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## A Comprehensive Review on Anti-Inflammatory Activity of The Traditional Plants *Plumbago zeylanica* (Chitra)



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### ABSTRACT

Medicinal plants have long been utilised as a source of medicine and are in high demand throughout the world. They've been around for a long time, and they've been utilised to cure and prevent ailments. *Plumbago zeylanica* is a medicinal plant that is frequently utilised for its medicinal properties. It contains several bioactive compounds like naphthoquinones, flavonoids, alkaloids, glycosides, steroids, tri-terpenoids, tannins, fixed oils, fats, proteins, etc. among all plumbagin is most important bioactive compounds. It possesses wide range of pharmaceutical activities such as anti-inflammatory, antimicrobial, anti-cancer, anti-ulcer, antidiabetic etc. Several investigations on its pharmacological activity have been conducted. The goal of this review is to provide a comprehensive understanding of *P. zeylanica*'s chemical composition and pharmacological action.



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## 1. INTRODUCTION

Inflammation is a temporary biological reaction of tissues to adverse stimuli such as injury, exogenous and endogenous antigens, with the goal of clearing or eliminating the stimulus and repairing the wounded tissue, eventually leading to regeneration and return to equilibrium. Although inflammation is a beneficial defense mechanism for the body, it has long been recognized as the root cause of a variety of diseases, including diabetes, allergies, atherosclerosis, obesity, cancer, and pain. Furthermore, inflammatory dysregulation that leads to chronic diseases contributes to rising health-care costs [1, 2]. The mode of action for inflammation is similar for all and having specific symptoms of inflammatory action that enhances the flow of blood and increased the cellular metabolism, vasodilation, soluble mediators releases, fluids extravasation and influx by cellular means instead of triggering cause [3]. When an inflammatory agent is present, cell membranes activate phospholipase A<sub>2</sub>, give the deleveriance of arachidonic acid and other inflammation mediators like cytokine, histamine, prostaglandin, and leukotrienes, which increase vascular permeability and allow leukocytes to migrate to the site of inflammation that enhances the permeability of vascular and allow leukocytes to migrate to the site of inflammation [4, 5]. At the initial stage of inflammation, the leukotrienes, prostaglandins, and histamine binding occur to the respective receptors on the endothelial cells, resulting the vasodilation and contraction of the endothelial cells and enhancement in its permeability of blood vessels. On endothelial cells that line the venules, histamine causes an increase in P-selectin (a cell adhesion protein) and platelet-activating factor (PAF). The results of P-selection and PAF bind is the occurrence of extravasion and binding occur to the leukocyte following its migration to the chemotactic chemicals like complement protein C5a and leukotriene B<sub>4</sub> that produces at the injury location of the cells. On other there is activation of macrophages and endothelial cells which releases the inflammation in cytokines like TNF and IL-1, results binding of receptors on the endothelial cells maintain the inflammation responses by up regulation of the adhesion molecules E-selecting and also maintains the P-selectin expression. The leukocyte attaches with E-selecting and moving via basement membrane for searching the chemokine's that are result of infection cells like IL-8 and monocyte chemotactic protein-1 (MCP-1) [1, 4, 5]. The reason inflammation can be various and if there is presence of inflammation in the body the body reacts at high level of biomarkers. The immune reaction when triggered by the physical parameters inflammation occurs in the body. There is not necessary that if inflammation occurs there is any type of infection in the body but if there is infection can cause the

inflammation. Treatment for inflammation depends upon the severity and type of inflammation as there is number of anti-inflammatory chemicals that helps in treating the disorders related to the inflammation. Sometimes if not treated in a proper manner can become life threatening as some infection entered into the blood and cause sepsis. Inflammation is taken as the protective response in the body for elimination of foreign stimuli. Number of herbal supplements helps in managing the inflammation including numerous medicinal plants and their constituents used traditionally all over the world to cure disorders of inflammation related to lungs and skin. Natural anti-inflammatory agents are some essential oils and their isolated constituents like monoterpenes that helps in searching the bioactive natural compounds against inflammation and their reported actions are mentioned below. The testing for confirmation in the results of anti-inflammatory agents mostly completed on the rates by keeping all the ethics in consideration and without harming them other models used for testing are carrageenan, formalin, and arachidonic acid for producing paw edema and also the in vivo and vitro protocols including the essential oils or monoterpenes [6]. The term pharmacognosy has been obtained from the Greek words *pharmacon*, which means drug or medicine, and *gnosis*, which means knowledge. In 1895, C.A. Seydler coined the word "analectapharmacognosia" in his dissertation "Analectapharmacognosia." Herbal remedies are effective in treating a variety of ailments and have been used in health care for decades as a traditional medicinal system for maintaining and healing human health [7, 8].

