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A review on Morphology, Phytochemistry and Pharmacological activities of medicinal herb *Plumbago Zeylanica* Linn.

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Abstract
Plumbagin is the most common and broad spectrum phytochemical of *P. zeylanica.* The leaves and root bark contains plumbagin. The root yield new pigments, viz, 3-chloroplumbagin, 3, 3- biplumbagin, binaphthoquinone identify as 3', 6'-biplumbagin, and four other pigments identify as isozeylanone, zeylanone, elliptinone, and droserone. The isolation of plumbagin, droserone, isoshinanolone and a new napthalenone 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. All parts of the plant are used, but the roots have tremendous pharmacological properties. The pulped roots or aerial parts are reported abortifacient, while powdered bark, root or leaves are used to treat gonorrhoea, syphilis, tuberculosis, rheumatic pain, swellings, wound healing dyspepsia, piles, diarrhoea, skin diseases, leprosy and also reported to possess antibacterial, antifungal, and cantharides.

Keywords: Plumbagin, Anticancer activity, phytochemical, Antioxidant, Antibacterial drug, naphthoquinones, *Plumbago zeylanica,* Nonyl 8-methyl-dodec-7-enoate.

1. Introduction
From thousands of years and a remarkable number of modern drugs have been obtained from natural sources, particularly from the plants. Plant based medicines have played an important role in primary health care needs of human as well as animals. Variety of plants exhibit antimicrobial, larvicidal, anti- inflammatory and antioxidant activities due to the presence of some active compounds like essential oils, flavonoids, terpenoids, tri-terpenoids, glycosides, alkaloids and other natural phenolic compounds play a dominant role in the maintenance of human health since ancient times[1]. Natural products play on important role in drug development programmes in the pharmaceutical industry [2].
There are a few reports on the use of plants in traditional healing by either tribal people or indigenous community [3-5]. Many reports show the effectiveness of traditional herbs against microorganisms; as a result, plants have become one of the bases of modern medicine [6]. As an alternative form of health care and the development of microbial resistance to the available antibiotics has led researchers to investigate the antimicrobial activity of medicinal plants [7-10]. Silver and Bostian [11] have documented the use of natural products as new antibacterial drugs. There is an urgent need to identify novel substances active towards highly resistant pathogens [12, 13]. It is thought that herbal remedies have the advantage of combining their active components with many other substances which appear to be inactive but which give the plant as a whole a level of safety and efficiency superior to that of its isolated, pure active components; moreover, in developing countries, synthetic drugs are presently too expensive and also are often adulterated [14]. *P. zeylanica* Linn (Plumbaginaceae) is a perennial herb commonly distributed in forest of the Uttarakhand, India, and cultivated in the gardens throughout India. It grows wild as a garden plant in eastern, northern and southern India and *has* been reported to be used in variety of folk medicine in Africa and Asia.
It has been using in the treatment of refractory prostate cancer [15] and shown anti fertility activity, antihyperlipidemic activity [16], anti estrogenic activity [17] to kill intestinal parasites, treat rheumatism, anemia due to "stagnant blood", external and internal trauma, toxic swelling and malignant furunculous scabies[18]. Antiplasmodial [19], antimicrobial [20], antifungal [21], anti-inflammatory [22], antibacterial [23], hypolipidaemic and antiatherosclerotic activities [24].

Plumbagin (5-hydroxy-2-methylnaphthalene-1,4-dione) is a naturally occurring yellow pigment produced by the members of *Plumbaginaceae*, accumulated mostly in root[25]. Plumbagin showed anticancer [26], antimicrobial and antibiotic [27, 28], antibacterial and antifungal activities [29]. Five coumarins – seselin [30], 5-methoxyseselin [31], suberosin [32], xanthyletin and xanthoxyletin have been isolated from the roots of *Plumbago zeylanica* [33].
The aim of this study was to emphasize the phytochemistry and pharmacological activities of *Plumbago zeylanica* herb.

2. Morphology
There is no consistency in the literature citing the classification of *P. zeylanica* as herb or shrub. Some authors have described it as a perennial dicot herb [34, 35], while it has also been designated as a shrub by others [36]. *P. zeylanica* plant attains a height of about 0.5–2 m (1.6–6.6 ft). The leaves are alternate, simple, ovate or ovate-lanceolate, elliptical or oblong, 0.5–12 cm in length with a tapered base 3 cm broad and often with a hairy margin. The stipules are absent and the petiole is narrow (0–5 mm long) with small auricles in young leaves. The inflorescence is of terminal raceme-type about 6–30 cm long and many-flowered. Flowers are white in colour [34, 37] long, inodorous, inbracteate, axillary and terminal elongated spikes, bisexual regular, pentamerous, pedicellate and sweet-scented. Calyx densely covered with stalked, sticky glands. Corolla is white, very slender, and tubular and Stamens 5, free. Ovary superior, 5-gonous, one celled, ovule one basal.

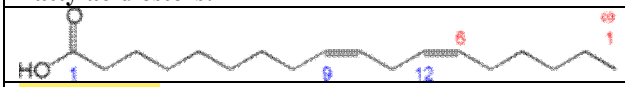
The style is filiform with five elongated stigma lobes and the ovary is superior, single-celled. The flowers are also characterized by having a tubular calyx (7–11 mm long and 5-ribbed) with glandular trichomes (hair) secreting a sticky mucilage. The plant flowers round the year and pollination is primarily by insects. The mucilaginous glands aid in trapping insects and fruit dispersal by animals. The fruit of the plant is an oblong (7.5–8 mm long) five-furrowed capsule containing single seed. Each seed is oblong in structure, 5–6 mm long and reddish- brown to dark brown in colour. Roots are straight, smooth, branched or unbranched, with or without secondary roots and about 30 cm or more in length and 6 cm in diameter [38]. They are light- yellow when fresh and become reddish-brown on drying. The roots have a strong and characteristic odour with acrid and bitter taste [34].

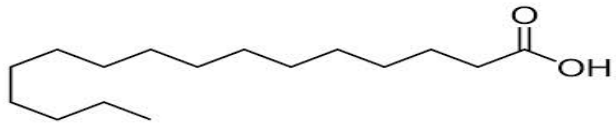
3. Phytochemistry
Plumbagin is the most common and broad spectrum phytochemical of *P. zeylanica*. The leaves and root bark contains plumbagin. The root yield new pigment, viz, 3-chloroplumbagin, 3, 3- biplumbagin, binaphthoquinone identify as 3', 6'-biplumbagin, and four other pigments identify as isozeylanone, zeylanone, elliptinone, and droserone. The isolation of plumbagin, droserone, isoshinanolone and a new napthalenone 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, maritinone, elliptinone and isoshinanolone), and five coumarins (seselin, methoxyseselin, suberosine, xanthyletin and xanthoxyletin) were isolated from the roots isolated by Lin and coworkers [33].
Some phytochemical from different parts of *P. zeylanica* are reported by different workers [36, 39, 40, 41]. Like in stem plumbagin, zeylanone, isozeylanone, sitosterol, stigmasterol, campesterol, and dihydroflavonol plumbagin. In leaves plumbagin and chitanone. Flowers contain plumbagin, zeylanone, and glucose. Fruit contains plumbagin, glucopyranoside and sitosterol.

