Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8196
JPP 2014; 3(4): 117-120
Received: 15-09-2014
Accepted: 01-10-2014

Nisha Sharma
Department of Botany and Microbiology, Gurukul Kangri University, Haridwar (U.K.), India.

Purshotam Kaushik
Department of Botany and Microbiology, Gurukul Kangri University, Haridwar (U.K.), India.

Correspondence:
Nisha Sharma
Department of Botany and Microbiology, Gurukul Kangri University, Haridwar (U.K.), India.

Medicinal, Biological and Pharmacological Aspects of *Plumbago zeylanica* (Linn.)

Nisha Sharma and Purshotam Kaushik

Abstract
The present review deals with chemical compounds, medicinal properties, biological activities and pharmacological effects of *Plumbago zeylanica*. *Plumbago zeylanica* (Linn.) belongs to family Plumbaginaceae, commonly known as Chitrak is one of the medicinal plants used in the Indian traditional system of medicine. Traditionally *P. zeylanica* is used as a stimulant digestant, expectorant, laxative and in the treatment of muscular pain and rheumatic diseases. Some parts of *P. zeylanica* are used in various pharmacological activities. The different parts of *P. zeylanica* are used for various ethnomedicinal purposes and investigations have been carried out on different chemical compounds such as plumbagin and other compounds of this plant. Its biological activities like antibacterial, antimycotic, antiviral, antiplasmodial, leishmanicidal, trypanocidal and anticarcinogenic have been studied along with pharmacological effects of it.

Keywords: *Plumbago zeylanica*, Plumbagin, Biological, Pharmacological effect

1. Introduction
Medicinal plants are the local heritage with global importance. The world is endowed with a rich wealth of medicinal plants [1]. Medicinal plants are the main constituents of many of drugs of Indian system of medicine [2]. Natural products play an important role in drug development programmes in the pharmaceutical industry [3]. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources, particularly from plants. Various medicinal plants have been used for years in daily life to treat diseases all over the world. There has been an increasing incidence of multiple resistances in human pathogenic microorganism in recent years, largely due to indiscriminate use of commercial antimicrobial drugs commonly employed in the treatment of infectious diseases [4].
Airy shaw in 1973 recorded its 12 species occurring in the wrma regions of the world of which three species are found in India [5]. Ninan and Geethamma (2009) on the basis of their plant collection trips of 1980s of the 20th century, conducted to various evergreens and rain forests of South India such as kodaikanal, Ootacamund, Munnar, Pulaney Hills, Palaruvi, Kallar, Ponmudi, Muthukuzhivayal, Agasthyakoodam, Vattakottai, Silent Valley, Mysore, Banglore, Kotagiri, recorded two species *Plumbago zeylanica* Linn. and *P. rosea* Linn. and regarded both of these on werge of extinction due to deforestation and adverse climatic conditions [6].
Plumbago zeyanica (L.) belongs to family Plumbaginaceae, commonly known as Chitrak is one of the common plants used in the Indian traditional system of medicine. Some parts of this plant species are used in various pharmacological activities [7-10]. Traditionally *P. zeylanica* is used as a stimulant digestant, expectorant, laxative and in the treatment of muscular pain and rheumatic diseases. In India it is usually used to treat fever or malaria. Pharmacological studies have indicated that *P. zeylanica* extract has antiplasmodial [11] antimicrobial [12] antifungal [13] anti-inflammatory [14] antihyperglycemic [15] hypolipidemic and antiatherosclerotic activities [16].

2. Traditional Medicinal Uses of *P. Zeylanica*
According to Paiva *et al*., (2003) flowers are used as digestant [17]. Leaves are caustic, vesicant, aphrodisiac, good for scabies stimulant and are also used in sore and swelling [18]. They are used to treat infections and digestive problems such as dysentery. Externally a paste is applied to painful rheumatic areas or to chronic and itchy skin problems [19].

The ethanolic stem extract inhibited the growth of *Leishmania amazonensis* promastigotes by 88% at 100 mg/ml [17]. Root is bitter, laxative, expectorant, tonic, abortifacient, good appetizer, useful in rheumatism, laryngitis, scabies and disease of spleen [19].

According to Chunekar its roots are mixed with *Abrus precatorius* and used in leucoderma [5]. It is also used as one of 10 constituents of 'Kaph-Promeh Nashak Dus Yog' in urinary disorders due to 'Kapha' [20]. Kaushik and Goyal (2011), however, have recorded two species only for use in traditional medicine, which are *Plumbago zeylanica* (= *Plumbago scandens*) and *Plumbago indica* (= *P. rosea*) [21]. According to Ninan and Geethamma (2009) while working in Department of Botany, University of Kerala, Kariavattom, Trivandrum; root, leaves and bark of *Plumbago zeylanica* are used by natives of Kerala in diarrhea and skin diseases while that of *P. rosea* are used to treat leprosy and ulcers [6].