In Ayurveda and Siddha, it was estimated that roughly around 1500 and 1200 species respectively are being used in the preparation of drugs for treating number of disorders. This Indian traditional medicine system used for decades and has proof of numerous successful outcomes and in practice for a long time but there is a lack of standardization related to the identification of crude drugs, their preparation procedures, and the quality of the final product. Recently pharmacognostical studies has been carried out on large number of plants viz. *Astercantha longifolia*, *Andrographis paniculata* [9], *Butea monosperma* [10], *Catheranthus roseus* [11], *Pedaliium mures* [12], *Ageratum conyzoids* [13], *Barleria prionitis*, *Phyllanthus spp.* [14], *Pogostemon* [15], *Salvia* [16], *Mentha spp.* [17], *Thymus spp.* [18], *Hibiscus sabdaritta* [19], *Rosmarinus spp.* [20], *Ocimum spp.*[19, 21], *Vasakhanda kushmandaka* [22], *Adhatoda vasica* [23-30].

## 2. MORPHOLOGICAL DESCRIPTION

The *Plumbago zeylanica* is commonly known as Ceylon leadwort, Chita, Chitra and Chitramoolam. *P. zeylanica* Linn (Plumbaginaceae) is perennial, sub-scandant shrub one of the common plants used in Indian traditional system of medicine **Figure 1**. The family Plumbaginaceae consists of 10 genera and 280 species. The genus Plumbago includes 3 species, namely *Plumbago indica* (*P. rosea*) *Plumbago capensis* and *Plumbago zeylanica*, which are distributed in several parts of India. Among these species; *P. zeylanica* grows all districts of plains in Andhra Pradesh, Karnataka, Maharashtra etc. common, wild or in cultivation due to its more therapeutic uses and the flowering tops of the *P. zeylanica* is showing in **Figure 2** [31].

Botanical classification of *P. zeylanica*

<b>Kingdom</b>	Plantae
<b>Order</b>	Caryophyllales
<b>Family</b>	Plumbaginaceae
<b>Genus</b>	Plumbago
<b>Species</b>	<i>P. zeylanica</i>

**Figure 1.** Botanical classification of *P. zeylanica*

The root is used as laxative, expectorant, astringent, abortifacient, and in dysentery[32]. Tincture of root bark is used as antiperiodic. The leaves are used as aphrodisiac and in scabies. Its roots are used in traditional system of medicine to cure various ailments like body pain, headache, fever and inflammation[33]. *P. zeylanica* roots were reported to possess antioxidant, hypolipidemic, anti atherosclerotic, central nervous system stimulant and anti-fertility properties [34, 35].



**Figure 2.** Fresh flowering top of *P. zeylanica*

*P. zeylanica* is a subscaudent, pretty perennial shrub with semi woody stems and numerous branches. Its leaves are simply alternate, ovate, narrowed into petiole, oblong-lanceolate and acute. Its flowers are borne in spikes, whereas the rachis of the spike is pubescent or glandular. The Corolla white tube is long and slender. The roots are cylindrical and are irregularly bent having transverse shallow fissures at bents. Its fruits are oblong and its capsules are enclosed by persistent viscid calyx [14, 32].

### **3. PHYTOCHEMICAL PROFILE**

Earlier chemical examination of this plant revealed that the root contains plumbagin, 3-chloroplumbagin, 2,3- biplumbagin, 6,6- biplumbagin, zeylinone, isozeylinone, chitranone (3, 3'-biplumbagin), droserone, plumbagic acid, plumbazeylanone, glucose, fructose, enzymes as protease and invertase. The leaves and stem contain little or no plumbagin. The aerial parts contain naphthoquinones, sitosterol, lupeol, lupenylacetate, hentriacontane, and amino acids. Plant contains naphthaquinones, plumbagin, chloroplumbagin, droserone, zeylinone, isozeylinone, plumbagic acid, plumba-zeylanone, naphthelenone, isonaphthelenone, isoshinanolone [14, 36]. Aspartic acid, tryptophan, tyrosine, threonine, alanine, histidine, glycine, methionine, hydroxyproline, were isolated from the aerial parts [37].