Seeds also contain plumbagin, and the root bark of *P. zeylanica* contains 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 droserone. The isolation of plumbagin, droserone, isoshinanolone and a new napthalenone 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, maritinone, elliptinone and isoshinanolone), and five coumarins (seselin, methoxyseselin, suberosine, xanthyletin and xanthoxyletin) were isolated from the roots**.** Plumbagin (2-methyl-5-hydroxy-1,4-naphthoquinone) is a yellow crystalline bioactive phytoconstituent present in the roots isolated from *P. zeylanica* by soxhlet apparatus followed by silica gel column chromatography [33, 42].

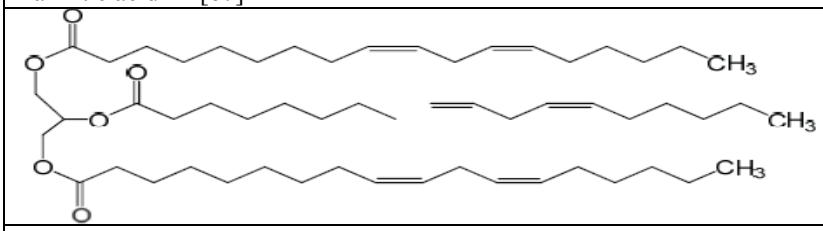
3.1 Phytochemicals isolated from *P. zeylanica*
Plumbagin is the major phytochemical isolated from *P. zeylanica* and it have tremendous medicinal values. Several other naphthoquinones, binaphthoquinones [43-47], coumarins [33, 48], di-phenyl sulfone [49], carboxylic acids and esters [50], meroterpenes [51], triterpenoids [52, 53], amino acids [54], anthraquinones [55], steroids [56], steroid glucosides [48], sugars [57] and other compounds [58-62]. Recently four other compounds one naphthoquinone and three difuranonaphthoquinones have been isolated and characterized [63, 64] Table 1. Some qualitative phytochemicals results in leaves of *P. zeylanica* revealed the presence of alkaloids, glycoside, reducing sugars, simple phenolics, tannins, Lignin, saponins and flavonoids reported qualitatively [41] and tested [84].

Table 1: List of phytochemicals isolated from different parts of *p. zeylanica*

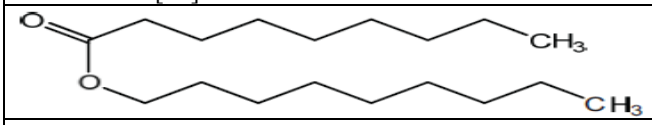
Compound names	**References**
Fatty acid esters:	
	
Linoleic acid	[67]



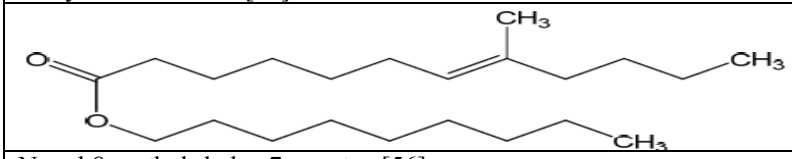
Palmitic acid [67]



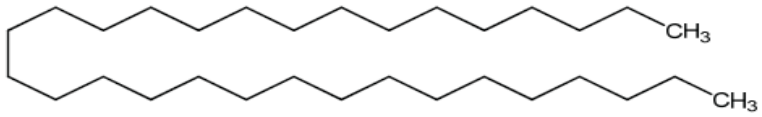
Trilinolein [83]



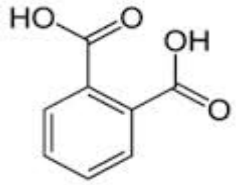
Nonyl nonanoate [56]



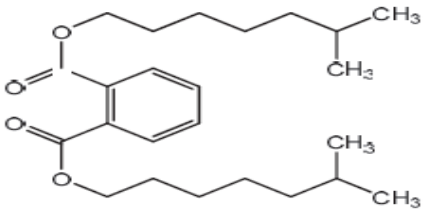
Nonyl 8-methyl-dodec-7-enoate [56]



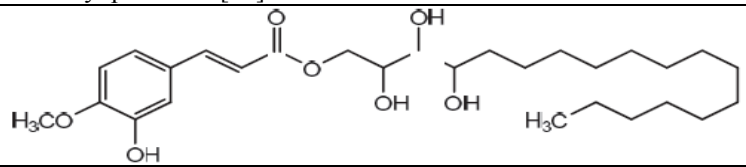
Hentriacontane [65]



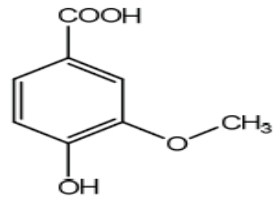
1,2-Benzenedicarboxylic acid [50]



Diisooctyl phthalate [50]

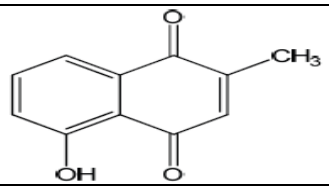
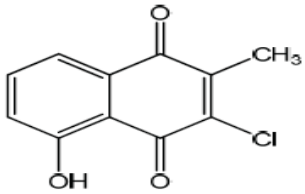
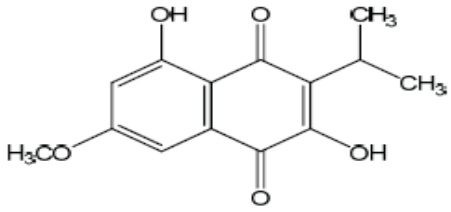
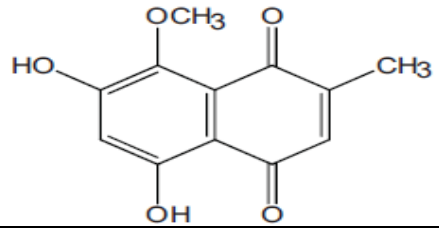
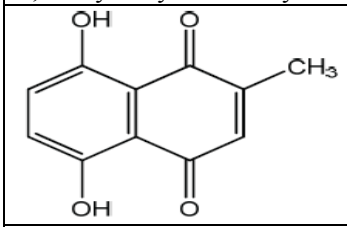
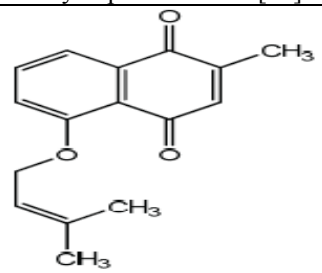
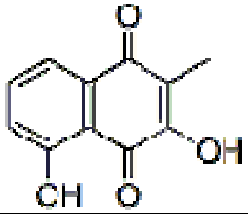


