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Review

A comprehensive review on *Plumbago zeylanica* Linn

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The present review aimed to compile up to date and comprehensive information of *Plumbago zeylanica* with special emphasis on its phytochemistry, various scientifically documented pharmacological activities, traditional and folk medicine uses. Traditional system of medicinal consists of large number of plants with various medicinal and pharmacological uses and hence represents a priceless tank of new bioactive molecules. *P. zeylanica* is one amongst these, found all over the world. In this review, we have attempted to highlight the work carried out on *P. zeylanica.* It is commonly known as 'Chitraka', and has been recognized in different traditional system of medicines for the treatment of various diseases of human beings in the form of paste and powder. Plant mainly contains naphthoquinones and steroidal compounds. Different parts of this plant are traditionally claimed to be used for the treatment of ailments including anti-fungal, anti-tumor, disease of heart, rheumatic pains, liver diseases, fever, diabetes, and kidney disease to list of few.

Key words: *Plumbago zeylanica,* phytochemistry, pharmacological activities.

INTRODUCTION

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. 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 (Chetty et al., 2006).

The root is used as laxative, expectorant, astringent, abortifacient, and in dysentery (Anonymous, 1989; Bhattacharjee, 1998). 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 (Mittal et al., 2010). *P. zeylanica* roots were reported to possess antioxidant, hypolipidemic, anti artherosclerotic, central nervous system stimulant and anti-fertility properties (Kirtikar and Basu, 1975; Mallikadevi and Paulsamy, 2010).

The main aim of reviewing this plant is to explore the usefulness of plant for human health. It is an important herb in the Indian and Chinese traditional medicine systems for over 3000 years. The medicinal properties attributed to several classes of naphthquinones, a group of naturally ocurring phenols based on the C6-C4 skeleton. The purpose of this article is to review recent literature regarding *P. zeylanica* in an attempt to establish a scientific basis for therapeutic use.

Botanical description:

Kingdom: Plantae
Order: Caryophyllales
Family: Plumbaginaceae
Genus: *Plumbago*
Species: *P. zeylanica*

Morphological description

P. zeylanica is a subscadent, pretty perennial shrub

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Figure 1. Leaves and roots of *P. zeylanica.*

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, wheras the rachis of the spike is pubescent or glandular (Figure 1). The Corolla white tube is long and slender. The roots are cylindrical and are irregularly bent having transverse shallow fissures at bents (Figure 1). Its fruits are oblong and its capsules are enclosed by persistent viscid calyx (Bhattacharjee, 1998; Chen et al., 2011).

Medicinal properties

Plant pacifies vitiated vata, kapha, diarrhea, inflammation, fever, nervous palsy, hemorrhoids, skin diseases, irritable bowel disease, epilepsy, ammenorrhoea and anemia. The roots are used as laxative, expectorant, astringent, abortifacient, and in dysentery, cirrhosis, arthritsetc (Table 1) (Bhattacharjee, 1998; Nadakarni and Nadakarni, 1999).

Phytochemistry

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 contains little or no plumbagin. The aerial parts contain naphthoquinones, sitosterol, lupeol, lupenylacetate, hentriacontane, and amino acids. Plant contains naphthaquinones (Figure 2a), plumbagin (Figure 2b), chloroplumbagin, droserone, zeylinone (Figure 2c), isozeylinone, plumbagic acid, plumba-zeylanone, naphthelenone, isonaphthelenone, isoshinanolone (Anonymous, 1989; Chen et al., 2011; Kumar et al., 2009). Aspartic acid, tryptophan, tyrosine, threonine, alanine, histidine, glycine, methionine, hydroxyproline, were isolated from the aerial parts (Elizabeth, 2002).

Analytical methods

Sudhakar et al. (2008) developed and validated a reverse phase HPLC method with UV detection to quantify plumbagin, the bioactive marker of the roots of *P. indica* and *P. zeylanica.* A quantitative high performance thin layer chromatography (HPTLC) method was also developed using hexane: ethyl acetate (8:2) as the mobile phase.

Kishore et al. (2010) characterized difuranonaphthoquinones from *P. zeylanica* roots by spectral analysis (UV, IR, 1D and 2D NMR and MS) and compound identified as naphthoquinones, lapachol, plumbagin, 2-isopropenyl-9-methoxy-1,8-di-oxa-di cyclopenta(*b,g*) naphthalene-4,10-dione, 9-hydroxy-2-isopropenyl-1,8-dioxa-dicyclopenta (*b,g*)naphthalene-4,10-dione, 2-(1-hydroxy-1-methyl-ethyl)-9-methoxy-1,8-dioxa-dicyclopenta(*b,g*)naphthalene-4,10-dione and 5,7 -dihydroxy-8-methoxy-2-methyl-1,4-naphthoquinone were isolated from roots of *P. zeylanica*.