### **4. PHARMACOLOGICAL PROFILE & ETHNOPHARMACOLOGICAL USES**

All parts of the plant have been used in Ayurvedic and Unani medicine to treat anaemia, rheumatoid discomfort, sprains, dysmenorrhea, carbuncles, fleabites, leprosy, internal injuries of the extremities and intestinal parasite eradication. Some of the potential healing properties of the plant's roots and ingredients are antiatherogenic, cardiogenic, neuroprotective, and central nervous system stimulating [38]. Several investigations have shown that *P. zeylanica*

possesses antidiarrheal, antiallergic, insecticidal, hepatoprotective, hypolipidaemic, anti-inflammatory and antitumour activity, as well as being antibacterial, antifungal and antibiotic, and can be taken orally to treat urinary tract infections [39]. Various disorders such as dyspepsia, piles, diarrhoea, and skin diseases are treated with the plant in Indian medicine. It is also deployed in a number of ayurvedic formulations. As a digestive aid, it is supposed to promote appetite and digestion. According to research, plumbago roots exhibit immunosuppressive and anticancer properties [40].

## 5. ANTI-INFLAMMATORY ACTIVITY

This plant has been studied extensively for its anti-cancer, anti-leishmanial, and anti-plasmodial properties, as well as for its anti-inflammatory and hypoglycemic, anti-atherosclerotic, antiallergic, central nervous system stimulatory, cytotoxic and insecticidal properties, among others. In this review we are emphasizing only on antiinflammatory activity of the *P. zeylanica* Li *et al.*. Studied proapoptotic and growth-inhibitory effects of Plumbagin on human gastric cancer cells via suppression of signal transducer and activator of transcription 3 and protein kinase B. Result showed that plumbagin suppressed the BAX, BCL-2, pro-caspase-3 expression and cleaved caspase-3 in gastric cancer cells. Plumbagin inhibits the apoptosis in human gastric cancer cells that may be due to its ability to suppress the STAT3 and Akt phosphorylation [41]. Shweta *et al.*, studied antimicrobial activity of leaves extract of *Plumbago zeylanica* plant against known drugs. Effect of crude extract of *P. zeylanica* leaves against *E.coli*, *Bacillus cereus*, *Staphylococcus aureus*, and *Candida* was observed and it was found that they exhibits inhibition zones which indicates the potential anti- microbial activity of *P. zeylanica* [42]. Honnegowda *et al.*, Reported the evidence of oxidative stress in the pathogenesis of non-healing ulcers. As the wound healing mainly depends on a low level of oxidant so the antioxidant nature of the plant extract obtained from *P. zeylanica* helps in controlling the wound oxidative stress thus accelerating wound healing [43]. Venkatadri *et al.*, reported anti-cancer activities of *P. zeylanica* extracts against MCF-7 and HT-29 cell lines. Result showed that methanolic extract of *P. zeylanica* were used against MCF-7 and HT-29 and it results in moderate anti-cancer activity and the inhibitory property compared with the standard tamoxifen for MCF-7 and 5-fluoro Uracil for HT-29. 50.23% of MCF-7 cell death and 25.17% of HT-29 cell inhibition were observed [44]. Jyothi *et al.*, investigated the wound healing activity of ethanolic root extract of *P. zeylanica* in wistar rats and found that the activity is due to the presence of phytochemicals such as alkaloids, terpenoids, flavonoids, saponins etc. and these compounds are responsible for the wound

