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Phytochemical and pharmacological profile of *Zanthoxylum armatum* DC. — An overview

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Zanthoxylum armatum DC. (Family — Rutaceace), also known as Toothache tree occupies an important place in the history of Indian system of medicines. It is used as carminative, stomachic and anthelmintic and in the treatment of toothache. It contains volatile oil with active constituents such as linalool, limonene and lignan. Various studies indicated that it possesses antilarvicidal, antifungal, hepatoprotective and allelopathic properties. This review focuses on the detailed phytochemical composition and medicinal uses along with pharmacological properties of different parts of *Z. armatum*.

Keywords: Indian Prickly Ash, Larvicidal, Lignans, Linalool, Monoterpenoids, Nepal Pepper, Toothache tree, *Zanthoxylum armatum*.

IPC code; Int. cl. (2011.01) — A61K 36/758, A23L 1/221

Introduction

Zanthoxylum armatum DC. (syn. *Z. alatum* Roxb.) of the Rutaceace family is an important medicinal plant which is commonly known as Indian Prickly Ash, Nepal Pepper or Toothache tree. Local names of this plant are: *Tejphal* (Hindi), *Tejowati* (Sanskrit), *Mukthrubi* (Manipuri) and *Timur* (Nepal).

It is widely distributed in India, from Kashmir to Bhutan at altitudes up to 2,500 m, also occurs throughout North East India. It is also found throughout most of China, Taiwan, Nepal, Philippines, Malaysia, Pakistan and Japan at altitudes of 1,300-1,500 m. Valleys and thickets in the mountains, wasteland and the under-storey of mixed forest are customary locations of the species[1-11].

It is a small tree or large spiny shrub. Leaves are distinctively trifoliolate with the leaf-stalk winged. Leaflets are stalk less, 2.0-7.5 × 1.0-1.7 cm, elliptic to ovate-lace like, entire to slightly toothed, sharp-tipped, base sometimes oblique. Minute yellow flowers arise in leaf axils. Flowers have 6-8 acute sepals. Petals are absent. Male flowers have 6-8 stamens and large anthers because of which the flowers look yellow. Female flowers have 1-3 celled ovary, 3 mm in diam., pale red, splitting into two when ripe. Seeds are round, 3 mm in diam., shining black. The flowering period is from March to April (Plate 1).

Traditional uses

The bark, fruits and seeds of *Z. armatum* are extensively used in indigenous system of medicine as a carminative, stomachic and anthelmintic. The fruit and seeds are employed as an aromatic tonic in fever and dyspepsia. An extract of the fruits is reported to be effective in expelling round worms. Because of their deodorant, disinfectant and antiseptic properties, the fruits are used in dental troubles, and their lotion for scabies. They are also used to ward-off houseflies[12]. The natives of North America crush the

Plate 1 — *Zanthoxylum armatum* DC.

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Table 1 — The traditional uses of *Zanthoxylum armatum* DC. in various countries

S. No.	Country	Traditional uses	Ref. No.
1.	India	The seeds and the bark are used in the treatment of fevers, dyspepsia and cholera.	16
		Root, fruit, bark and leaf are used for catching fishes (piscicidal).	17
2.	Japan	Seed is used for indigestion, flatulence and depression.	18
3.	Nepal	Fruit decoction is used for abdominal pain.	19
		Berries are carminative, antispasmodic and used for rheumatism and skin diseases. Bark is used for cholera, diabetes and asthma.	20
		Pickles from the fruits are useful for cold & cough, tonsillitis, headache, fever, high altitude sickness, limbs numbness, vertigo/dizziness, diarrhoea and dysentery. Powdered dried fruits are taken with hot water to cure diarrhoea, dysentery and stomachache.	21
4.	Pakistan	The dried fruit is used as a spice.	22
		Powder of its dried fruit, *Mentha longifolia* dried leaves, *Trachyspermum ammi* seeds and black salt is taken with water during cholera and indigestion. Twigs are used as toothbrush during gum problems and toothache.	23
5.	China	An infusion in vinegar is used to expel bugs or worms infecting ear.	24
		Scabies is treated by the plant, using a lotion applied to the skin.	25

bark and apply on their gums for relief hence it is known as the toothache tree.