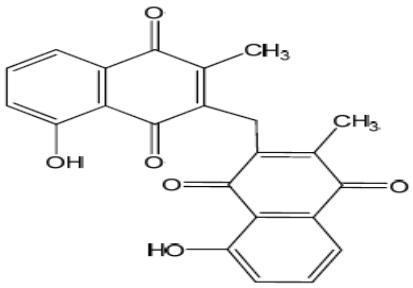
Gugultetrol-18-ferrulate [65]



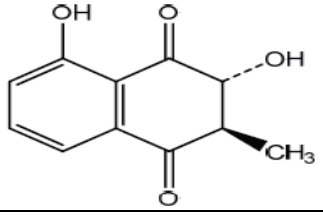
Vanillic acid [68]

Naphthoquinones:

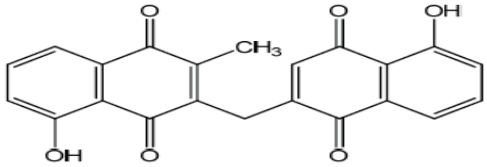

Plumbagin [56,69,70]

3-chloroplumbagin [71]

3,8-dihydroxy-6-methoxy-2-isopropyl-1,4-napthoquinone [44]

5,7-dihydroxy-8-methoxy-2-methyl-1,4- naphthoquinone [44]

2-methylnaphthazarin [43]

2-methyl-5-(3'-methyl-but-2'-enyloxy)- [1,4]naphthoquinone [63]

Droserone (3,5-Dihydroxy-2-methyl-1,4-naphthoquinone) [47,55]



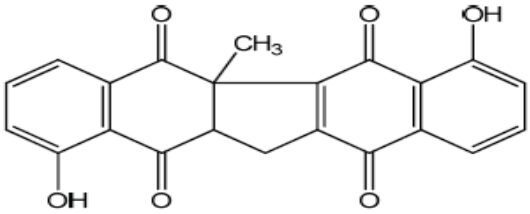
Methylene-3,3'-diplumbagin [43]



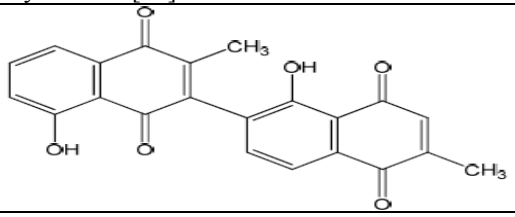
Dihydrogesterone [72]



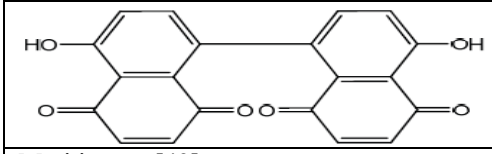
Isozeylanone [73]



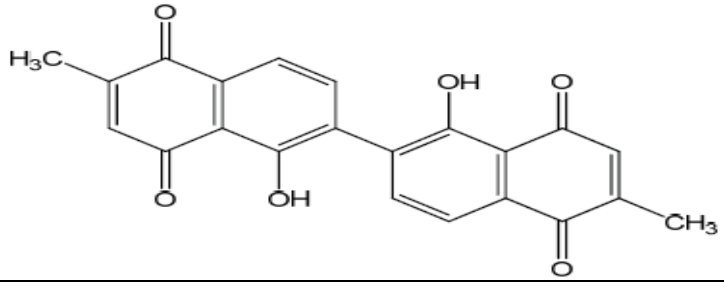
Zeylanone [73]



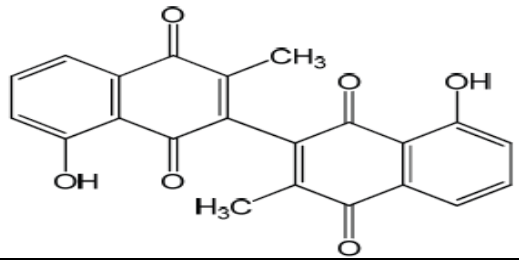
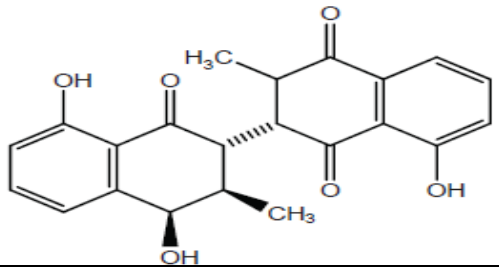
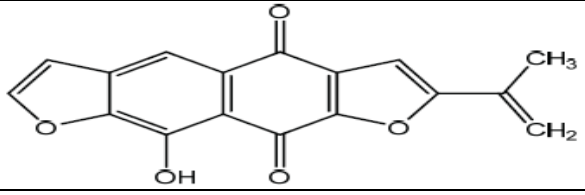
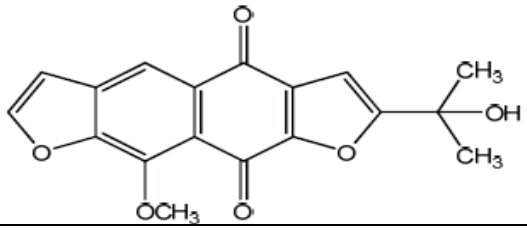
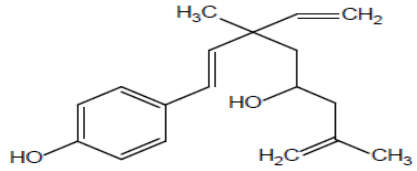
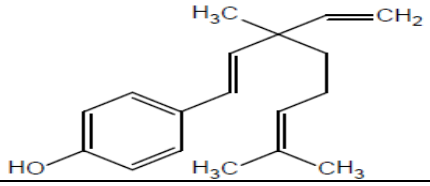
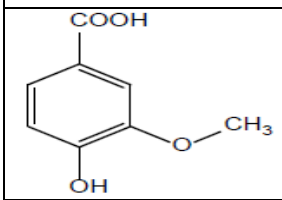
Chitranone [45]

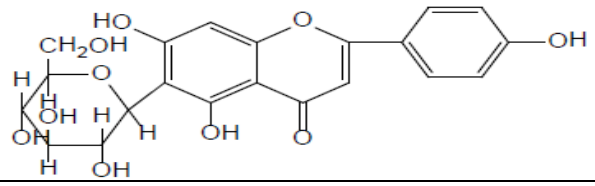


Maritinone [43]

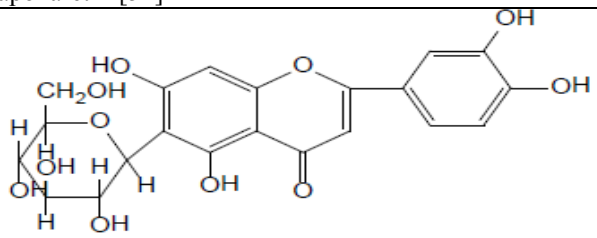


Elliptinone [47]

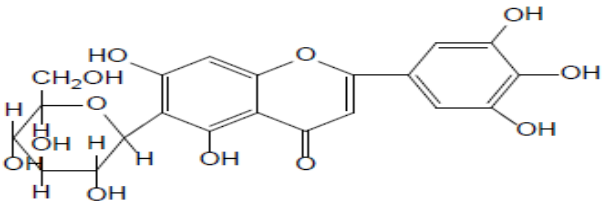

3,3-diplumbagin [74]

