

**A REVIEW ON PHARMACOLOGICAL PROFILES OF  
*Plumbago indica* L. AND *P. zeylanica* L.**

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(REVIEW ARTICLE)

*Plumbago indica* L. (known as Pink Doctorbush) and *Plumbago zeylanica* L. (also known as Doctorbush) are shrubby, widely distributed throughout the tropical and sub-tropical regions of the world. The literature reveals their wide range of applications in traditional system of medicines against various diseases, as antiinflammatory, anti-malarial, anti-fertility, anti-microbial, anti-oxidant, wound healing, memory enhancer and anti-cancer. The therapeutic uses of the plant have been attributed to the presence of number of bioactive compounds, such as elliptinone, zeylanone, sistosterol and plumbagin.

Atharveda (around 1200 BC), Charak Samhita and Sushrut Samhita (1000-5000 BC) are the main classics that give detailed description of over 700 herbs. India has about 45,000 plant species. According to the World Health Organization (WHO), approximately 80% of the world's population currently uses herbal traditional system of medicine for their primary health care. *Plumbago zeylanica* L. (chromosome number  $2n=24$ ) is a multipurpose medicinal herb of family Plumbaginaceae. *P. zeylanica* is the most common plant used in Indian traditional system of medicine. A native of South Asia, the species is distributed throughout most of the tropics and

subtropics; growing in deciduous woodland, savannas and scrub lands from sea level up to 2000 m. altitude [Vijber (1971); Aditi G (1999); Vishnukanta (2010)]. The root is used as laxative, expectorant, astringent, abortifacient and in dysentery. Tincture of root bark is used as antiperiodic. The leaves are caustic and used in treatment of scabies. *Plumbago* are chemically characterized by the presence of naphthoquinones, flavonoids, terpenoids and steroids, many of them being responsible for several biodynamic activities. Popular name of *Plumbago zeylanica* is lead wort. This plant is also known by several names in different parts of the world. In India its common name is "Chitrak".

#### PHYTOCHEMISTRY

**Stem:** Stem contain plumbagin, zeylanone, isozeylanone, sitosterol, stigmasterol, campesterol, and dihydroflavinolplumbaginol.

**Leaves:** Leaves contain plumbagin, chitanone.

**Flower:** Flowers contain plumbagin, zeylanone, and glucose.

**Fruit:** It contains plumbagin, glucopyranoside and sitosterol.

**Seeds:** Seeds contain plumbagin.

**Roots:** The root bark of *P. indica* and *P. zeylanica* contain plumbagin. The root yield new pigment, viz, 3-chloroplumbagin, 3, 3- biplumbagin, binaphthoquinone identify as 3', 6'-biplumbagin, and four other pigments identify as isozeylanone, zeylanone, elliptinone, and

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droserone 2, 3. The isolation of plumbagin, droserone, isoshinanolone and a new naphthalenone i.e., 1, 2 (3)-tetrahydro-3, 3'plumbagin is reported from the phenolic fraction of the light petrol extract of the roots. Two plumbagic acid glucosides; 3'-o-beta-glucopyranosyl plumbagic acid and 3'-o-beta- glucopyranosyl plumbagic acid methyl ester along with five naphthaquinones (plumbagin, chitranone, maritnone, elliptinone and isoshinanolone), and five coumarins (seselin, methoxyseselin, suberosine, xanthyletin and xanthoxyletin) were isolated from the roots [Lin *et al.*, (2003)].

### PHARMACOLOGICAL ACTIVITIES

The plant *P. indica* L. and *P. zeylanica* L. exhibits large numbers of pharmacological activities:-

#### 1. Anti-inflammatory activity

Plumbago species are one of the most important medicinal plants which are used for anti-inflammatory diseases. The root of *P. zeylanica* extracted with methanol was used for determining the anti inflammatory effects. The methanolic extracts at 300 and 500 mg/kg produced 31.03% and 60.3% inhibition of acute inflammation, respectively, in Carrageenin induced raw paw oedema confirming that *P. zeylanica* roots are effective against acute inflammation. Sheeja *et al.*, (2010) studied the anti-inflammatory of various leaf extracts of *P. zeylanica* using *in vivo* experimental models. The acetone extract significantly ( $p < 0.01$ ) reduced inflammation in the carrageenan induced rats when compared to the control group. Yedapo (1996) investigated the phosphate buffered saline extract of the roots of *P. zeylanica* for anti-inflammatory activity. The plant has been used for anti-inflammatory properties.(Oyedapo (1996); Reddy *et al* (2002). Three medicinal plants namely *Phyllanthus emblica*, *P. zeylanica* and *Cyperus rotundus* were used to analyse two models of acute inflammation and result showed that *P. zeylanica* reduce the oedema while the combination of *P. emblica* compared to aspirin. (Dang *et al.*, 2011) Also *P.zeylanica* brought to suppress the activation of NF-kappa B in tumor cells and prevented Graft Versus Host Disease induced mortality in mice (Checker *et al.*, 2009).