It is used in China and India as snake-bite remedy[13]. In China the dried fruits are marketed, and appear as small red carpels containing the black, shinning, pungent and somewhat acrid-tasting seeds, which are about 3.1 mm across. The fruits have also been used, since classical times, for pickling[14,15]. The traditional uses of *Z. armatum* in various countries are listed in Table 1[(Refs 16-25)].

Chemical constituents

Various phytochemical constituents like alkaloids, sterols, phenolics, lignins, coumarins, terpenoids, flavonoids and their glycosides and benzenoids, fatty acids, alkenic acids, amino acids have been isolated from this plant. In Table 2, different types of phytochemical compounds are listed[26-51].

Kalia *et al*[26] extracted armamide (amide), asarin and fargesin (lignan) from the bark of *Z. armatum*. Other constituents of bark are mainly of zanthonitrile[37] and berberine[36] (alkaloid), *L*-asarin, *L*-sesamin and *L*-planinin[33] which are lignans. Volatile constituents linalool, limonene and methyl cinnamate are also found from seed[27]. Ramidi *et al* isolated tambulin (flavonoid) from the seed[51].

An essential oil from this plant, collected from Kashmir and Jammu, contain linalool, (64.1%), linalyl acetate, citral, geraniol methyl cinnamate, limonene and sabines[1]. Leaves from Garhwal, further east in the Himalaya, yield 0.04% essential oil, containing methyl-n-nonyl ketone, 44.0; linalool, 19.5; linalyl acetate, 10.7; and sesquiterpenes, 13.0%. The structure of some of the main constituents are given in Figure 1.

Biological activities

Various biological activities reported from different extracts of the plant are summarized in Table 3[52-73], and some major ones are discussed below:

Mosquito repellent

Das *et al*[52] studied the mosquito repellent property of its oil against mosquitoes in mustard and coconut oil base and compared with synthetic repellent dimethyl phthalate (DMP) as standard. It afforded better protection in both the base at all the concentrations. Repellents in mustard oil gave longer protection time than those in coconut oil. At 0.57 mg/cm^2 concentration the oil gave significantly higher protection both in mustard (445 min) as well as coconut oil (404 min) than DMP.

Cardiovascular disorders

The crude extract exhibits spasmolytic effects, mediated probably through Ca^{2++} antagonist mechanism, which provides pharmacological base for its medicinal use in the gastrointestinal, respiratory and cardiovascular disorders[53]. The extract exhibited concentration-dependent relaxation of spontaneous and high K^+ (80 mM) induced contractions against isolated rabbit jejunum (*in vitro*), being more effective against K^+ and suggestive of Ca^{2++} antagonist effect, which was confirmed when

Table 2 — Chemical constituents of *Zanthoxylum armatum* DC.

S. No.	Compound	Source	Country	Percentage of essential oil/compound yield	Reference No.
TERPENOIDS					
1.	α-Fenchol	SD	India	0.68	26
2.	α-Terpinene	SD	India	0.4	27
3.	α-Thujene	SD	India	1.65	26
4.	α-Thujone	SD	India	0.1	27
5.	α-Pinene	SD	India	0.1	27
6.	α-Terpineol	SD	India	0.31	26
		SD	India	1.1	27
		LO	Vietnam	4.1	28
7.	β-Pinene	SD	India	0.1	27
8.	β-Cymene	LO	Vietnam	1.3	28
9.	β-Phellandrene	SD	India	5.7	29
		PFT	India	5.3	30
10.	β-Terpineol	LO	Vietnam	2.1	28
11.	Camphor	SD	India	0.25	26
12.	Carvone	SD	India	0.20	26
		SD	India	0.4	27
13.	Citral	DF	India	-	1
14.	Citronellol	SD	Japan	-	31
15.	Citronellal	SD	Japan	-	31
16.	1,8-Cineole	SD	India	0.25	26
		SD	India	t	27
		LO	Vietnam	41.0	28
		AP	German	15.7	32
17.	*cis*-Ocimene	SD	India	0.12	26
18.	Geraniol	DF	India	-	1
		SD	India	0.4	27
		FT	India	-	33
19.	γ-Terpinene	SD	India	0.08	26
20.	*(E)*-Carveol	SD	India	2.6	27
21.	*(E)*-Linalool oxide	SD	India	1.0	27
22.	Limonene	SD	India	24.46	26
		SD	India	19.8	27
		SD	India	8.2	29
		PFT	India	6.2	30
		SD	Japan	12.6	31
23.	Linalool	SD	India	58.3	26
		SD	India Vietnam	57.0	27
		LO	India	-	28
		SD	India	4.5	29
		PFT	Japan	71.0	30
		SD	German	62.2	31
		AP	India	18.8	32
		FT	India	-	34
		SO	USA	87.7	35
		SD		72.0	36
24.	Linanyl acetate	DF	India	-	1
		FT	India	-	34

