Plumbago indica* Linn. This plant is regarded as toxic and is used mostly for external applications to cure skin conditions. The root is thought to be the most active component of the plant. It is regarded as an emmenagogue, abortifacient, alterative, carminative, stimulant, tomachic, and vesicant. The root is used internally to improve menstrual flow, cleanse the blood, stimulate digestion, and induce abortion. Leprosy, rheumatism, paralysis, tumors, headaches, toothaches, hemorrhoids, and swollen glands can all be treated with a poultice made from the roots. A vesicant is created using the root-bark. The leaves are applied as a poultice to cure headaches and rheumatism.

Keywords: phytochemistry, pharmacology, anti-tumor, review, *Plumbago indica*

## INTRODUCTION

Traditional medical systems have used medicinal plants for centuries to treat various ailments [1]. According to WHO guideline. The biggest genus of flowering plants in the Plumbaginaceae family is called *Plumbago indica* Linn. This plant, formerly known as *Plumbago rosea*, may flourish in a variety of climates. One of the most significant medicinal herbs is *Plumbago indica*. Ayurveda, Siddha, Unani, and homeopathy all employ the upright or spreading, half-woody plant known as *Plumbago indica*. The Sikkim and Khasi highlands of India are where this species originated, and it has since nations including Sri Lanka [2]. The herbal medicines are a sustainable alternative solution for detoxification [3]. Traditional medical systems have used *Plumbago indica* Linn, a wild medicinal plant, for centuries [4].

*Plumbago indica* has wide range of pharmacological activities against many diseases. Currently plumbagin is mainly extracted from *Plumbago indica* roots [5]. As plant does not produce seeds, shoot cuttings are mainly used for the vegetative propagation [6]. This plant has a slow growth and take considerably long period of time for roots to be ready for medicinal purposes [7]. *Plumbago indica* rapidly

decline from their natural habitat due to over exploitation for commercial uses [8]. Normally distractive harvesting is done as the root system of this plant used in preparation of traditional medicines [9]. Therefore in vitro plant propagation methods are used as an alternate strategy for sustainable conservation and propagation of *Plumbago indica* .[10]

## DESCRIPTION

Kingdom	Plantae
Subkingdom	Tracheobionta
Class	Magnoliopsida
Subclass	Caryophyllidac
Superdivision	Spermatophyta
Division	Magnoliophta
Order	Caryophyllales
Family	Plumbaginaceae
Genus	Plumbago
Species	Indica



Fig 1: *Plumbago indica* flower

### Morphology

#### Macroscopic characters

*Plumbago indica* is perennial herb or small shrub grows well under warm tropical climate. These small shrubs are grown up to 1.0 – 1.5 m height and stem is erect, trailing or climbing. The stem is simple or branched from the base [11]. Leaves are about 10 cm in length, ovate-elliptic in shape, simple, having alternate arrangement with entire margin and exstipulated. Base of the leaf is tapering in to a short somewhat clasping petiole.[12]

Bisexual, regular and pentamery flowers are red in color and inflorescence on glabrous elongated spike or raceme which has 10-30 cm length. Flowers have ovate shaped 2-3 mm bracts and 8-9 mm long, tubular shape, glandular and red calyx. Five sepals are fused to form the calyx [13]. Five petals are fused in to 2.5 cm long, spreading, apiculate, tubular silverform corolla. Filaments of stamens are as long as the corolla tube. Anthers are exerted just beyond the throat. Ovary is superior, five carpellary, unilocular with basal placentation and one anatropous ovule. There are five stigmas on about 2.2 cm long style. Pollinated flowers form membranous circumscissile capsule which enclosed by persistent calyx [14]. *Plumbago* species show carnivorous behavior during flowering. Glands on *Plumbago* sepals produce resinous secretion that helps to capture small insects. *P. indica* is capable of producing Proteases in response to

the stimuli as insects or decomposing insects [15]. Fruit and seeds are not known in this species. Therefore vegetative propagation is the main propagation method, thus in nature this species shows a low genetic variability.[16]

## GROWTH AND DISTRIBUTION

Indian leadwort, also known as *Plumbago indica*, is a well liked traditional remedy in India as well as in several regions of Africa and Southeast Asia - particularly in areas with a sizable Indian population.

## MEDICINAL USES

The plant is regarded as an emmenagogue, abortifacient, alterative, carminative, stimulant, and vesicant. Excessive dosages are risky and can be fatal. The naphthoquinone plumbagin is the plant's main active ingredient. Leucodelphinidin, 6-hydroxyplumbagin, plumbaginol (a flavonol), and steroids (Such as - itosterol, stigmasterol, and campesterol) are other chemicals identified from the aerial portions. The pharmacological properties of plumbagin include antibacterial, anticancer and antifertility effects. The leaves' ethanol extract has anti-herpes simplex virus type 1 activity (HSV1). The root is used internally to improve menstrual flow, cleanse the blood, stimulate digestion, and induce abortion. Leprosy, rheumatism, paralysis, tumors, headaches, toothaches, hemorrhoids, and swollen glands can all be treated with a poultice made from the roots. A vesicant is created using the root-bark. To do this, extremely thin slices of the fresh root are cut and fastened to the skin. Similar to how they may be used on the forehead to treat headaches. The leaves are applied as a poultice to cure headaches and rheumatism [14].