In another study, Okamoto et al. (2001) utilized a method for a biomimetic synthesis of the binaphthoquinone, 3,3′-biplumbagin, isolated from *P. zeylanica.* The aryl–aryl coupling reaction of 1-naphthol with $SnCl_4$ for 2,2′-binaphthol synthesis and its application to the biomimetic synthesis of binaphthoquinone was isolated from *P. zeylanica*. A simple method for the direct synthesis of 2,2′-binaphthols was developed, utilizing aryl–aryl coupling reaction via electron donor–acceptor complexes of 1-naphthols with $SnCl_4$.

Hsieh et al. (2006) performed measurement and pharmacokinetic study of plumbagin in a conscious freely

Table 1. Medicinal use of different parts of *P. zeylanica.*

S/N	Disorder	Parts used	Description
1	Diarrhoea	root	The paste made out of root (1 to 2 g) is taken with butter milk (30 to 60 ml), 2 to 3 times a day
2	Dysentery, abdominal disorders, peptic ulcers, piles and improves appetite	root bark	The decoction prepared out of the root bark churnam is taken orally (30 to 60 ml) twice in day for about 1 to 2 weeks. In children the dosage should be limited to 5 to 10 ml in divided doses.
3	Hypercholostremia	root	The fine powder of the root is taken orally (2 to 5 g) with honey twice a day for a period of 3 months
4	Abortifacient	root	Local administration of fine root paste (3-5 g) of chitraka into the vaginal track for a period of 3 to 5 days
5	Anemia and improves blood formation	root	The fine powders of chitraka and *Abutilon indicum*(L.) Sweet. root in equal proportion is given in dosages of 1 to 3 g with milk ones in a day for 3 months
6	Leucoderma and psoriasis	root	The fine powder of chitraka (1 part), dry zinger, *Piper longum*L. and *Piper nigrum*L. (1 part each) are taken orally 2 to 3 g with ghee or honey, twice a day for period of 3 months

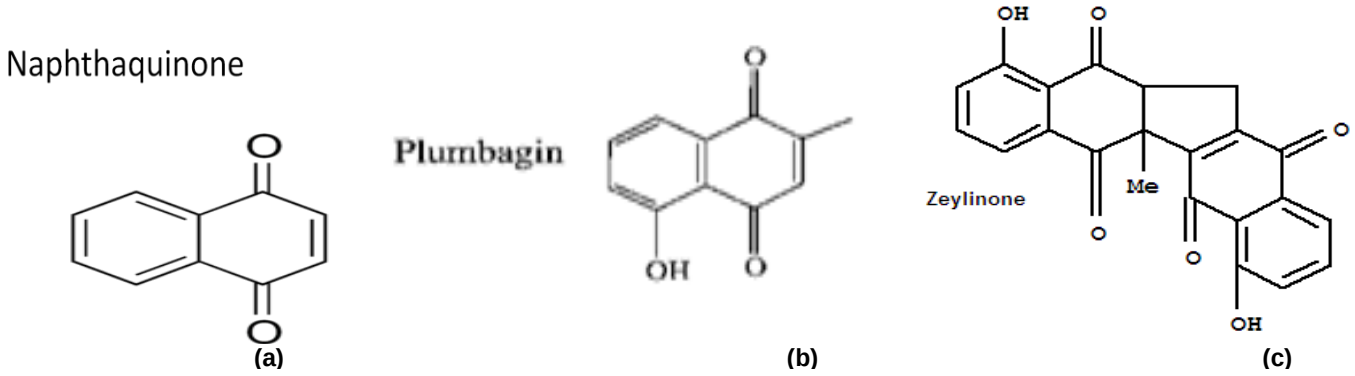

Figure 2. Chemical structure of constituents of *P. zeylanica.*

moving rat using liquid chromatography/tandem mass spectrometry. Plumbagin, an herbal ingredient, was isolated from P. zeylanica. Recovery of plumbagin from the rat plasma was about 80%.

Advancement in pharmacological activities

P. zeylanica used for centuries to treat a wide range of diseases, showed great potential as safe and efficacious multi-purpose medicinal agent. Beside its traditional uses, several recent reports have demonstrated hepato-protective, immunomodulatory, antitumor, hypolipidemic and cardioprotective. Moreover, various parts of plants are reported to possess abortificient, and anticancer properties.