(*Contd.*)

Table 2 — Chemical constituents of *Zanthoxylum armatum* DC.— *Contd.*

S. No.	Compound	Source	Country	Percentage of essential oil/compound yield	Reference No.
25.	Myrcene	SD	India	3.55	26
		SD	India	1.3	27
26.	Nerol	SD	India	0.3	27
27.	1-α-Phellandrene	SD	USA	-	36
28.	Phellandrene	FT	China	-	37
29.	*p*-Cymene	SD	India	0.65	26
30.	Piperitone	SD	India	0.3	27
31.	Sabinene	SD	India	0.1	27
		LO	Vietnam	8.4	28
		FT	Paris	-	33
		FT	China	-	37
32.	Tagetonol	SD	India	0.16	26
33.	Terpinen-4-ol	SD	India	2.3	27
		LO	Vietnam	5.2	28
34.	*(Z)*-Sabinene hydrate	SD	India	t	27
35.	*(Z)*-Linalool oxide	SD	India	1.0	27
36.	*(Z)*-Pinene hydrate	SD	India	0.5	27
37.	*allo*-Aromadendrene	SD	India	0.98	26
38.	β-Caryophyllene	SD	India	0.50	26
39.	(*E*)-Nerolidol	SD	India	0.6	27
40.	α-Amyrins	BK	India	-	38
41.	β-Amyrone	BK	China	-	39
42.	β-Amyrins	BK	India China	-	38
		BK		-	39
43.	Lupeol	BK	India	-	38
ALKALOIDS					
1.	Berberine	BK	India	-	40
2.	Chelelactam	PNS	UK	-	41
3.	Dictamnine	RT	USA	-	36
4.	Fargarine	PNS	UK	-	41
5.	Haplopine	PNS	UK	-	41
6.	Magnoflorine	RT	USA	-	36
7.	Nitidine	PNS	UK	-	41
8.	Nevadensin	SO	India	-	35
9.	Robustine	PNS	UK	-	41
10.	Sanguinarine	PNS	UK	-	41
11.	Skimmianine	BK	China	-	42
		RT	USA	-	36
12.	Zanthonitrile	BK	China	-	42
STEROLS & STEROIDS					
1.	β-Daucosterol	BK	China	-	39
2.	β-Sitosterol	BK	China	-	39
		SO	India	-	35
3.	Stigmasta-5-en-3β-D-glucopyranoside	SD	India	t	43
4.	β-Sitosterol-β-D-glucoside	BK	India	-	40

(*Contd.*)