Root powder showed the presence of protease enzyme, trace quantity of Vit, A, B_1, B_2 and C and was found to be GIT Flora normalizer. It stimulates the proliferation of coliform bacteria in mice [22]. Root is used in filariasis, depigmentation of the skin and anasarca generalized swelling all over the body. In rheumatic joints, its paste applied is beneficial. It is recommended in the treatment of non-bleeding piles. The same is extremely helpful in colitis. The root is a powerful acronarcotic poison.

Chitrak effectively used in the enlarged liver and spleen. It relieves the obstructed phlegm in chronic colds and cough. Chitrak is a bitter tonic and recommended as a rejuvenator. Orally Chitrak is used in digestive disorders like loss of appetite, Indigestion, also in piles, worms, colitis, ascites and liver diseases. It augments the appetite, improves digestion, relieves constipation and alleviates the urticaria- the allergic skin rashes [23].

3. Chemical Constituents of *P. Zeylanica*

According to Satyavati *et al.,* (1987) and Kapoor (1990) flowers contain plumbagin, zeylanone and glucose. Leaves contain plumbagin chitanone. Stem contains pumbagin, zeylanone, isozeylanone, sitosterol stigmasterol, campesterol and dihydroflavonol plumbagin. The root bark of *P. zeylanica* contains plumbagin. The root yields new pigment, viz. 3-Chloroplumbagin, 3, 3-biplumbagin binaphthoquinone identify as 3',6'- bipumbagin and four other pigments identified as isozeylanone, zeylanone, elliptinone and droserone [22, 23].

4. Biological Activities

4.1 Antibacterial Activity

The aqueous extract and its partition (Petroleum ether, dichloromethane, methanol, aqueous residue) were effective against *Salmonella gallinarum*, *Escherichia coli, Proteus vulgaris, Salmonella typhimurium, Pseudomonas aeruginosa* and *Staphylococcus aureus*. The alcoholic extract from roots of *Plumbago zeylanica* was tested against multi-drug resistant of clinical origin (*Salmonella paratyphi, Staphylococcus aureus, Escherichia coli* and *Shigella dysenteriae)*. The extract exhibited strong antibacterial activity against all tested bacteria. Plumbagin augments and macrophage bactericidal activity by potentiating the Oxyradical release at low concentration, whereas at the higher concentration it has inhibitory activity in BALB/C mice [24]. Antibiotic resistant strains of *E. coli* and *Staphylococcus aureus* inoculated in an antibiotic (streptomycin, rifampicin) medium showed a delayed growth due to the resistance. However, the growth was completely prevented when the bacteria were grown in medium with antibiotic and Plumbagin [25].

When *P. zeylanica* was tested against the resistant strain of *Mycobacterium tuberculosis* (H37, RV) the inhibitory activity of Plumbagin was < 12.5 mg/ml. The anticyanobacterial activity of isonicotin acid hydrazide against *Mycobacterium intracellurum, M. smegmatis, M. xenopei* and *M. chelonei* combined with plumbagin was lowered from a MIC value of 1.25-2.5 to 0.15-0.3 mg/ml [26]. Wang and Huang (2005) used water, ethanol, ethyl acetate and acetone extract of *Plumbago zeylanica* to evaluate the anti-helicobacter pylori activity. Ethyl acetate extract exhibited the lowest minimum inhibitory concentration (MIC) against five *H. pylori* strains, which ranged from 0.32 to 1.28 mg/ml in ascending order by acetone, ethanol and water analogs. Bactericidal activity was also determined, with the lowest minimum bactericidal concentrations demonstrated for the ethyl acetate in ascending order, by the acetone and ethanol analogs [27].

4.2 Antifungal Activity

According to Mehmood *et al*., (1999) alcoholic extracts of *Plumbago zeylanica* showed strong antifungal against the pathogenic yeast, Candida albicans and dermatophytes, *Epidermophyton floccosum, Microsporum gypseum* and *Trichophyton rubrum,* Minimum inhibitory concentration (MIC) was found to be 4 mg/ml [13].

4.3 Antiviral Activity

Marian *et al*., (2006) examined the antiviral activities of the 80% methanolic extracts of *Plumbago zeylanica* against Coxsackie Virus 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. They also found that CVB3 was inhibited by the extract of *Plumbago zeylanica* [28].

4.4 Antiplasmodial Activity

Plumbagin shows antimalarial effects on *Plasmodium falciparum enzyme,* the succinate dehydrogenase (SDH). The activity has been 50% inhibited by the naphthoquinone plumbagin at an inhibitory concentration of 5 mM. It also inhibited the *in vitro* growth of the parasite with a 50% in an inhibitory concentration of 0.27 mM [17].

4.5 Leishmanicidal Activity

In the case of leishmaniasis *Plumbago* species have been shown to contain compounds with significant activity. The quinones corresponds to promising antileishmanial substances. Plumbagin a naphthoquinone isolated from *Plumbago* species is reported to have an activity (IC 50) of 0.42 and 1.1 mg/ml against amastigotes of *Leishmania donovani* and *L. amazonesis.* Plumbagin and its dimmers, 3, 3'- bis- plumbagin and 8, 8'- bisplumbagin have been used in the treatment of cutaneous leishmaniasis in Amazonian Bolikia [17].