Cytotoxic and antibacterial activity

Aziz et al. (2008) studied a inhibitory effect of plumbagin on growth and invasion of hormone in refractory prostate cancer. The results indicate for the first time, using both *in vitro* and in *vivo* preclinical models, that PL inhibits the growth and invasion of PCa. Plumbagin inhibits multiple molecular targets including PKCepsilon, a predictive

biomarker of PCa aggressiveness. Plumbagin may be a novel agent for therapy of hormone-refractory PCa.

Chen et al. (2011) synthesized, characterized and evaluate preliminary cytotoxicity of five lanthanide (iii)–plumbagin complexes-plumbagin (5-hydroxy-2-methyl-1,4-naphtho quinone, H-PLN) was isolated from *P. zeylanica*, the anticancer traditional Chinese medicine (TCM). Five new lanthanide (III) complexes of deprotonated plumbagin were synthesized.

Xu and Lu (2010) investigated plumbagin induces ros-mediated apoptosis in human promyelocytic leukemia cells *in vivo*-plumbagin, a naphtoquinone from the roots of *P. zeylanica* is known to possess anticancer and anti-bacterial activity. The results showed that i.p. injection of plumbagin (2 mg/kg body weight) daily for 3 weeks resulted in a 64.49% reduction of tumor volume compared with the control. These results indicate that plumbagin has potential as a novel therapeutic agent for myeloid leukemia.

In another study, Yang et al. (2010) reported that plumbagin activates erk1/2 and akt via superoxide, src and pi3-kinase in 3t3-l1 cells. Plumbagin, derived from the plant *P. zeylanica*, has been shown to chronically activate ERK1/2 and inhibit Akt activity in cancer cells. These results suggest that plumbagin activates NAD(P)H oxidase, Src, and PI3K, and that the activated PI3K or PDK1 subsequently stimulate Akt and Ras–Raf–MEK1/2–ERK1/2 in 3T3-L1 cells.

Genotoxicity

Demma et al. (2009) studied potential genotoxicity of plant extracts used in Ethiopian traditional medicine. In the present study, hydroalcoholic extracts of *Glinus lotoides*, *P. zeylanica*, *Rumex steudelii* and *Thymus schimperi* were evaluated for their DNA damaging effects using the comet assay. In the absence of S9, all extracts were found to induce significant DNA damage without affecting the cell viability. *T. schimperi* and *R. steudelii* were the most potent DNA-damaging extracts, and *G. lotoides* and *P. zeylanica* the least potent.Demma et al. (2009) carried out a study to elucidate the potential genotoxicity and antigenotoxicity of plumbagin in mouse lymphoma L5178Y cells, using the comet assay. Without affecting the cell viability, plumbagin itself was found to induce significant DNA damage at concentrations as low as 0.25 ng/ml. When the cells were exposed to non-DNA damaging concentrations of plumbagin, together with NQNO (known to interact with DNA in many different ways) or catechol (known to induce oxidative DNA damage), plumbagin was found to significantly reduce the catechol-induced DNA damage, but to be without protective effect against the NQNO-induced damage.

In another study, Chen et al. (2009) investigated the effect of plumbagin on the growth of human pancreatic carcinoma cells and its possible underlying mechanisms. Liu's staining and transmission electron microscopy demonstrated morphological changes resembling apoptosis in Panc-1 cells treated with plumbagin. Plumbagin may induce apoptosis in human pancreatic cancer cells primarily through the mitochondria-related pathway followed by both caspase-dependent and caspase-independent cascades. It indicates that plumbagin can be potentially developed as a novel therapeutic agent against pancreatic cancer.

Chen et al. (2009) were isolated plumbagin (PLN) from *P. zeylanica.* Reaction of plumbagin with Cu^{II} salt, afforded $[Cu(PLN)_2]\cdot 2H_2O$ (1). With 2,2′-bipyridine (bipy) as a co-ligand, PLN reacts with Cu^{II} to give $[Cu(PLN)(bipy)(H_2O)]_2(NO_3)_2\cdot 4H_2O$ (2). The *in vitro* cytotoxicity of PLN, 1 and 2 against seven human tumour cell lines was assayed. The binding properties of PLN, 1 and 2 to DNA were investigated through UV-vis, fluorescence, CD spectra, and gel mobility shift assay, which indicated that 1 and 2 were non-covalent binding and mainly intercalated the neighboring base pairs of DNA. PLN, 1 and 2 exhibit inhibition activity to topoisomerase I (TOPO I), but 1 and 2 were more effective than PLN.