Table 2 — Chemical constituents of *Zanthoxylum armatum* DC.— *Contd.*

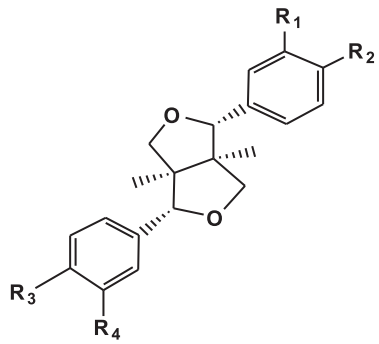
S. No.	Compound	Source	Country	Percentage of essential oil/compound yield	Reference No.
LIGNINS					
1.	Asarinin	BK	India	-	40
		PNS	Budapest	-	44
		PNS	-	-	45
2.	Eudesmin	PNS	-	-	45
3.	Epieudesmin	PNS	-	-	45
4.	Fargesin	BK	India	-	38
		PNS	-	-	45
5.	Kobusin	PNS	-	-	45
6.	*L*-Asarinin	BK	China	-	39
7.	*L*-Sesamin	BK	China	-	39
8.	*L*-Planinin	BK	China	-	39
9.	Magnolin	PNS	-	-	29
10.	Phylligenin	PNS	-	-	45
11.	Planinin	PNS	-	-	45
12.	Sesamin	PNS	Budapest	-	44
		PNS	-	-	45
FLAVONOIDS					
1.	3,5-Diactyltambulin	BK	China	-	42
2.	Kaempferol	BK	China	-	42
3.	Tambulin	PNS	Budapest India	-	44
		SD		-	46
4.	3,5,3′-Trihydroxy-6,7-dimethoxy-4′-(7″-hydroxygeranyl-1″-ether) flavone	SD	India	-	47
5.	3,5,3′,4′-Tetrahydroxy-7,8-dimethoxy flavone	SD	India	-	47
6.	Tambuletin	SD	India	-	47
COUMARINS					
1.	Bergapten	BK	China	-	42
2.	Umbelliferone	BK	China	-	42
		SO	India	-	35
AMIDES					
1.	Armatamide	BK	India	-	38
2.	Hydroxyl-α-sanshooil	P	India	-	48
3.	Hydroxyl-β-sanshooil	P	India	-	48
CARBONYL COMPOUNDS					
1.	Cuminal	FT	China	-	37
2.	Cuminaldehyde	SD	India	0.3	27
3.	Cuminic aldehydes	FT	Paris	-	25
4.	Cinnamic aldehyde	FT	Paris	-	25
5.	Dimethylic ether of phloroacetophenon	FT	Paris	-	25
6.	Phellandral	SD	India	1.3	27

(*Contd.*)

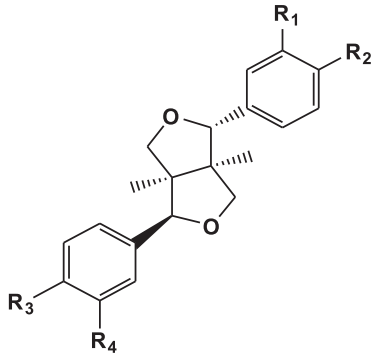
Table 2 — Chemical constituents of *Zanthoxylum armatum* DC.— *Contd.*

S. No.	Compound	Source	Country	Percentage of essential oil/compound yield	Reference No.
7.	2-Tridecanone	LO	Vietnam	1.8	28
8.	Undecan-2-one	AP	German	17.0	32
AROMATIC COMPOUNDS					
1.	1-Hydroxy-6,13-anthraquinone	SD	India	0.0064	43
2.	2-Hydroxybenzoic acid	SD	India	0.0038	43
3.	2-Hydroxy-4-methoxy benzoic acid	SD	India	0.0047	43
4.	*trans*-Cinnamic acid	SO	India	-	35
5.	Vanillic acid	BK	China	-	39
6.	(*E*)-Methyl cinnamate	SD	India	5.7	27
7.	Methyl cinnamate	SD	India	8.92	26
		SD	Japan	8.8	31
		PFT	India	12.2	30
8.	(*Z*)-Methyl cinnamate	SD	India	4.9	29
9.	3-Methoxy-11-hydroxy-6,8-dimethylcarboxylate biphenyl	SD	India	0.0211	43
10.	3,5,6,7-Tetrahydroxy-3',4'-dimethoxyflavone-5-*β*-D-xylopyranoside	SD	India	0.0075	43
11.	Monoterpenetriol-3,7-dimethyl-1-octane-3,6,7-triol	SO	India	-	35
12.	1-Methoxy-1,6,3-anthraquinone	SD	India	0.0083	43
OTHER ALIPHATIC COMPOUNDS					
1.	*cis*-9-Hexa-decenoic	SO	India	15.4	49
2.	*cis*-10-Octadecenoic acid	PNS	India	25.5	50
		SO	India		51
3.	*cis*-9,12-Octadecadienoic acid	PNS	India	18.76	50
4.	*cis*-9,12,15-Octadecatrienoic acid	PNS	India	12.65	50
5.	2,6-Dimethyl-1,3,5,7-octatetraene	LO	Vietnam	1.5	28
6.	6-Hydroxynonadec-*(4Z)*-enoic acid	SD	India	-	26
7.	8-Hydroxypentadec-(4*Z*)-enoic acid	SD	India	-	26
8.	7-Hydroxy-7-vinylhexadec-(4*Z*)-enoic acid	SD	India	-	26
9.	Hexadec-(4*Z*)-enoic acid	SD	India	-	26
10.	6-Methylheptanoic	SD	Japan	-	31
11.	8-Methylnonanoic acid	SD	Japan	-	31
12.	Oleic acid	SD	India	t	27
13.	Palmitic acid	PNS	India	10.5	50
		SD	India	0.9	27
14.	Palmitolic acid	PNS	India	31.47	50
15.	Methyl palmitate	SD	India	t	27