#### 2. Lipid metabolism activity

Plumbagin (2-methyl-5-hydroxy, 1:4naphthoquinone) isolated from the roots of *P. zeylanica* when administered to hyperlipidaemic rabbits, reduced serum cholesteroland. Plumbagin was reported to reduce serum cholesterol and LDL-cholesterol by 53%-86% and 61%-91% respectively; lower cholesterol/phospholipid ratio by 45.8%; elevates decreased HDL-cholesterol significantly in rabbits [Alpana Ram (1996)].

#### 3. Wound healing activity

The wound healing activity of *Plumbago indica* and *Pzeylanica* was investigated by Devender Rao Kodati *et al* (2011) and Reddy *et.al.*, (2002) in rat. Significant wound healing activity of methanolic root extract of *Plumbago zeylanica* was observed.

#### 4. Antidiabetic activity

Olagunju *et al.*,(1999) investigate antihyperglycemic effect of *P. zeylanica* on induced diabetic animals.Zarmouh *et al.*,(2010) shows that 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 of glucose-6-phosphatase ( $P < 0.001$ ) in streptozotocin treated diabetic rats. Christudas Sunil and *et al.*,(2012) also evaluated the antidiabetic effects of plumbagin isolated from *P. zeylanica* root and its effect on GLUT4 translocation in STZ-induced diabetic rats.

#### 5. Memory-inducing activity

Mittal *et al.*,(2010) reported the effect of *P. zeylanica* roots 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.).

#### 6. Antifertility activity

Some worker reported that *Plumbago indica* and *P. zeylanica* treatment during first 7 days of pregnancy abolished uterine proteins of 13000, 19000 and 26000 and 75000 Da molecular weights resulting in preimplantation loss. Proteins having molecular weights 55000 and 65000 Da were absent in aborted rats, that were given *Plumbago indica* and *P. zeylanica* root powder since day 6 to day 17 of pregnancy Devarshi *et al.*, (1991). In another study, Inclusion complex of plumbagin with hydroxyl propyl betacyclodextrin (HPBCD) was prepared with a view to increase the efficacy and solubility. The complex was entrapped in the aqueous layer of niosomes and evaluated for antifertility activity. Given intraperitoneally, at a dose of 5 mg/kg the niosomes of the complex showed promising antifertility activity when compared to the control and niosomes with lipid layer entrapment D' Souza *et al.*, (1998).

#### 7. Anti-viral activity

Chen *et al.*,(2007) examined the antiviral activities of the 80% methanolic extracts of *Plumbago indica* and *P. zeylanica* against coxsackievirus B3 (CVB3), influenza A virus and herpes simplex virus type 1 Kupka (HSV-1) using cytopathic effect (CPE) inhibitory assays in HeLa, MDCK, and GMK cells, respectively. The antiviral activity of the most active compound was confirmed with plaque reduction assays. *Plumbago zeylanica* L had marked inhibition effects on HBeAg and HBsAg which is expressed by cells. In addition, CVB3 was inhibited by the extracts of *Plumbago indica* and *P. zeylanica* Marian *et al.*, (2006).

#### 8. Anti-bacterial activity

The alcoholic extract from roots of *Plumbago zeylanica* was tested against multi-drug resistant of clinical origin (*Salmonella paratyphi*, *Staphylococcus aureus*, *Escherichia coli*

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and *Shigella dysenteriae*) Abdul K *et al.*, (1995). The chloroform extract of *Plumbago indica* and *P. zeylanica* L. root showed antibacterial activity against *Escherichia coli* (16.7,0.14 mm), *Salmonella typhi* (14.3,0.04 mm) and *Staphylococcus aureus* (12.0,0.54 mm). Moderate inhibition is shown against *Klebsiella pneumonia* (9.2,0.73mm), *Serratia marcescens* (8.6,0.07 mm) and *Bacillus subtilis* (8.0,0.61 mm), and lowest against *Proteus vulgaris* (5.9,0.55mm) and *Pseudomonas aeruginosa* (4.8,0.87mm). The methanolic extract exhibited moderate activity while aqueous extract has been found weak against the bacterial strains [Jayachandran *et al* (2009)].