healing activity of the plant [45]. Falang *et al.*, revealed the anti-ulcer activity of *P. zeylanica* root extract (aqueous) on aspirin and indomethacin induced acute gastric ulcer in albino rats. By determining and comparing the ulcer index, score and percentage protection of extract with that of the control and negative experiment groups, it was found that 50 ml/kg and 100ml/kg showed significant dose-dependent inhibition in case of aspirin and 50 mg/kg and 100 mg/kg in case of indomethacin. Also, oral acute toxicity testing showed that LD50 was greater than 5000 mg/kg which indicates the wide margin of root extract safety [46]. Sunil *et al.*, evaluated the antidiabetic effects of plumbagin isolated from *P. zeylanica* root and its effect on GLUT4 translocation in STZ-induced diabetic rats [47]. Patil *et al.*, Tested extracts of *P. zeylanica* and *C. nocturnum* for larvicidal activity against second, third, and fourth instar larvae of *Aedes aegypti*. The LC (50) values of all the extracts in different solvents of both the plants were less than 50 ppm (15.40 to 38.50 ppm) against all tested larval instars. Plant extracts also affected the life cycle of *A. aegypti* by inhibition of pupal development and adult emergence with increasing concentrations [48]. Dang *et al.*, analysed three medicinal plants namely *Phyllanthus emblica*, *P. zeylanica* and *Cyperus rotundus* on two models of acute inflammation and result showed that *P. zeylanica* reduce the oedema while the combination of *P. emblica* compared to aspirin[49]. Kodati *et al.*, investigated wound healing activity of *Plumbago zeylanica* in rat. Significant wound healing activity of methanolic root extract of *Plumbago zeylanica* was observed [50]. Zarmough *et al.*, showed that In streptozotocin-treated diabetic rats, oral administration of ethanolic root extract of *P. zeylanica* (100 mg, 200 mg/kg/p.o) and tolbutamide (250 mg/kg/p.o) boosted hexokinase activity and lowered glucose-6-phosphatase activity ( $P < 0.001$ ) [51]. Vishnukanta & Rana evaluated in female wistar rats, the hydroalcoholic extract of *Plumbago zeylanica* leaves has antifertility action. Because of anti-estrogenic activity, which antagonises estrogen's effect and produces structural and functional alterations in the uterus, *Plumbago zeylanica* leaves demonstrated highly powerful (95.167 %) anti-implantation activity. The antiestrogenic action is also supported by a decrease in glycogen content, endometrial width and thickness, myometrium, uterine lumen with fewer pits and folds, uterine gland number and size, vaginal opening, and cornification [52]. Sheeja *et al.*, studied using in vivo experimental models, researchers investigated the anti-inflammatory properties of several *P. zeylanica* leaf extracts. When compared to the control group, the acetone extract significantly ( $p < 0.01$ ) decreased inflammation in the carrageenan-induced rats [53]. Mittal *et al.*, Reported the effect of *P. zeylanica* roots on scopolamine-induced amnesia in rats in terms of learning and memory In mice, a chloroform extract of the plant at a concentration of 200 mg/kg had a potential