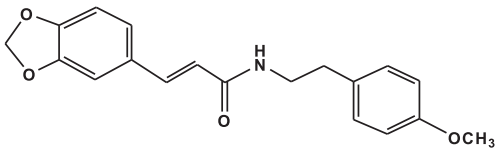
SD = Seed, SO = Seed Oil, Ft = Fruit, BK = Bark, AP = Aerial Part, LO = Leaf Oil, RT = Root, C = Carpels, DF = Dry Fruit, PFT = Pericarp of Fruit, PNS = Part Not Specified, t = trace & - = Not assigned.



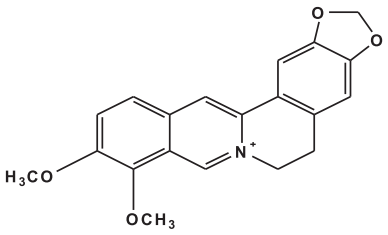
(+)-Sesamin R_1/R_2= OCH_2O, R_3/R_4 = OCH_2O
(+)-Kobusin R_1=R_2= OCH_3, R_3/R_4 = OCH_2O
Eudesmin R_1=R_2= R_3=R_4 = OCH_3



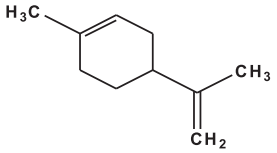
(+)-Asarinin R_1/R_2= OCH_2O, R_3/R_4 = OCH_2O
(+)-Fargesin R_1=R_2= OCH_3, R_3/R_4 = OCH_2O
Planinin R_1/R_2= OCH_2O, R_3?R_4 = OCH_3
(-)-Phylligenin R_1 = OCH_3, R_2= OH R_3=R_4 = OCH_3
Epleudesmin R_1=R_2= R_3=R_4 = OCH_3



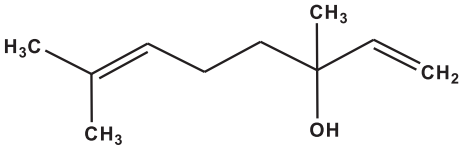
Armatamide



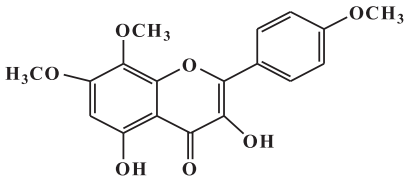
Berberine



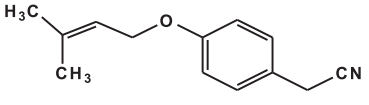
Limonene



Linalool



Tambulin



Zanthonitrile

Fig. 1 — Main constituents of *Zanthoxylum armatum* DC.

Table 3 — Biological activities of essential oil/and different extracts of *Zanthoxylum armatum* DC.