1,2(3)-tetrahydro-3,3'-biplumbagin [75]

9-hydroxy-2-isopropenyl-1,8-dioxa-dicyclopenta[b,g]naphthalene-4,10-dione [64]

2-(1-hydroxy-1-methyl-ethyl)-9-methoxy-1,8- [64]
dioxa-dicyclopenta [b,g]naphthalene-4,10-dione
Meroterpenes:

12‑ hydroxyisobakuchiol [51]

Bakuchiol [51]
Flavonoid and flavonoid glucosides:

2-(2, 4-Dihydroxy-phenyl)-3, 6,8-trihydroxy-chromen-4-one [76]



Saponaretin [51]

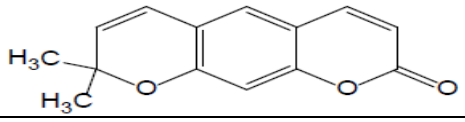


Isoorientin [51]

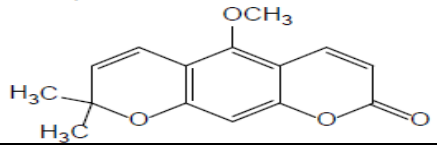


Isoaffinetin [51]

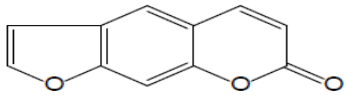
Coumarins:



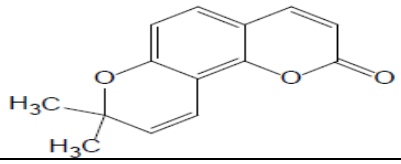
Xanthyletin [51]



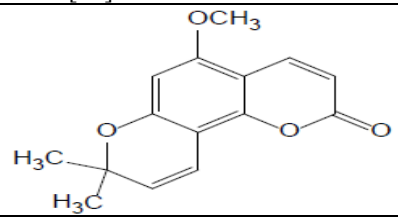
Xanthoxyletin [51]



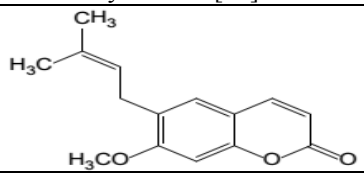
Psoralen [51]



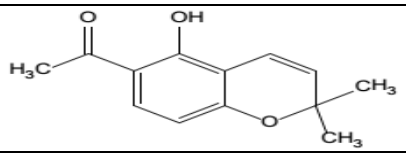
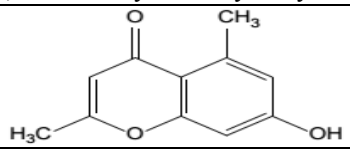
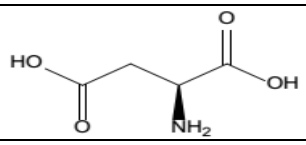
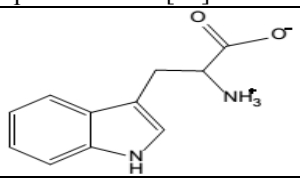
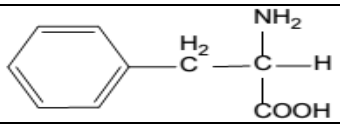
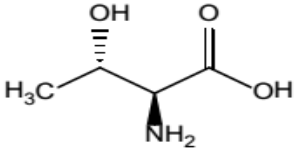
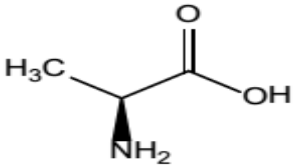
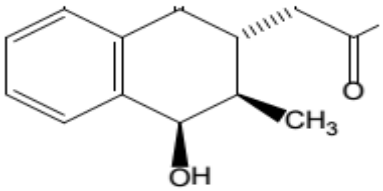
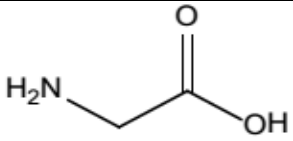
Seselin [33]

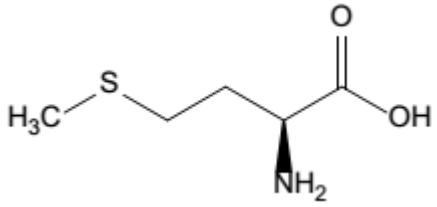


5‑ methoxyseselin [33]

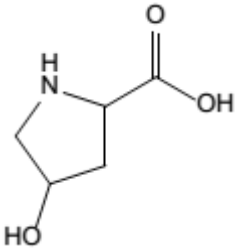


Suberosin [33]

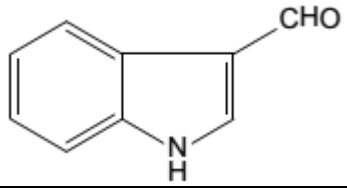

2,2- dimethyl- 5- hydroxy- 6- acetyl chromene [56]

2, 5- dimethyl- 7- hydroxychromone [77]
Amino acids and alkaloids:

Aspartic acid [54]

Tryptophan [54]

Tyrosine [54]

Threonine [54]

Alanine [54]

Histidine [54]

Glycine [54]



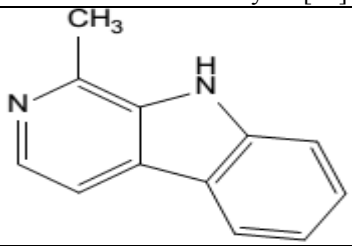
Methionine [54]



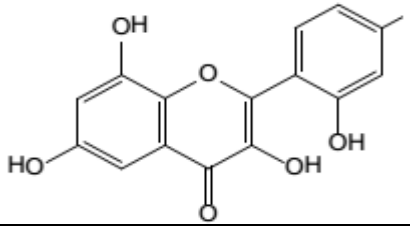
Hydroxyproline [54]



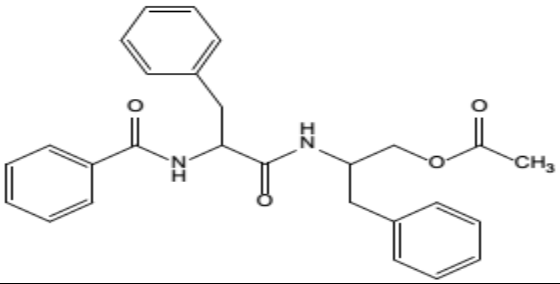
Indole‐3‐carboxaldehyde [77]



Harman [78]

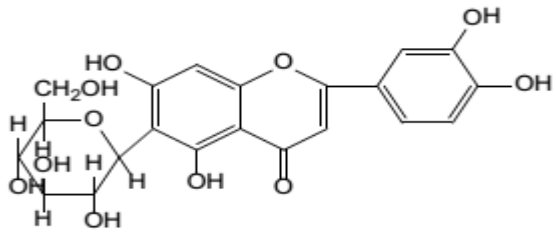


Neoechinulin A [78]