Nazeem et al. (2009) investigated the copper-mediated anticancer mechanism of plumbagin in human cancer cells using 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt assay for cell growth inhibition, histone/DNA ELISA, homogeneous caspase-3/7 assay for apoptosis as well as alkaline comet assay for DNA single-strand breaks detection; in this report, authors confirm that plumbagin causes effective cell growth inhibition, induces apoptosis and generates single-strand breaks in cancer cells. Incubation of cancer cells with scavengers of ROS and neocuproine inhibited the cytotoxic action of plumbagin proving that generation of ROS and Cu(I) are the critical mediators in plumbagin-induced cell growth inhibition.

Powolny and Shingh (2008) investigated the mechanism of human prostate cancer cell growth inhibition by plumbagin, a constituent of the widely used medicinal herb *P. zeylanica.* Plumbagin treatment decreased viability of human prostate cancer cells (PC-3, LNCaP, and C4-2) irrespective of their androgen responsiveness or p53 status. The present study points towards an important role of ROS in plumbagin-induced apoptosis in human prostate cancer cells.

Lin et al. (2003) carried out cytotoxic naphthoquinones and plumbagic acid glucosides from *P. zeylanica.* Two plumbagic acid glucosides, 30-O-b-glucopyranosyl plumbagic acid and 30-O-b-glucopyranosyl plumbagic acid methylester along with five naphthoquinones, and five coumarins were isolated from the roots of *P. zeylanica*. Cytotoxicity of these compounds to various tumor cells lines was evaluated, and plumbagin significantly suppressed growth of Raji, Calu-1, HeLa, and Wish tumor cell lines.

Wang and Huang (2005) carried out screening of anti-*helicobacter pylori* herbs derived from Taiwanese folk medicinal plants. In this study, extracts from 50 Taiwanese folk medicinal plants were examined and screened for anti-*helicobacter pylori* activity. *P. zeylanica* and *other* five plant demonstrated strong anti-*Helicobacter pylori* activities.

In another study, Wang and Huang (2005) established the anti-*H. pylori* activities of different extracts of-*P. zeylanica.* Bactericidal activity was determined for *P. zeylanica* extracts with the lowest minimum bactericidal concentrations (5.12 to 20.48 mg ml^{-1}) demonstrated for the ethyl acetate, followed, in ascending order, by the acetone and ethanol.

Jetty et al. (2010) isolated, separated and evaluated the antimicrobial properties of compounds such as neoisoshinanolone and 1-epineo-isoshinanolone from the roots of *P. zeylanica*. 1-epineo-isoshinanolone is more active with a MIC of 12.5 to 25 μg/ml, whereas neoisoshinanolone has recorded a MIC of 50 to 100 μg/ml. The activities are compared with plumbagin (0.78 to 3.13 μ/ml) and standards streptomycin for bacteria and nystatin for fungi. The root extract of *P. zeylanica* possesses good antimicrobial activity, which suggests its therapeutic use in the Ayurvedic system of medicine to cure skin diseases.

Iqbal and Aqil (2007) studied *in-vitro* efficacy of bioactive extracts (alcoholic crude extracts and some fractions) of 15 medicinal plants against extended spectrum *β*-lactamases (ES*β*L) producing multidrug-resistant enteric bacteria. *P. zeylanica* demonstrated relatively high activity as compared to other plant extracts.

Aquil and ahmad (2007) screened 66 ethanolic plant extracts against nine different bacteria. The highest activity against all groups of bacteria was found in *P. zeylanic*a. In addition, these extracts showed synergistic interaction with tetracycline, chloramphenicol and ciprofloxacin against *S. aureus* and/or *E. coli.* Six plants, *P. zeylanica, H. indicus, A. calamus, P. granatum, H. antidysenterica* and *D. regia*, were further subjected to fractionation-based study. Gram-positive and Gram-negative MDR bacteria are almost equally sensitive to these extracts/fractions, indicating their broad-spectrum nature.

The Aquil and ahmad (2007) investigated alcoholic crude extracts and some fractions from 15 traditionally used Indian medicinal plants for their ability to inhibit the growth of extended spectrum beta-lactamases (ESbetaL)-producing multidrug-resistant enteric bacteria. The test bacteria *E. coli* and *Shigella* were resistant to 16 to 23 antibiotics with intermediate or resistance to beta-lactams (MIC) value range 16-1024 microg/ml). From all 15 plants the ethyl acetate fraction of *P. zeylanica* was most active.