S.No.	Extract	Plant part	Country	LC50/ED50 Conc.used/MGI	Species	Reference No.
A.	LARVICIDAL ACTIVITY:					
1.	EO	SD	India	-49 ppm	*Culex quinquefasciatus*	27
2.	EO	SD	India	-58 ppm	*Anopheles stephensi*	27
3.	EO	FL	China	-6.895 µg cm^{-3}	*Culex pipiens quinquefasciatus*	61
B.	ANTIFUNGAL ACTIVITY:					
1.	DCM	LF	India	+18 mm	*Alternaria alternata*	62
2.	DCM	LF	India	+15 mm	*Curvularia lunata*	62
3.	EO	FT	India	*2.0 x 10^3 µll^{-1}	*Aspergillus flavus*	63
4.	EO	FT	India	*2.0 x 10^3 µll^{-1}	*Aspergillus parasiticus*	63
5.	Acetone	P	India	*340 cm^{-2}	*Sitophilus oryzae*	64
6.	Acetone	P	India	*340 cm^{-2}	*Callosobruchus maculatus*	64
7.	Aqueous	PX	India	@	*Candida albicans*	65
8.	Aqueous	PX	India	@	*Cryptococcus neoformans*	65
9.	EO	SD	India	-+39.5 %	*Microsporum gypseum*	66
10.	EO	SD	India	-+28.8 %	*Trichophyton mentagrophytes*	66
11.	EO	LF	India	--353.4 µg ml^{-1}	*Sclerotium rolfsii*	67
12.	EO	LF	India	--250.0 µg ml^{-1}	*Rhizoctonia bataticola*	67
13.	EO	SDP	Nepal	*10 µl ml^{-1}	*Alternaria brassicicola*	68
C.	HEPATOPROTECTIVE ACTIVITY:					
1.	Ethanol	BK	India	*100 mg kg^{-1}	Male Wistar rats	69
D.	INHIBITION OF KERATINOCYTE GROWTH:					
1.	Methanol	BK	German	++11 µg mL^{-1}	Human keratinocytes (HaCaT cells)	70
E.	ANTIVIRAL ACTIVITY:					
1.	Methanol	DP	Nepal	*2 mg ml^{-1}.	HSV-1/Vero cells	71
2.	Methanol	DP	Nepal	*2 mg ml^{-1}.	Influenza A/MDCK cells	71
3.	Aqueous	PX	India	@	*Japanese B encephalitis* virus	65
F.	ANTI-PROTOZOAN					
1.	Aqueous	PX	India	@	*Plasmodium berghei*	65
2.	Aqueous	PX	India	@	*Giardia lamblia*	65
G.	PESTICIDAL /INSECTICIDAL ACTIVITIES:					
1	EO	PNS	India	-55-60 ppm	*Aphis cracccivora*	72
2.	EO	PNS	India	-55-60 ppm	*Tetranychus urticae*	72
3.	EO	FT	India	*2.0 x 10^3 µll^{-1}	*Allacophora foveicollis*	62
4.	PET	PNS	India	#20.45 ppm	*Culex pipiens quinquefasciatus*	50
5.	Petroleum	PNS	India	#315.50 ppm	*Culex pipiens quinquefasciatus*	50
H.	ANTIBACTERIAL					
1.	Aqueous	PX	India	@	*Staphylococcus aureus*	65
2.	Aqueous	PX	India	@	*Escherichia coli*	65
I.	Antifertility					
1.	Aqueous	PX	India	@	Anti-implantation in rats	65
J.	ANTIHELMINTIC					
1.	Aqueous	PX	India	@	*Pseudomonas aeruginosa*	65
K.	ALLELOPATHIC ACTIVITY:					
1.	Aqueous	LF	India	**52.0 %	*Triticum aestivum* Linn.	73
2.	Aqueous	LF	India	**100.0 %	*Hordium vulgare* Linn.	73
3.	Aqueous	LF	India	**63.0 %	*Brassica campestris* Hook. f. & Thoms.	73

** = Percent germination of field crops, - = LC_{50}, -- = ED_{50}, # = $LD_{50,}$ + = Inhibition zone,* = Conc, ++ = IC50, -+ = Mycelial growth inhibition (MGI), EO = Essential oil, DCM = Dichloromethane, PET= Petroleum ether & @ = Not specified.

pretreatment of the tissues with extract shifted Ca^{2++} concentration-response curves to the right, like that caused by Verapamil extract which inhibited the castor-oil-induced diarrhoea in mice at 300-1000 mg/kg. The extract relaxed the carbachol (1μM) and high K^+-induced contractions in rabbit tracheal preparation, in a pattern similar to that of Verapamil. In case of isolated rabbit aortic rings, extract exhibited vasodilator effect against phenylephrine (1μM) and K^+-induced contractions. Also, the extract caused inhibition of both atria force and rate of spontaneous contractions, similar to Verapamil, in case of Guinea pig atria.