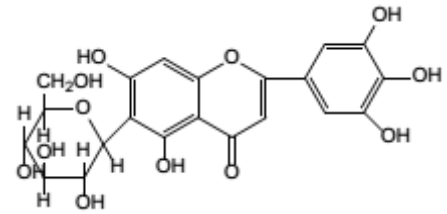


N‐(N′‐benzoyl‐S‐phenylalaninyl)‐S‐phenylalaninol [78]

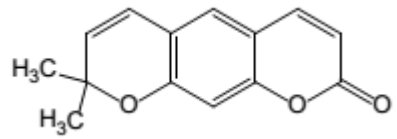
Steroids:



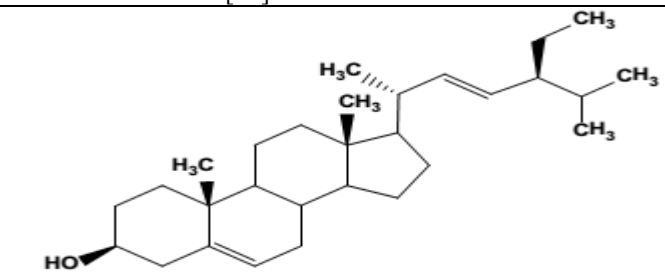
β-sitosterol [49,172]



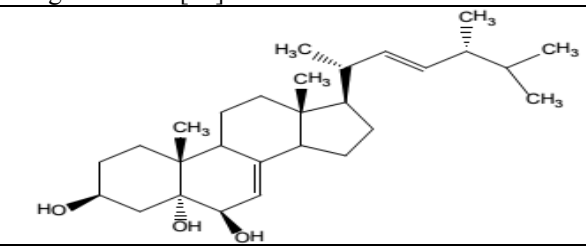
Stigmasterol acetate [56]



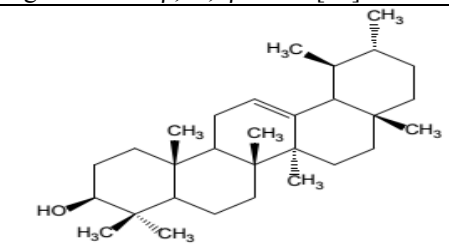
Sitosterone [56]



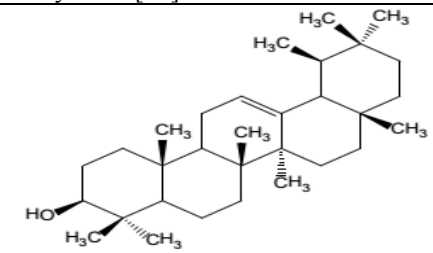
Stigmasterol [56]



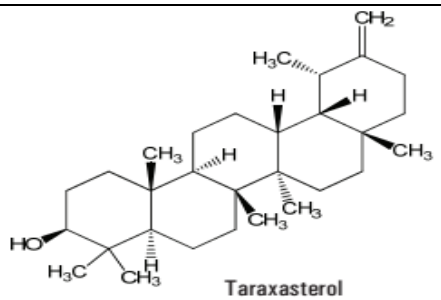
Ergostadiene-3β,5α,6β-triol [78]



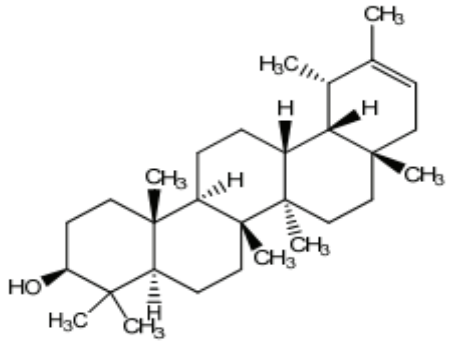
α-amyrin [53]



β-amyrin [53]

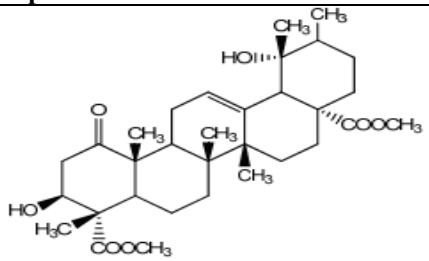


Taraxasterol [53]

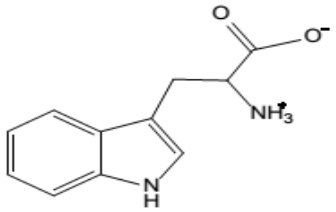


ψ –taraxasterol [79]

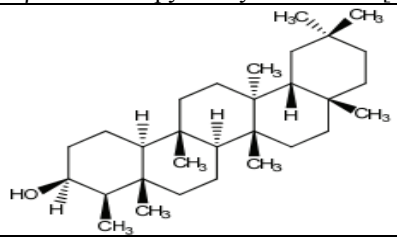
Terpenoids:



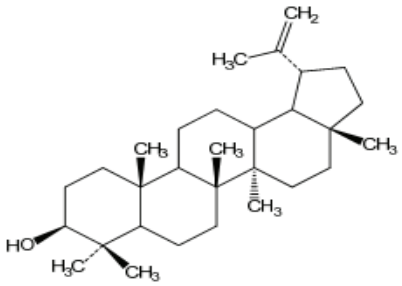
1-keto-3 β,19 α-ainyaroxyurs-12-ene-24,28-dioic acid dimethyl ester [52]



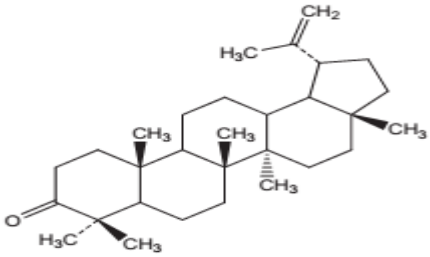
3-O-β-D-arabinopyranosy derivative [52]



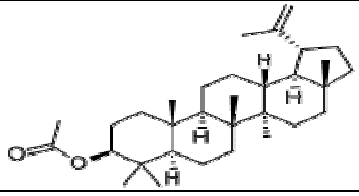
Friedelinol [56]



Lupeol [53]

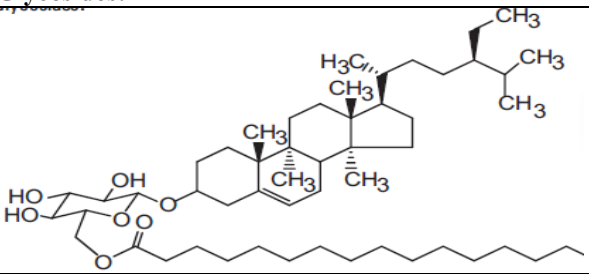


Lupanone [56]

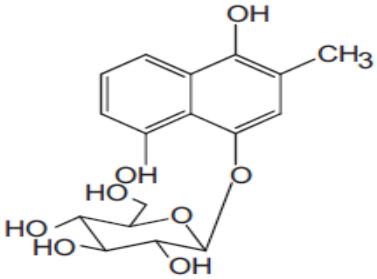


Lupeol acetate [83]