Aqil et al. (2006) studied the anti-methicillin-resistant *Staphylococcus aureus* (MRSA) activity of ethanolic extracts of four medicinal plants namely *Acorus calamus* (rhizome) *Hemidesmus indicus* (stem), *Holarrhena antidysenterica* (bark), and *P. zeylanica* (root), were detected with inhibition zone size ranged from 11 to 44 mm and MIC varied from 0.32 to 3.25 mg/ml. Time kill assay with most promising fractions of these plant extracts, demonstrated concentration-dependent killing of MRSA within 9 to 12 h of incubation.

Lemma et al. (2002) studied anti-bacterial activity of *P. zeylanica* roots on some pneumonia causing pathogens. The anti bacterial activity of polar (aqueous) and non-polar (pet. Ether) extracts was prepared from the roots of *P. zeylanica*. Minimum inhibitory concentration value of this particular compound showed comparative activity resembling the commonly used broad spectrum antibiotic, tetracycline.

Larvicidal activity

Patil et al. (2011) 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. The larvicidal stability of the extracts at five constant temperatures (19, 22, 25, 28 and 31°C) evaluated against fourth instar larvae revealed that toxicity of both plant extracts increases with increase in temperature.

Patil et al. (2010) carried out larvicidal activity of crude chloroform, dichloromethane and methanol extracts of the leaves and roots of six Indian plants *Aegle marmelos*, *Balanites aegyptiaca*, *Calvatia gigantica*, *Murraya koenigii*, *Nyctanthes arbor-tristis* and *P. zeylanica* were tested against the early fourth instar larvae of *Aedes aegypti* and *Anopheles stephensi*. The larval mortality was observed after 24 h of exposure. The highest larval mortality was found in methanol extracts of *P. zeylanica* roots and *B. aegyptica* roots against *Ae. aegypti* (LC_{50} 169.61 mg/L and 289.59 mg/L) and *An. stephensi* (LC_{50} 222.34 and 102.29 mg/L), respectively.

Maniafu et al. (2009) tested three *Plumbago spp.* for mosquito larvicidal activity. The crude extracts exhibiting the highest larvicidal activity against *An. gambiae* were hexane and chloroform extracts from *P. zeylanica* showed LC_{50} 6.4 and 6.7 μg/ml respectively.

Antiviral activities

Neubert et al. (2006) studied antiviral activities of some Ethiopian medicinal plants used for the treatment of dermatological disorders. In this study, the antiviral activities of the 80% methanolic extracts of *Acokanthera schimperi*, *Euphorbiae schimperi*, *Inula confertiflora*,

Mutinus elegans, and *P. zeylanica* plants have been examined against cox-sackievirus B3 (CVB3), influenza A virus and herpes simplex virus type1 Kupka (HSV-1) using cytopathic effect (CPE) inhibitory assays in HeLa, MDCK, and GMK cells, respective lym CVB3 was inhibited by the extracts of *P. zeylanica* and HSV-1 by *I. confertiflora*.

Anti-invasive activity

Sathya et al. (2010) studied 3β-Hydroxylup-20(29)-ene-27,28-dioic acid dimethyl ester, a novel natural product from *P. zeylanica* inhibits the proliferation and migration of MDA-MB-231 cells. In this study, the anti-invasive activities of *P. zeylanica* methanol extract (PME) and pure compound 3β-hydroxylup-20(29)-ene-27,28-dioic acid (PZP) isolated from it are investigated *in vitro*. PME and PZP were noted to have the ability to induce apoptosis as assessed by flow cytometry. Obtained data provide the molecular basis of the anti-proliferative and anti-metastatic effects of PME and PZP.

Immunomodulatory agent

Sakamoto et al. (2008) developed an enzyme-linked immunosorbent assay (ELISA) using highly-specific monoclonal antibodies against plumbagin. The prepared monoclonal antibody against plumbagin which is secreted from established hybridoma cell line 3A3 (MAb 3A3) has been proven to have highly-specific to plumbagin resulting from cross-reactivities test. The range for calibration of plumbagin by ELISA was 0.2-25 microg mL(-1). Based on validation analysis, this analytical method by ELISA is a precise, accurate, and sensitive method for the determination of plumbagin in plant.

Checker et al. (2009) described novel immunomodulatory effects of plumbagin. Plumbagin inhibited T cell proliferation in response to polyclonal mitogen Concanavalin A (Con A) by blocking cell cycle progression. Immunosuppressive effects of plumbagin on cytokine levels were seen *in vivo*. Plumbagin completely inhibited Con A induced I kB-alpha degradation and NF-kB activation. Further, plumbagin prevented graft versus host disease-induced mortality in mice.