Piscicidal

The piscicidal activity of the ethyl alcohol extract of the fruits was evaluated on Mg^{2+}- and Na^+, K^+-ATPase activity in different tissues of a carnivorous air-breathing catfish, *Heteropneustes fossilis*[54]. On exposure of fish to different concentrations of extract, and at LC_{50} concentration for different time intervals revealed significant inhibition of enzyme activity in brain, liver and muscle tissues. The inhibition was both dose and time dependent and reversible. Activity of Mg^{2+}-ATPase was inhibited more than that of Na^+, K^+-ATPase. *In vitro* studies on Mg^{2+}-ATPase activity revealed that inhibition of brain tissue extract was more than muscle and gill extracts. Kinetic studies on Mg^{2+}-ATPase activity suggested that piscicide is a non-competitive inhibitor. Noxious effect of extract was reversible.

Leech repellent

Essential oil of it possesses leech repellent activity. Experiments on persistence of repellent properties of N,N-diethyl phenyl acetamide (DEPA), N,N-diethyl-m-toluamide (DEET), 3 acetyl 2(2-6-dimethyl-5-heptenyl) oxazolidine (citronyl), dimethyl phthalate (DMP) and N-benzoyl piperidine (NBP) on cloth were tested against land leeches in evergreen rain and deciduous forests of Assam[55]. Results obtained were compared with volatile oil of it to evaluate its efficacy as leech repellent. *Z. armatum* oil was at par with Citronyl and exhibited better results than DMP and NBP though DEPA and DEET were found to be the best.

Inhibits skin sensitivity

A lipophilic extract of the fruits was credited for reducing mouth irritation due to food[56]. Dilution of this extract with oleyl alcohol gives an ingredient of cosmetic which is easy to formulate and is endowed with a remarkable soothing effect based on inhibition of sensory irritation from sun bathing, shaving, depilation, insect bites, chemical treatments and other causes.

Lousicidal

The seeds exhibit lousicidal potential against tropical hen louse, *Lipeurus lawrensis tropicalis*[57]. The seed extracts were diluted to the desired level (1:0, 1:1, 1:5, 1:10 and 1:100) and the lousicidal properties varied in proportion to the dilution and exposure time. Mortality was observed after 6, 12, 24 and 48 h of exposure to the respective dilutions. The undiluted extract showed 100% mortality after 12 h; the 1:1 dilution gave similar results. 1:5 dilution imparted 20, 53.3, 73.3 and 93.3% mortality after the respective exposure times. 1:10 dilutions gave values of 10.0, 33.3, 56.7 and 83.3% after the respective exposure times. The 1:100 dilutions gave only 10.0, 26.7 and 56.7% mortality after 12, 24 and 48 h, respectively.

Anti-inflammatory

Bergapten, a coumarin extracted from the plant exhibited significant inhibition of the production of pro-inflammatory cytokines, namely tumour necrotic factor-α (TNF-α) and interleukin-6 (IL-6) by PBMCs stimulated with lipopolysaccharide in a concentration-dependent manner[58]. Also, linalool and linalyl acetate are known to acquire inflammatory activity[59].

Antibacterial, antifungal and cytotoxic activities

The main flavonoid, 3,5-diacetyltambulin reported from *Z. armatum*[60] showed significant antibacterial activity against Gram positive bacteria (*Bacillus subtilis*, *B. megaterium*, *Staphylococcus aureus*) and Gram negative bacteria (*Escherichia coli*, *Shigella dysenteriae*, *S. sonnei*, *S. flexneri*, *Pseudomonus aeruginosa*, *Salmonella typhi*). The MIC values against these bacteria ranged from 8-64 μg/ml. However, this flavonoid and monoterpenoid (geraniol) shows weak antifungal activity[45,60].

Conclusion

The plant has been utilized in various traditional uses of which some have been proved clinically. The essential oils of *Z. armatum* have been used widely for larvicidal and insecticidal activities. Further studies on other secondary metabolites mainly of alkaloids and individual terpenoids need to be examined, to explore further findings. This review would be useful in promoting research aiming at the

development of new agents for therapeutic and agro-industries application, based on bioactive chemical compounds from indigenous plant sources as an alternative to synthetic chemical compounds.

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