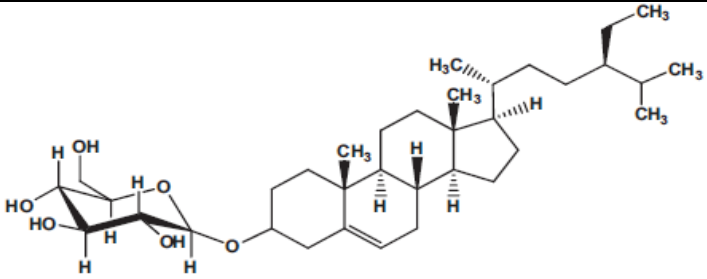
Glycosides:



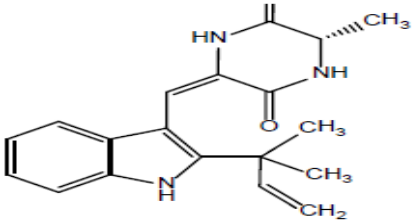
β-sitosterol-3 β-glucopyranoside-6'-O-palmitate [60]



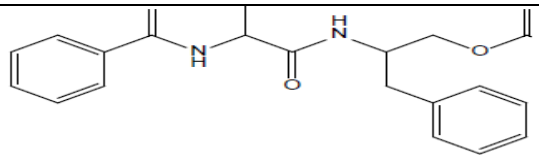
Hydroplumbagin glucoside [80]



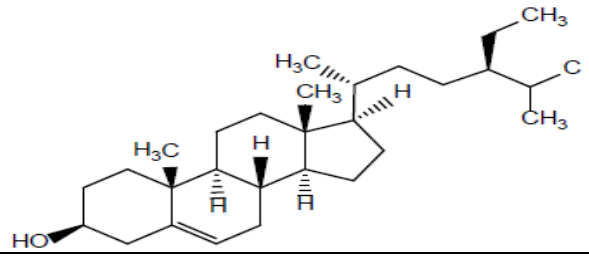
β-sitosteryl glucoside [83]



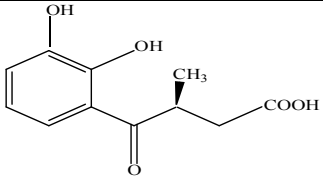
3'-O- β-glucopyranosyl plumbagic acid [33]



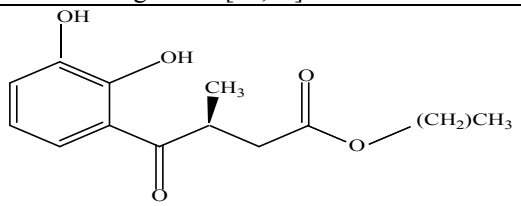
1-hydroxy-3-methyl-6-methoxyanthraquinone-8-O-β-D-xylopyranoside [55]



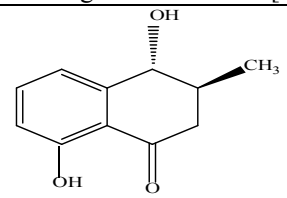
3'-O- β-glucopyranosyl plumbagic acid methylester [33]



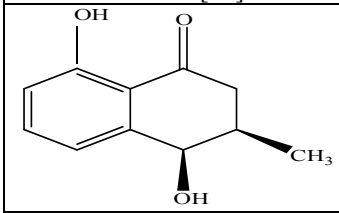
Plumbagic acid [68,91]



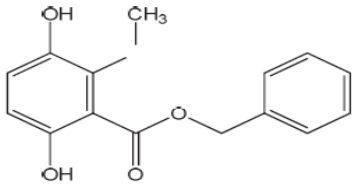
Plumbagic acid Bu. Ester [51]



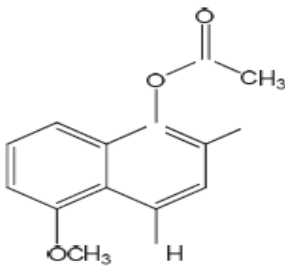
Isoshinznolone [78]



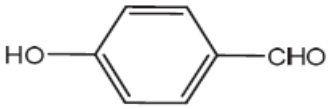
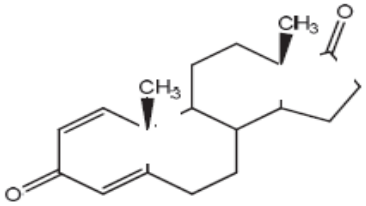
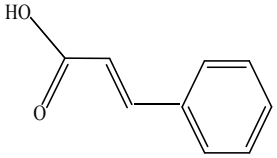
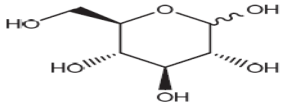
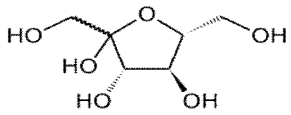
Isoshinanolone [46,51]



Benzyl 2,5-dihydroxy-6-methoxybenzoate [56]



1-acetoxy-4-hydroxy-2-methyl-5-methoxynaphthalene [74]


4-hydroxybenzaldehyde [77]

Androsta-1,4-diene-3,17-dione [78]

Trans-cinnamic acid [77]

Glucose [82]

Fructose [82]

3.2 Macro, micro and some essential elements detected in *P. zeylanica:*

Some elemental analysis has been done for leaves, stems and roots of *P. zeylanica* exists with abundant amounts of elements like four macro-elements (Na, K, Ca and Mg), five essential microelements (Zn, Fe, Mn, Cr and Co), and eight other elements (Mo, Sb, Bi, Cd, Sr, Pb, Cd and As) respectively were detected by inductively Coupled plasma atomic emission spectrometry (ICP-AES) [85].

4. Pharmacological activities of *P. zeylanica.*

The whole plant and its root have been used as a folk medicine in Taiwan for the treatment of rheumatic pain, menostasis, carbuncle and injury by bumping [86] . All parts of the plant are used, but the roots have tremendous pharmacological properties. The pulped roots or aerial parts are reported abortifacient, while powdered bark, root or leaves are used to treat gonorrhea, syphilis, tuberculosis, rheumatic pain, swellings, wound healing [87] dyspepsia, piles, diarrhoea, skin diseases, leprosy and also reported to possess antibacterial, antifungal [88], cantharides [83].

The pharmacological importance of this perennial shrub lies in its ability to produce a napthoquinone, called plumbagin [89]. The main constituent in the root and leaves is Plumbagin (2-methyl-5-hydroxy-1,4-naphtho-quinone). Plumbagin is a yellow crystalline bioactive phytoconstituent [42] about 0.03% of dry weight of the roots. Plumbagin showing a broad range of pharmaceutical activities. Table 2 & 4

Pharmacological effects of plumbagin have been investigated on shortness of breath [90]. In Ayurvedic and Unani system of medicines, the plant has been described for significant anticancer [83, 91], antitumor [92], anti-inflammatory [22], antioxidant [93, 94], anti-mycobacterial [95] and antimicrobial activities [25, 39, 96, 97], rheumatic pain, sprains, scabies, skin diseases, and wounds. The roots of the plant and its constituents are credited with potential therapeutic properties including anti-atherogenic, cardiotonic, hepatoprotective, neuroprotective, and central nervous system stimulating properties [98], activity against canine distemper virus [99].