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### 10. Anti-oxidant activity

Antioxidant effects of the aqueous/alcoholic extracts of root, corresponding to medicinal preparations, and the active ingredient, plumbagin, were studied by Tilak *et al.*, Methods used included: ferric reducing/antioxidant power (FRAP), radical scavenging of 1,1-diphenyl-2-picryl hydrazyl (DPPH) and 2, 2'-azobis-3- ethylbenzthiazoline-6-sulfonic acid (ABTS), lipid peroxidation in rat liver mitochondria induced by different agents, and estimating phenolic and flavonoid content. In FRAP/DPPH assays, boiled ethanolic extracts was the most effective, while in the ABTS assay boiled aqueous extracts was the most efficient. These extracts also significantly inhibited lipid peroxidation induced by cumene hydroperoxide, ascorbate-Fe<sup>2+</sup> and peroxy nitrite and contained high amounts of polyphenols and flavonoids. In conclusion, various studies reveal that extracts of *Plumbago indica* and *P. zeylanica* and its active ingredient plumbagin have significant antioxidant abilities that may possibly explain some of the reported therapeutic effects. The isolation and spectral data for new flavonoid 2-(2,4-Dihydroxy-phenyl)-3,6,8 trihydroxy chromen-4-one from the roots of *Plumbago indica* and *P. zeylanica* were determined and in the other studies carried out by Nile *et al.* (2010) the antioxidant activity was studied by free radical scavenging and superoxide radical scavenging methods.

### 11. Anti cancer activity

It was observed that the plant *Plumbago indica* and *P. zeylanica* show anti cancer activity against various cancer cell lines. Sachin Hiradeve *et al.* carried out the preliminary phytochemical screening and anticancer evaluation of *Plumbago indica* and *P. zeylanica*

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against Ehrlich Ascites Carcinoma in animal model. They observed that the ethanolic extract of *Plumbago indica* and *P. zeylanica* possess significant anticancer activity and also reduce elevated level of lipid peroxidation due to higher content of terpenoids and flavonoids.

Zhao YL and Lu DP investigated the effects of plumbagin on the proliferation, cell cycle and apoptosis of APL cell line NB4 Cells. The results demonstrated that 2-15 micromol/L plumbagin inhibited the proliferation of NB4 cells in a dose-dependent manner. The morphologic changes of cell apoptosis, such as chromosome condensation and apoptotic body formation, were observed by light microscope and transmission electron microscope. Cell cycle analysis showed that NB4 cells were blocked in G2/M phase of cell cycle. Plumbagin induced annexin V+/PI- cell increase and DNA fragmentation. There was a correlation between cell apoptosis rates and the concentrations of plumbagin in dose-dependent manner ( $P < 0.05$ ). The study show that plumbagin can inhibit cell proliferation, block cell cycle and induce apoptosis of APL cell line NB4 cells.

Nguyen *et al.* isolated betasitosterol, beta-sitosteryl-3beta-glucopyranoside, beta-sitosteryl-3beta-glucopyranoside-6'-Opalmitate (1), lupenone, lupeol acetate, plumbagin and trilinolein from the dichloromethane extract of aerial parts of *Plumbago zeylanica*. Compound 1 showed cytotoxic activity against MCF7 and Bowes cancer cell lines (IC<sub>50</sub> 113 microM and 152 microM, respectively), beta-sitosterol inhibited Bowes cell growth (IC<sub>50</sub> 36.5 microM) and plumbagin was cytotoxic against MCF7 and Bowes cells (IC<sub>50</sub> 1.28 microM and 1.39 microM, respectively).

Anticancer evaluation of *Plumbago zeylanica* L. leaves against Ehrlich Ascites Carcinoma was done by Hiradeve S 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 % 107 cells/ml (4.85,0.23) in a dose dependent manner Hiradeve *et al.* (2010).

### 12. Larvicidal activity

Barasa M Maniafu *et al.* (2009). tested three *Plumbago spp.* for mosquito larvicidal activity. The crude extracts exhibiting the highest larvicidal activity against gambiae were hexane and chloroform extracts from *Plumbago indica* and *P. zeylanica* exhibited LC<sub>50</sub> 6.4 and 6.7 µg/ml respectively.

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