## PHYTOCHEMISTRY

*Plumbago indica* is rich in different types of alkaloids, flavonoids, saponins, glycosides and tannins [15]. Plumbagin (5-Hydroxy-2-methyl-1, 4-naphthoquinone) is one of the naturally occurring bioactive organic compound which is isolated from roots of *P. indica* [16]. It is a simple hydroxy naphthoquinone which is commercially important for its broad range of pharmacological activities [17]. Plumbagin is yellow needle shaped crystals which is soluble in alcohol, acetone, chloroform, benzene, and acetic acid and slightly soluble in hot water. Plumbagin has melting point ranging 78-79°C. [18]

## PHARMACOLOGY STUDIES

### Anti - Cancer Activity

Plumbagin is an important naphthoquinone, mainly found in the roots of plant species from Family Plumbaginaceae are used in treatment of cancer [19]. A study was conducted on SK MEL 28 human melanoma cell lines and lymphocytes which were treated with different concentrations of plumbagin and plant root extract of *Plumbago indica*. Growth inhibition in a dose-dependent manner occurred by both when treated for 24 hours. SK MEL 28 cells showed a 50% cell proliferation inhibition at 84.74 µg/ml and 30.48 µg/ml when treated with plant root extracts and purified plumbagin respectively. Usually inhibition of proliferation occurs through mechanisms such as cell cycle arrest, DNA damage, apoptosis, and suppression of telomere and telomerase activity [20]. Nuclear morphology was analyzed quantitatively by staining and suggested that apoptotic cell death mechanism was more potentially involved in the anti-proliferative effect by plant root extracts compared to plumbagin. Furthermore, colony formation assay was also performed to compare the long-term effect of purified plumbagin and root extract on SK

MEL 28 cells. Although root extract treated cells showed lesser colony formation over 10 days compared to purified plumbagin treated cell.[21]

#### Anti – Microbial Activity

Tannins, ability to inhibit pathogenic activities, primarily fungal infections such as *C. albicans*, even at higher concentrations was observed. A higher antibacterial activity towards gram-positive bacteria. [22] Methanol extract of *P. indica* was tested using disc diffusion method for determining anti-bacterial properties against four-gram positive bacteria *Bacillus subtilis*, *B. megaterium*, *B. cereus*, *S. aureus* and seven-gram negative bacteria, *P. aeruginosa*, *E. coli*, *Shigella dysenteriae*, *Shigella sonnei*, *Salmonella typhi*, *Vibrio cholera*, *Salmonella paratyphi*. Methanol extract had been shown varying degree of zone of inhibition ranging from 7.0 to 14.0 mm at 250.0 µg/disc. Zone of inhibition was increased up to 17.0 to 25.0 mm when concentration of methanol extract in disc increase up to 500 µg/disc [65,66,67]. Methanol extract of *P. indica* 500 µg /disc showed a significantly high zone of inhibition (17 – 25 mm) for gram positive bacteria like *Bacillus cereus*, *B. megaterium*, *B. subtilis*, *Staphylococcus aureus* and zone of inhibition (18 - 23 mm) for gram negative bacteria like *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella paratyphi*, *S. typhi*, *Shigella dysenteriae*, *S. sonnei*, *Vibrio cholera*. [23]

#### Anti – Acne Activity

Among skin disorders, commonly presenting one is Acne which affects almost everybody during adolescence. This occurs due to increased production of sebum followed by infections caused by micro-organisms like *Propionibacterium acnes*, *Staphylococcus epidermidis* bacteria and fungi like *Malassezia furfur* [24]. The potential antimicrobial activity of the *Plumbago indica* in agar disc diffusion method was determined for the anti-acne activity with different concentrations of acetone extracts. Plant extract at concentration of 10 mg/ml showed largest zone of inhibition in all three micro-organism.[25]

#### Antioxidant Activity

Methanolic extract of roots of *P. indica* showed the presence of phenolic and non-phenolic compounds which are mainly responsible for anti-oxidant activity. *Plumbago indica* roots extract has active compounds which have the ability to donate hydrogen to free radicals. The IC<sub>50</sub> value for methanolic extract of *P. indica* roots was 79.1 µg/ml while that for reference ascorbic acid was 4.2 µg/ml. For anti-oxidant activity can also be measured by the reducing power potential. Reducing power of methanolic extract of *P. indica* roots have been evaluated by the transformation of Fe<sup>3+</sup> to Fe<sup>2+</sup> through electron transfer ability. The reductive activity of the extract increased with the increasing concentration of the extract and when compared with the standard ascorbic acid, it has substantial reducing power in *P. indica* root extract was confirmed [26].