4.6 Trypanocidal Activity

Plumbagin exhibited high potency (IC 90 = 1-5 mg/ml) against six strains of *T. cruzi* epimastigotes, while the dimer 3,3'-bisplumbagin and 8, 8'- bisplumbagin were less effective, with IC 90 in the 25-100 mg/ml range [17].

4.7 Anticarcinogenic Activity

Male F344 rats, administered with plumbagin at 200 ppm in the diet for two weeks beginning one week before azoxymethane (AOM) injection had a lower incidence and multiplicity of tumors in the small intestine than those administered AOM alone. This suggests that plumbagin could be a promising neoplasia. Hexokinase, phosphoglucoisomerse and aldolase levels increased in hepatoma-bearing rats, but they decreased to near-normal levels in animals administered plumbagin. Levels of the gluconeogenic enzymes, glucose- 6-phosphate and fructose -1, 6-disphosphatase decreased in hepatoma bearing animals, but increased in the animals treated with plumbagin [29].

Plumbagin inhibit NF-kB activation induced by TNF, and other carcinogens and inflammatory stimuli (e.g. Phorbol 12 – myristate 13-acetate, H2O2, cigarette smoke condensate, interleukin- 1β, lipopolysaccharide and okadaic acid). It also suppressed the constitutive NF-kB activation in certain tumor cells. The suppression of NF-KB activation correlated with sequential inhibition of tumour necrosis factor (TNF)- induced activation of IkBα kinase, IkBα phosphorylation, IkBα degradation, P65 Phosphorylation, P65 nuclear translocation and the NF-kB- dependent reporter gene expression activated by TNF, $TNFR_1$ $TRAF_2$, NIK, IKK-B, and the p65 subunit of NF-k B. It is also suppressed the direct binding of nuclear p65 and recombinant p65 to the DNA and this binding was reversed by dithiothreitol both *in vitro* and *in vivo*. It indicates that plumbagin is a potent inhibitor of NF-kB – regulated gene products. This may explain its cell growth modulatory, anticarcinogenic and radiosensitizing effects [30].

5. Pharmacological Effects of *P. Zeylanica*

Swiss Albino mice pre-treated with an alcoholic root extract of *P. zeylanica* (250 and 500 mg/kg body weight) showed protection against cyclophosphamide-induced genotozicity, reduced the frequency of micronucleated polychromatic erythrocytes, and increased the normochromatic erythrocyte ratio in the bone marrow [31]. In albino rats a *P. zeylanica* extract (2 mg/kg body weight) was tested for blood characteristics after chronic administration (after 1 day, after 15 days, after 31 days). There was no change in platelet count. But the platelet adhesion was significantly decreased [32]. In hyperlipidaemic rabbits plumbagin, isolated from roots of *P. zeylanica* reduced the serum cholesterol and LDL- Cholesterol Values by 53 to 86% and 61 to 91% respectively. Plumbagin treated hyperlipidaemic subjects excreted more faecal cholesterol and triglycerides in the liver and aorta and lowered atheromatous plaques of thoracic and abdominal aorta [16].

In male wistar rats plumbagin (4 mg/kg body weight) from *P. zeylanica* reduced the growth in 3-methyl-4- dimethyl aminoazobenzene (3 Me DAB) induced hepatoma. In hepatoma bearing rats levels of hexokinase, phosphoglucoisomerase and aldolase increased ($P<0.001$), but they decreased in only plumbagin treated rats to near normal levels. In tumour hosts glucose-6-po_4 and fructose-1, 6-diphosphatase decreased ($p<0.001$). In hyperglycaemic rats the effects of ethanol extracts from the roots of *P. zeylanica* were studied on key enzymes of glycolysis and other biochemical parameters. Thigh muscle hexokinase, phosphofructokinase, pyruvate kinase, lactate dehydrogenase activities were significantly ($p<0.05$) reduced by 12.7%, 51.02%, 24.32% and 25.16% in the treated animals [15].

6. Conclusion

Numerous phytochemical and Biological studies have been conducted on different parts of *Plumbago zeylanica.* This has made an attempt to congregate the traditional medicinal use, phytochemical constituents, biological activities and pharmacological effects of *Plumbago zeylanica.* Scientific research on this plant reported the antibacterial, antifungal, antiviral, antiplasmodial, leishmanicidal, trypanocidal and anticariogenic activity of various parts of this plant in the literature.

Unfortunately, most of the compounds have not properly been evaluated for the exploitation of new lead molecules. Moreover, mechanisms of action of a few bioactive compounds have been identified so far. Hence, extensive research is required to find out the mechanisms of action as well as bioactivity of the various phytochemicals and efficacy of the medicinal values of *P. zeylanica*. Thus, in the near future extracts of *P. zeylanica* could be further exploited as a source of useful phytochemical compounds and may play a very important role in modern system of medicine.

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