4.1 Pharmacological activities of different solvent extracts of *P. zeylanica.*

Acetone extract of *P. zeylanica* also effects on chromosomal aberrations induced by ethinylestradiol in cultured human lymphocytes [100]. hypolipidemic effect [101], anti-tumor [102-104], antimicrobial, anticancer, wound healing [105], anti-inflammatory and altered T-cell

proliferative activities [106, 107], and anti-fertility actions [108-112]. Plumbagin has also shown antibacterial activity against both gram-positive and gram-negative bacteria [28, 113-117], antihyperglycemic [118], insecticidal [119, 120], anti-allergic [121, 122] and antigonorrhoeal activity [123]. Besides, it has been also found active against certain yeasts fungi [124, 125], protozoa [19] and in tumor inhibitory activity [125]. It has also demonstrated significant hyperglycemia, hypolipidemic, and antiatherosclerotic effects in rats [24, 65, 126-129]. The root of *P. zeylanica* has been reported to be a powerful poison when given orally or applied to ostiumuteri, causes abortion [130] cytotoxic and anti-insecticidal property [48, 131, 132]. Different kinds of solvent extracts of *P. zeylanica* have shown their broad spectrum pharmacological activities. Table-3

Table 2: Pharmacological activities of plumbagin (2-methyl-5-hydroxy-1,4-naphtho-quinone)

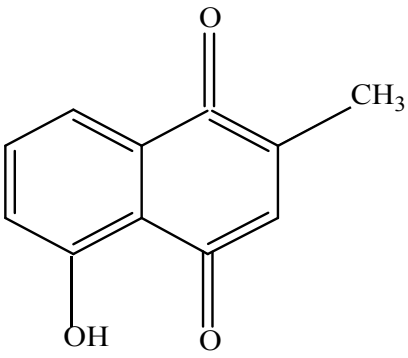
 Plumbagin	Antibacterial activity Antitumour activity Antyfertility activity Synergistic activity Anticoagulant activity Hypolipidaemic activity GST activity Antibacterial activity Blood coagulation activity AntiHelicobacter pylori activity	[28] [103,104] [104,111] [95] [127] [24] [93] [97] [129] [113]

Table 3: Pharmacological activities of some solvent extracts of *Plumbago Zeylanica* herb.

Type of plant extract	Dose ranges	Negative Control	Animal model / Microorganisms	Duration of the study	Results	Ref.
Methanolic extract of leaves	25, 50 & 100 mg	-	Indian earthworm (*Pheretima posthuma*)	2 days	Anthelmintic activity	133
Methanolic extract of root	50,100, &150 µg/ml	-	*Helicobacter pylori*	1 day	Anti- bacterial activity	134
Ethanol, acetone or ethyl acetate of Rhizome	30 µl	-	*Helicobacter pylori*	3 day	Anti- bacterial activity	113
Ethanolic extract of root	0.64-10.24 mg/ml	Ethanol	*E. coli* and *Shigella*	2 days	Anti- bacterial activity	135
Plumbago zeylanica root	100 mg/kg	-	Human study	14 days	Anti- hyper Cholesterolemic activity	34
Ethanolic extract of stems	500, 1000 mg/kg	48/80	Wistar Mice	2 days	Antiallergic activity	121
Methanol, chloroform and alcoholic extracts of leaves	50, 100 mg/ ml	-	*Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa*	1 day	Antibacterial activity	41
Methanol, Chloroform and	1 mg/ml	-	*E. coli, Salmonella typhi, Klebsiella*	2 days	Antibacterial activity	23

aqueous extract of root			*pneumoniae, Serratia marcescens, Proteus vulgaris, Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus cereus*			
Petrol. ether, ethanol and aqueous extract of root	1200 µg/ml	-	*Staphylococcus aureus* and *Micrococcus luteus*	2 days	Antibacterial activity	39 172
Methanolic extract of leaves	50, 100 mg/ml	-	*Baci. subtilis, Staphylococcus aureus, Escherichia coli* and *Salmonella typhi*	2 days	Antibacterial activity	133 172
Ethanolic extract of root	100, 200 mg/kg	Cancer cell line	Male Swiss albino mice	14 days	Anticancer activity	136
Ethanolic extract of root	250 mg/kg bw	3-methyl-4- di methyl amino azo-benzine	Wistar albino rats	7 days	Anticarcinogenic activity	137
Hydroalcoholic extract of leaves	250, 500 mg/kg	Pentylenetetrazole	Wistar albino rats	1 hour	Anti-convulsion activity	138
Methanolic extract of root	4–10 mg/ml	Occluded dermal irritation	Albino rabbits, Swiss mice and Albino rats	1 day	Anti-dermatotoxicity	90
Ethanolic extract of root	250 mg/kg bw	Alloxan	Wistar albino rats	21 day	Antidiabetic activity	118
Aqueous extract of root	100, 200 mg/kg	STZ	Wistar albino rats	42 day	Antidiabetic activity	139
Aqueous extract of leaves	100, 200 mg/kg	STZ	Wistar albino rats	28 day	Antidiabetic activity	140
Aqueous extract of leaves	100, 200 mg/kg	STZ	Wistar albino rats	28 day	Antidiabetic activity	141
Methanol, chloroform extract of whole plant	50 µl	-	*Rhizoctonia solani Kuhn, Bipolaris* spp., *Ustilago maydis* and *Alternaria alternate*	2 day	Antifungal activity	142 172
Ethanolic extract of root	250, 500 mg /kg bw	Cyclopho sphamide	Swiss albino mice	7 day	Antigenotoxic activity	94
Petroleum ether extract of root	300 mg/kg	Parace- tamol	Wistar albino rats	7 days	Antihepatot oxic activity	143
Methanolic extract of aerial parts	35, 70 mg/kg	CCl4	Wistar albino rats	14 days	Antihepatot oxic activity	36
Aqueous extract of root	20,40, and 80 mg/kg	Diet-induced hyperlipidemic rats	Wistar albino rats	7 days	Antihyperli pidemic effect	17
Methanol, extract of root	300, 500 mg /kg	Carrageenin	Wistar albino rats	7 days	Anti-inflam-matory activity	66
Petroleum ether, chloroform and acetone extract of root	0.1 ml	-	*Salmonella typhi, Staphylococcus aureus, Escherichia coli,*	2 days	Antimicrobial activity	144