memory-enhancing effect. Scopolamine (0.4 mg/kg i.p.)-induced amnesia was significantly restored by the extract [33]. Nile & Khobragade determined Spectral data for the novel flavonoid 2-(2,4-Dihydroxyphenyl)-3,6,8 trihydroxy chromen-4-one from *P. zeylanica* roots. Free radical scavenging and superoxide radical scavenging methods were used to investigate antioxidant activity. The antioxidant activity measured by DPPH was 96 g/ml and by NBT was 4.6 g/ml, both of which were higher than the reference (quercetin), which was 45 g/ml by DPPH and 10 g/ml by NBT assay [54]. Chauhan *et al.*, In his study carried out *Plumbago zeylanica* was subjected to preliminary phytochemical screening and anticancer testing in an animal model of Ehrlich Ascites Carcinoma. Because of the greater quantity of terpenoids and flavonoids in the ethanolic extract of *Plumbago zeylanica*, they discovered that it has substantial anticancer potential and also reduces elevated levels of lipid peroxidation [55]. Maniafu *et al.*, reported Extracts from three *Plumbago* species have larvicidal action against *A. gambiae*. Hexane (LC50 = 6.4 g/mL) and chloroform (LC50 = 6.7 g/mL) extracts were shown to have the strongest larvicidal activity against *Anopheles gambiae* [56]. Edwin *et al.*, investigated that the acetone and ethanol extracts of *P. zeylanica* were the most effective at interrupting the estrous cycle, resulting in a prolonged diestrous stage of the cycle and a transient suppression of ovulation. *P. zeylanica* also serves as a family planning and anti-implantation agent in humans, obstructing progesterone production or usage [57]. Checker *et al.*, studied Plumbagin's anti-inflammatory properties are due to its inhibition of NF kappa B activation in lymphocytes. *P. zeylanica* inhibited NF-kappa B activation in tumour cells and reduced mortality in mice with Graft Versus Host Disease [58]. Vishnukanta & Rana evaluated *Plumbago zeylanica* leaf hydroalcoholic extract for central nervous system activity. The extract had considerable CNS depressive effects as well as muscle relaxant effects, according to the researchers. It also had anxiolytic properties [52]. Kotecha & Rao *et al.*, Investigated the effect of 500 mg of *Plumbago zeylanica* and 1gm of haridra powder in capsules given four times a day for 45 days to obese patients on a low-calorie diet. When compared to haridra, the results showed that *P. zeylanica* is significantly significant in the weight loss of the patient [59]. Sandur *et al.*, Showed that Plumbagin, a compound produced from *P. zeylanica*, inhibits cell growth, carcinogenesis, and radio resistance. The activation of the transcription factor NF-kappa B activation pathway should govern all of these events. Plumbagin prevents TNF, other carcinogens, and inflammatory triggers like phorbol myristate acetate from activating NF-kappa B [60]. Dai *et al.*, Investigated ethanolic extracts (70%) from *P. zeylanica* stems cause allergic responses. The extracts (500, 1000 mg/kg orally) reduced homologous passive cutaneous anaphylaxis and skin reactions generated by



histamine or serotonin in rats and prevented dose-dependently systemic anaphylactic shocks generated by compound 48/80 in mice. At a dose of 1000mg/kg, significant variations were detected [61]. D'Souza *et al.*, Inclusion To improve efficacy and solubility, a combination of plumbagin and hydroxyl propyl  $\beta$ -Cyclodextrin (HP $\beta$ CD) was created. The antifertility action of the combination was tested after it was entrapped in the aqueous layer of niosomes. When compared to the control and niosomes with lipid layer entrapment, the complex's niosomes showed promising anti-fertility action when given intraperitoneally at a dose of 5 mg/kg [62]. Alpana *et al.*, also revealed When hyperlipidemic rabbits were given 500 mg/kg ethanolic extract of *P. zeylanica*, blood cholesterol, LDL cholesterol, and triglycerides all decreased significantly [63]. Rout *et al.*, evaluated When taken orally or administered to the ostium uteri, the roots of *Plumbago zeylanica* have been known to be a strong poison that causes abortion [64]. Premakumari *et al.*, reported In albino rats, plumbagin has strong anti-implantation and abortifacient activity without causing teratogenic effects at dosages of 1mg/100g [65]. Arunachalam *et al.*, revealed the Chitrak plant (*Plumbago zeylanica*) was discovered to have an anti-inflammatory effect in carrageenin-induced raw paw oedema in rats. Four groups were used in the study, two of which were given 300 mg/kg and the other two were given 500 mg/kg, confirming the acute inflammation inhibition of 31.03 percent and 60.30 %, respectively [40].

## 6. CONCLUSION

The numerous studies such as morphology, pharmacognostic, phytochemical and physiochemical review of the *Plumbago zeylanica* were done by literature review concluded that plants of *Plumbago zeylanica* exhibited anti-inflammatory activities. This plant has been utilised in Ayurvedic medicine for thousands of years to improve longevity and vigour. In herbal formulations, it's the most important medicinal plant. As a multifunctional medicinal agent, it contains a variety of active chemicals, including plumbazin, chitranone, zeylanone, and several valuable naphthaquinone components. *P. zeylanica* and its botanical ingredients have been studied as antiinflammatory agents in this study. This review provides the exhaustive evidence of anti-inflammatory activity of *P. zeylanica*. More studies need to be done for finding of pharmacological and chemical characters finding to know the accurate mechanism of action of the formulation for isolating the active principles responsible for this type of actions.

### Conflict of interest

Authors declare no conflict of interest.

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