Sakamoto et al. (2010) carried out a study on single-chain variable fragment (scFv) antibody, fusion of the variable regions of the heavy chain and light chain of immunoglobulin against plumbagin (PL-scFv). The recombinant purified PL-scFv expressed in Sf9 insect cells was found to be different from that expressed in *E. coli* and parental MAb 3A3, although the detectable level (0.2 to25 µg/ml) was the same in ELISA using each antibody. Even more interestingly, the characteristics of PL-scFv, which have wide cross-reactivity against 1,4-napththoquinone, suggest its potential use as a tool for plant immunomodulation.

Tsai et al. (2008) identified effects of seselin from *P. zeylanica* on phytohem agglutinin (PHA)-stimulated cell proliferation in human peripheral blood mononuclear cells (PBMC). The data demonstrated that seselin inhibited PBMC proliferation-activated with PHA with an IC_{50} of 53.87±0.74_M. Cell viability test indicated that inhibitory effects of seselin on PBMC proliferation were not through direct cytotoxicity. Seselin significantly decreased the IL-2 and IFN-gene expression in PHA-activated PBMC. Therefore, results elucidated for the first time that seselin is likely an immunomodulatory agent for PBMC.

Chen et al. (2007) investigated extracts of *P. zeylanica* containing suberosin inhibits proliferation of human peripheral blood mononuclear cells through the modulation of the transcription factors NF-AT and NF-kappaB. The inhibitory effects of suberosin on PHA-induced PBMC proliferation, were mediated, at least in part, through reduction of $[Ca^{2+}]i$, ERK, NF-AT, and NF-kappaB activation, and early gene expression in PBMC including cyclins and cytokines, and arrest of cell cycle progression in the cells. Our observations provide an explanation for the anti-inflammatory activity of *P. zeylanica.*

In another study, Kamal and Rao (1995) studied modulatory effect of plumbagin on macrophage functions in balb/c mice. The data indicate that plumbagin augments the macrophage bactericidal activity by potentiating the oxyradical release at low concentration whereas at the higher concentration it has inhibitory activity.

Acaricidal properties

Kofi et al. (2009) carried out acaricidal effects of extracts and compounds derived from *P. zeylanica* roots against different stages of *Amblyomma variegatum*. The results indicated that the naphthoquinone plumbagin possesses acaricidal properties thus giving scientific justification for the folkloric use of the plant in animal husbandry.

Mutagenic screening

Akintonwa et al. (2009) carried out a research to determine the mutagenic potentials of *Morinda lucida* (root), *Acalypha indica* (leaf), *Tetrapleura tetraptera* (fruit), *P. zeylanica* (root), *Xylopia aethiopica* (fruit), *Nitzschia laevis* (leaf), *Aciduliprofundum boonei* (bark), *Enantia chlorantha* (bark), and *Rauvolfia vomitoria* (root) using the *Allium cepa* model and the modified Ames assay. The modified Ames test showed an alteration in the biochemical characteristics of *E. coli* (0157:H7) for all plants except *R. vomitoria* and *P. zeylanica*.

Aqil et al. (2008) tested methanolic extracts of *Acorus calamus* (rhizome), *Hemidesmus indicus* (stem), *H.*

antidysenterica (bark) and *P. zeylanica* (root), for their antimutagenic potential. These extracts, at tested concentrations, showed no sign of mutagenicity to *Salmonella typhimurium* tester strains. At a dose of 100 µg/plate, the extracts exhibited the inhibition of His+ revertants from 18.51 to 82.66% against direct acting mutagens, methyl methanesulphonate (MMS) and sodium azide (NaN_3) induced mutagenicity in *Salmonella tester* strains TA 97a, TA 100, TA 102 and TA 104. The overall antimutagenic potential of the aforementioned four extracts was found to be in order of *A. calamus* > *H. indicus* > *H. antidysenterica* > *P. zeylanica*.

Antiplasmodial activity

Simonsen et al. (2001) carried out *in-vitro* screening of Indian medicinal plants for antiplasmodial properties against *Plasmodium falciparum*. Of 80 analyzed ethanol extracts, from 47 species, significant effects were found for 31 of the extracts one of that was *P. zeylanica*.

Anticonvulsant activity

Vishnukanta and Rana (2010) carried out a study on pharmacological and clinical therapeutical uses of Ayurvedic medicinal plants, one of which was *P. zeylanica*. Leaf extract of this plant were evaluated for anticonvulsant activity using PTZ induced convulsion and maximum electro shocked induced convulsion. It was found that extract has no anticonvulsant activity.