			Aspergillus niger, Pencillium sp. And *Fusarium oxysporum*			
Methanolic extract of root	7.5 mg/ml	RPMI & Dimethyl Sulfoxide	male Sprague–Dawley rats	3 hours	Antimutagenic effect	145
Root powder	7.5 mg/kg bw	Phenyl-hyd ra zine	Male Wistar Albino rats	21 hours	Antioxidant activity	146
Ethanolic extract of root	1 mg/L	DPPH(1,1-di phenyl -2-picrylhydra zyl)ABTS (2,2-azinobis-3-ethy lbenzothiazo line-6-sulfonic acid diammoni um salt	*In-vitro* study	1 hour	Antioxidant activity	76
Ethanolic extract of root	100 mg/kg	-	*In-vitro*	2 hours	Antioxidant activity	147
Methanolic extract of leaves	50,100 mg /ml	Butylated hydroxy anisole	*In-vitro*	2 hours	Antioxidant actvity	133
Methanolic extract of root	0.8–200 µg /ml	Guanidine hydrochloride, amantadine, and phosphonoformic acid	coxsackievirus B3 Nancy (CVB3), influenza A virus Hong Kong/1/68 (H3N2), and herpes simplex virus type 1 Kupka (HSV-1)	2 days	Antiviral activity	148
Aqueous extract of plant	0.5 µg/ml	-	Hepatitis B-virus	2 days	Antiviral activity	149
Ethanolic extract of root	250 mg/kg	Cholesterol	Rabbit	28 days	Hypolipidaemic activity	150
Ethanolic extract of root	250 mg/kg	Diet-induced hyperlipidemic rats	Rabbit	28 days	Hypolipidemic activity	151
Ethanolic extract of root	250 mg/kg bw	-	BALB/C mice	6 weeks	Immunomodu-latory activity	152
Aqueous root extract	4 mg/ml	Turkey egg albumin	Balb/c mice	56 days	Immunosuppr-essive activity	153
Chloroform extract of root	100, 200 & 400 mg/kg.	Scopolamine	Swiss albino mice	10 days	Memory Enha-ncing effect	154

Table 4: Plumbagin with putative anticancer and anti-proliferative tested in either *in vivo* or *in vitro* models

Cancer Cells	Results	Ref
Human Prostate cancer cell (PC-3, LNCaP, and C4-2)	Decrease in cell viability, apoptosis induction, Generation of ROS, depletion of intra cellular GSH	155

Human Melanoma A375.S2	Reduced amounts of cyclin B1, cyclin A, Cdc2, and Cdc25C and enhanced the levels of inactivated phosphorylated Cdc2 and Cdc25C, increased the activation of apoptosis signal-regulating kinase 1, JNK and extracellular signal-regulated kinase 1/2 (ERK1/2) and finally blocking ERK and JNK	156
Human non small cell lung cancer cells, A549	Activation of JNK and SP600125 (Aanthra [1,9-cd]pyrazol-6(2H)-one-1,9- pyrazoloanthrone), a specific inhibitor of JNK, decreased apoptosis by inhibiting the phosphorylation of p53 and subsequent increased in the interaction of p53 and MDM2. SP6000125 also inhibited the phosphorylation of Bcl-2 (Ser70	157
Human Peripheral blood lymphocytes	Effective cell growth inhibition, induces apoptosis, generates single-strand of DNA breaks and cytotoxic action	158
Human Prostate Cancer	Inhibition of both cultured Prostate Cancer cells and DU145 xenografts (a) the expression of protein kinase Cepsilon (PKCepsilon), phosphatidylinositol 3- kinase, phosphorylated AKT, phosphorylated Janus-activated kinase-2, and phosphorylated signal transducer and activator of transcription 3 (Stat3); (b) the DNA-binding activity of transcription factors activator protein-1, nuclear factor kappaB, and Stat3; and (c) Bcl-xL, cdc25A, and cyclooxygenase-2 expression	159
Human acute promyelocytic leukemia cells	Inhibition of proliferation of NB4 cells, chromosomes condensation and apoptotic body formation, cell proliferation and induce apoptosis of APL cell line NB4 cells	160
MCF7 and Bowes cancer cell lines	Inhibition of the proliferation of MCF7 and Bowes cells	83
Human hepatoma	Inhibition of the certain glycolytic enzymes and gluconeogenesis.	137
Human peripheral blood mononuclear cells	Involve the regulation of cell cycle progression, interleukin-2 and interferon production	161
MDA-MB-231 cells	Inhibitory effect on the protein levels of p- PI3K, p-Akt, p-JNK, p-ERK1/2, MMP-2, MMP-9, VEGF and HIF- 1α	162
Human breast cancer cells	Inactivation of NF-kappaB and Bcl-2	163
Human breast cancer cells	Inhibit Akt activity and enhanced the activation of Chk2, resulting in increased inactive phosphorylation of Cdc25C and Cdc2.	164
Lung A549 cells	Increased the expression of p53 and phosphorylated p53 (Ser15 and Ser392) and regulates the levels of cell cycle related molecules in A549 and activates JNK	157
Human ovarian cancer cells	Bound to the active site of ER-α and inhibit classical ER-α signaling pathways	165
Cervical cancer cells	Lower dose of radiation in combination with plumbagin could induce apoptosis more effectively and activation of caspase 3 in C33A cells. Induction of apoptosis by irradiation and involves caspase-dependent pathways.	166
Human promyelocytic leukemia cells	Induced apoptotic cell death and inhibits tumor growth without obvious toxicity and triggering the mitochondria-dependent apoptosis of tumor cells by increasing ROS	91
Ovarian cancer cells	Induced loss of mitochondrial membrane potential, nuclear condensation, DNA fragmentation, and morphological changes	167
Human cervical cancer	Induced cell death is through the generation of ROS and subsequent induction of apoptosis caused loss of mitochondrial membrane potential and morphological changes characteristic of apoptosis, such as the translocation of phosphatidyl serine, nuclear condensation, and DNA fragmentation.	168
sarcoma-180	Ehrlich ascites model was evaluated and identified as less toxic, justified with the help of LD50 survival studies and stud	169

Azoxymethane induced intestinal carcinogenesis	Promising chemopreventive agents for human intestinal neoplasia	170
3T3-L1 cells	Activated PI3-kinase and/or PDK1 stimulate Akt activity with Ras–Raf–MEK1/2–ERK1/2 pathway	171

5. Conclusion

The study showed that the ethanol and petroleum ether and other solvent extract from the leaves, roots and stems of Plumbago zylanica have anti microbial, antiviral, antioxidant, antifungal, anti-allergic and other wonderful medicinal properties. It is the most important medicinal plant extensively used in herbal formulations for centuries. The evidence presented in this review has shown that *Plumbago zeylanica* L. has tremendous potential to be integrated into conventional medical practice for the treatment and management of various metabolic syndromes, hepatotoxic, diabetes, inflammation, cancer and other disease complications. Some phenolic compounds have also been known as antioxidant agents, which act as free radical terminators and have shown medicinal activity as well as exhibiting physiological functions. It was reported that compounds such as flavonoids, which contain hydroxyls, are responsible for the radical scavenging effects of most plants. Development and research on *Plumbago zylanica* through modern pharmaceutical technologies and analytical protocols is essential to assure its quality, safety and efficacy. It is anticipated that this review will provide some valuable information for ongoing explorations of this fascinating species its phytochemicals and pharmacological dynamics.

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