#### Anti – Diarrheal Activity

Anti-diarrheal activity of *Plumbago indica* was observed using castor oil-induced diarrhea in mice Loperamide 3 mg/kg was used as positive control mice. Total number of 8.6 ± 1.20 feces for total latent period (1.24 ± 5.25 hour) was observed in mice treated with 500 mg/kg and Loperamide 3 mg/kg was used as positive control. Loperamide showed total number of feces (6.4 ± 1.151) for total latent period (1.35 ± 6.02 hour) [27]. Plumbagin prevents secretory diarrhea by inhibiting calcium-activated

chloride channels (CaCC) and cystic fibrosis transmembrane conductance regulators (CFTR) [28]. It significantly delayed intestinal motility and inhibited intestinal smooth muscle contractility without an evident impact on contractive frequency, indicating anti-diarrheal activity of *Plumbago indica*. [29]

### Anti - Fertility Activity

There are studies on anti-fertility activity of *Plumbago indica*. Anti-fertility activity of ethanolic extracts of *Plumbago indica* roots in combination with aerial parts of *Aerva lanata* was evaluated using anti-implantation, abortifacient, and motility of Albino rat spermatozoa (in-vitro) models. Ethanol extract of *Plumbago indica* roots was administered orally for pregnant albino rats during 10th -18th days of their pregnancy. The percentage of abortions at 400 mg/kg b/w was 70%. Anti-implantation activity was also measured by administering ethanolic extract orally to pregnant albino rats within 1st to 7th days of pregnancy. *Plumbago indica* showed 50% anti-implantation activity at 400 mg/kg b/w, while at lower concentrations no motility of rat spermatozoa within 60 seconds and no motility by 90 seconds at a concentration of 10% and 5%, respectively was recorded [30]. High concentration of *P. indica* roots (800 mg/kg) extract on fetuses of mice suggested 100% fetotoxicity effect causing poisoning or degenerative effects in a developing fetus or embryo [31]. This could lead to abortions or congenital abnormalities. Acetone extract of stems and acetone and ethanol extract of leaves of *Plumbago indica* also showed a temporary and reversible modification of the estrous cycle in rats when administered orally by prolonging the diestrus phase. Acetone extract of stems and acetone and ethanol extract of leaves of *Plumbago indica* was exhibited estrogenic activity by increasing in diameter of the uterus, uterine weight, and thickness of the endometrial epithelium. According to literature, flavonoids and plumbagin compounds found in *Plumbago indica* are known to exhibit antifertility activity [32]. When stems of *P. indica* were studied on estrous cycle at two dose levels, 200 and 400 mg/kg respectively using acetone extracts showed antifertility activity was shown in female Wistar rats [33]. A significant estrogenic activity was observed only when given together with ethinyl estradiol, the estrogenic activity produced by ethinyl estradiol causing an increase in the uterine wet weight.[34]

### Analgesic and Anti – Inflammatory

A significant inhibition in the Carrageenan induced paw oedema at those of 300 mg/kg body weight was observed in comparison to the control group which was given standard drug Indomethacin. Inhibition of writhing scores for *Plumbago capensis* and *Plumbago indica* against 1% acetic acid were 67.32% and 70.29% respectively and Eddy's hot plate method exhibited an index of analgesia of about 68.29% and 45.2% respectively for *Plumbago capensis* and *Plumbago indica*. Additional studies are required by using more animals and to isolate the mechanism responsible for this pharmacological activity .[34]

### TOXICOLOGY

It is reported that, Plumbagin causes side effects including diarrhea, skin rashes, leukocytosis and increased serum phosphatase levels when high concentrations were administered to mice [35]. Therefore, toxic effect of the extract should evaluate to identify the safe dose for treatments. Mice administered extracts through oral route showed high tolerance than intraperitoneal administration. The LD50 of the extract by oral route was 1148.15 mg/kg and intraperitoneal administration was 239.88 mg/kg. Dark spots on liver, green color thyroid, increased weight of spleen and reduction of weight of liver, thymus, testes and kidneys were observed in male rats. Female rats showed a weight loss of thymus and increased weight in uterus on autopsy [36]. Cytotoxic activity of methanolic extract of *Plumbago indica* was evaluated by using brine shrimp lethality assay and LD50 was reported as 4.57 µg/ml [37]. GSH is non-

enzymatic intracellular antioxidant which oxidized in to GSSG during oxidative stress. Plumbagin and *Plumbago indica* L. extract induce oxidant - anti oxidant imbalance in liver by depleting the hepatic GSH content while the hepatic GSSG content was increased. This increased hepatic oxidative stress causes chronic inflammation and cellular injury in liver.[38]

## CONCLUSION

General *Plumbago* has a wide range of medicinal properties. Among them, *Plumbago indica* contain vast range of phytochemical compounds that help to cure different kind of diseases in human and other animals. *Plumbago indica* is widely used in Ayurveda, Siddha, Unani, and Homeopathy like traditional systems of medicine and currently subjected to different experimental research to find out its curing ability on cancer. Demand for dry *Plumbago indica* plant parts have increased dramatically over past few decades. Therefore, it is rapidly declining from their natural environment due to over exploitation for commercial uses. This plant is not produced seeds and has slow growth. Introduction of suitable propagation method will help to preserve it in their natural environment as well as it'll enough supply of raw materials for medicinal preparations. This article included scientifically proven data about its propagation, photochemistry and biological activities to encourage the future studies.

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