Antioxidant activity

Zahin et al. (2009) carried out *in vitro* antioxidant activity and total phenolic content of methanolic extracts of *P. zeylanica* (root), *A. calamus* (rhizome), *H. indicus* (stem) and *H. antidysenterica* (bark). The order of antioxidant potential according to FTC assay was found to be highest in *P. zeylanica.*

Natarajan et al. (2006) carried out antioxidant activity of a salt–spice–herbal mixture against frees radical induction. A combination of spices (*P. nigrum*, *P. longum* and *Z. officinale*), herbs (*C. rotundus* and *P. zeylanica*) and salts make up *Amrita Bindu*. It was interesting to note that rats with *Amrita Bindu* pretreatment showed significantly lower levels of free radicals, lipid peroxidation and protein carbonyls along with significantly higher levels of antioxidants when compared with rats without *A. Bindu* pretreatment on PHZ administration. These results reveal that *A. Bindu*, a salt–spice–herbal mixture exerts a promising antioxidant potential against free radical induced oxidative damage.

Hepatoprotective activity

Rajesh et al. (2009) conducted a study to evaluate the hepatoprotective activity of methanolic extract of aerial parts of *P. zeylanica* in CCl_4-induced hepatotoxicity in wistar rats. The extract of aerial parts of-*P. zeylanica* have shown very significant hepatoprotection against CCl_4-induced hepatotoxicity in wistar rats by reducing serum total bilirubin, SGPT, SGOT and ALP levels. Histopathological studies also confirmed the hepatoprotective nature of the extract.

Anti-fertility activity

Edwin et al. (2009) evaluated the antifertility properties of extracts of leaves of *P. zeylanica*. The effects of petroleum ether, chloroform, acetone, ethanol and aqueous extracts of the leaves of *P. zeylanica* on the estrous cycle of rats were studied at two dose levels, namely, 200 and 400 mg/kg. The acetone and ethanol extracts were most effective in interrupting the estrous cycle of the rats ($p < 0.05$). The animals exhibited a prolonged diestrous stage of the estrous cycle corresponding to a temporary inhibition of ovulation. The antiovulatory activity was reversible on discontinuation of treatment. Both extracts showed significant oestrogenic and anti-oestrogenic activity ($p < 0.05$).

Toxicity studies

Teshome et al. (2008) carried out toxicity studies on dermal application of plant extract of *P. zeylanica* used in Ethiopian traditional medicine. Repeated dose toxicity test was associated with increased relative testis weight ($P < 0.05$) as well as higher values for blood urea nitrogen and K^+ ($P < 0.05$) in both sexes with the highest dose (1000 mg/kg) group, although histopathological analyses failed to lend support to these observations. Taken together, the dermatotoxicity test results from this study suggest that *P. zeylanica* toxic effects might be limited to effects like moderate irritation.

Anti-inflammatory activity

Dang et al. (2011) conducted experimental study to evaluate anti-inflammatory activity of *Phyllanthus emblica, P. zeylanica* and *C. rotundus* in acute models of inflammation, namely carrageenan induced rat paw edema and acetic acid induced peritonitis in mice. In carrageenan induced paw edema, *P. emblica, P. zeylanica* and *C. rotundus* showed a trend to reduce the edema while the combination of *P. emblica* + *P. zeylanica* (PI: 20.64%) showed results comparable to aspirin (23.74%). Whereas in a model of acetic acid induced peritonitis, all the plant drugs, that is, *P. emblica*, *P. zeylanica*, *C. rotundus* and a combination of *P. emblica* + *P. zeylanica* showed a significant decrease in the protein content of the peritoneal exudates compared with the

disease control group ($p < 0.05$).

Sheeja et al. (2010) carried out the anti-inflammatory and antinociceptive activities of various leaf extracts of *P. zeylanica* (petroleum ether, chloroform, acetone, ethanol, and aqueous) using *in vivo* experimental models at two dose levels (200 and 400 mg/kg, p.o.). The acetone extract significantly ($p < 0.01$) reduced inflammation in the carrageenan induced rats when compared to the control group. As for the analgesia effect, the acetone and petroleum ether extracts significantly ($p < 0.01$) decreased the pain stimulus only in the later phase of the formalin test, suggesting that the drug could be peripherally acting.

Yedapo (1996) investigated the phosphate buffered saline extract of the roots of *P. zeylanica* for anti-inflammatory activity. The extract stabilized red blood cells subjected to both heat and hypotonic induced lyses. The extract exhibited a biphasic response. The enzymatic activities of both alkaline and acid phosphatases were reduced, while adenosine triphosphatase activity was stimulated in the liver homogenates of formaldehyde induced arthritic rats.

Antiarthritic activity

Poosarla and Athota (2007) investigated the role of an ethyl acetate fraction of the root extract of *P. zeylanica* in its antiarthritic activity in collagen type II–induced arthritis in DBA/1 mice and in the suppression of humoral antibody and stimulation of T cell mediated responses. PZE-6 suppressed collagen type II–induced arthritis in DBA/1 mice in a dose-dependent manner. In addition, the treatment with *P. zeylanica* stimulated Con A induced T-cell proliferation to normal levels in arthritic mice.

Wound healing activity

Reddy et al. (2002) studied wound healing effects of *H. indicum*, *P. zeylanica* and *A. indica* in rats. The ethanolic extracts of *H. indicum*, *P. zeylanica* and *A. indica* were evaluated for their wound healing activity in rats. *H. indicum* possesses better wound healing activity than *P. zeylanica* and *A. indica*.

Locomotorbehaviour and central dopaminergic activity

Bopaiah and Pradhan (2001) studied the effects of a 50% ethanol extract of the root of *P. zeylanica* on locomotor behavior and central dopaminergic activity in rats. The results showed that the extract specifically enhanced the spontaneous ambulatory activity without inducing stereotypic behavior. The neurochemical estimations revealed elevated levels of DA and HVA in striatum compared with the control rats ($p < 0.01$).

Hyperlipidaemic activity

Alpana (1996) studied effect of *P. zeylanica* in hyperlipidaemic rabbits and its modification by vitamin E. There was significant reduction in serum total cholesterol, LDL cholesterol and triglyceride levels. Marked reduction was observed with the formulation of *P. zeylanica* and vitamin E. The total cholesterol/HDL and LDL/HDL cholesterol ratios were found significantly ($p<0.01$) decreased.

Some other research

Giday et al. (2007) conducted a study in two sub-districts of the Shinasha, Agew-awi and Amhara peoples in northwest Ethiopia to compile and analyzed knowledge on the use of medicinal plants for treatment or prevention of human ailments by three socio-cultural groups, Large proportions of medicinal plants were found to have been used for the treatments of gastro-intestinal complaints (26%), skin diseases (24%) and malaria (22%). Relatively, higher numbers of informants agreed on the use of *Zehneria scabra* against malaria (13%). The species *Croton macrostachyus*, *Cattleya aurea*, *Canephora hirsuta* and *P. zeylanica* were found to have the highest diversity of medicinal applications.

Sandur et al. (2010) investigated whether 5-hydroxy-2-methyl-1,4-naphthoquinone (plumbagin), an analogue of vitamin K, and isolated from chitrak (*Plumbago zeylanica*), Plumbagin significantly potentiated the apoptotic effects of thalidomide and bortezomib in MM cells. Overall, these results suggest that the plumbagin inhibits STAT3 activation pathway through the induction of SHP-1 and this may mediate the sensitization of STAT3 overexpressing cancers to chemotherapeutic agents.

Effect of *P. zeylanica* on key enzymes of glycolysis

Olagunju et al. (1999) studied the effects of the ethanol extract of the root of *P. zeylanica* on key enzymes of glycolysis and other biochemical parameters in the rat.
The results show that thigh muscle hexokinase, phosphofructokinase, pyruvate kinase and lactate dehydrogenase activities were significantly reduced ($p < 0.05$) by 12.07, 51.02, 24.32 and 25.16%, respectively in rats treated with the ethanol extract of *P. zeylanica* when compared with the controls.

Conclusion

*P. zeylanica*is is used for centuries in Ayurvedic medicine to increase longitivity and vitality. It is the most important medicinal plant extensively used in herbal formulations. It is chemically rich with its diverse content of active

compounds, such as plumbazin, chitranone, zeylanone and many useful naphthaquinone constituents as a multi-purpose medicinal agentwere present. In this study, we have reviewed literature pertaining to *P. zeylanica* and its botanical constituents as immunostimulatory, hepatoprotective, and hypolipidamic agents and *P. zeylanica* can exhibit varying degrees of therapeutic values in the treatment of fungal, malaria and bacterial infections including cancer. From review of article it can be said that plant act as a very good anticancer drug. Future research with respect to clinical study need to be carried out to explore its uses.

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