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A REVIEW ON THERAPEUTIC USES OF TIMUR (ZANTHOXYLUM SPECIES [ARMATUM])

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ABSTRACT

Zanthoxylum, often known as "Timoor," is used as a spice, mouth freshener, and fish intoxicant. In this work, the separated chemical components and biological activity of the genus Zanthoxylum are documented. The Rutaceae family of aromatic deciduous trees and shrubs includes zanthoxylum limonella. Different portions of Z. limonella are used in traditional medicine to cure conditions like dental cavities, diarrhea, stomach aches, and rheumatism. The fruits, stem barks, and stems have been found to contain secondary metabolites. Alkaloid, amide, lignin, coumarin, and terpenoid chemicals are found in the plant. Native Americans have long employed the roots/rhizomes of black cohosh (Actaea racemosa L. syn. Cimicifuga racemosa [L]. Nutt., Ranunculaceae) to treat colds, rheumatism, and several diseases connected to women's health. Many plant species were found to be employed as food ingredients and in the treatment of hypertension, inflammation, pain, and mental disorders. The biological activities of both plant extracts and their phytoconstituents, including their modes of action, are reviewed. Over 500 chemicals have been identified from Z. species. Traditional medicines made from zanthoxylum piperitum DC. (ZP) are mostly used in Asian nations like Japan. This investigation is into the antinociceptive properties of ZP essential oil (ZPEO). The essential oil's primary ingredient was beta-(29.39%) Phellandrene. It is local to the Caribbean, Focal America, and South America. The species is generally developed in tropical and subtropical districts for its sweet-smelling leaves, which are utilized in culinary dishes and as a customary medication. Xanthophylum pipertium is a little tree or bush that normally develops to a level of 2-5 m (6.6-16.4 ft). The leaves are straightforward, elongated to curved, and measure 2-10 cm (0.79-3.94 in) long and 1-3 cm (0.39-1.18 in) in width. The leaves are sweet-smelling and have a sharp taste. The blossoms are little, white, and borne in groups. The natural product is a little, beefy berry that becomes yellow or orange when ready. This essay compiles an overview of research on Zanthoxylum armatum DC's pharmacological effects, phytochemical composition, and problems. Indigenous medicines are prepared using diverse plant parts such as leaves, fruits, stems, bark, seeds, and roots to treat a variety of ailments. It has antioxidant, anticancer, anti-inflammatory, analgesic, antibacterial, insecticidal/larvicidal, and other biological actions. A plant with several therapeutic properties called Zanthoxylum armatum DC. is widely used in traditional medicine to treat a wide range of illnesses, including cancer. The purpose of the current work is to molecularly identify Zanthoxylum armatum, which was gathered from various locations in Manipur, India.

KEYWORD: Anti- inflammatory, Analgesic, Zanthoxyulum Armatum.

INTRODUCTION

The world's temperate and tropical regions are home to around 150 genera and 1,600 species of trees, shrubs, and climbers that belong to the Rutaceae family.[1] The majority of the Rutaceae are fragrant plants with volatile scent molecules in their leaves, fruits, or cotyledons in seeds.[2] Rutaceae family members have been employed in traditional medicine, cuisine, and perfumes. Additionally, it has been noted in numerous publications that Rutaceae contains secondary chemical components. Alkaloids, coumarins, flavonoids, limonoids, and volatile oils are found in this family's plants.[3] An essential medicinal plant called Zanthoxylum armatum, also known as the toothache tree, Nepal pepper, and Indian prickly bush. This plant is extensively distributed in Northeast India and is locally known as Tejphal in Hindi, Tejowati in Sanskrit, Timur in Nepali, and Mukthrub in Manipuri. It is also known as the Szechuan pepper in China.[4] It is traditionally used by the Bhotiya communities in Uttaranchal, India's Himalayas, for food, medicine, and trade. The Bhotiyas of the Kamoli area of Garhwal have pioneered the collecting and trade of Armatum adheres to visitors to the Badrinath, Kedarnath, Gangotri, and Yamunotri shrines. The Bhotiyas of the Pithoragarh district of the Kumaon region uses the

Zanthoxylum armatum fruit.[5] Citrus, Zanthoxylum, Ruta, Ptelea, Murraya, and Fortunella are their principal genera.[6] More than 200 species of the genus Zanthoxylum exist around the world in tropical and temperate regions of North America, South America, Africa, Asia, and Australia.[7] In traditional medicine, perfumery, and pharmaceutical industries, members of the Zanthoxylum have been used by Supabphol & Tangjitjareonkun.[8] Based on their use in conventional folk medicine, these plants are a source of valuable bioactive chemicals that can be employed in ethnopharmaceutical products. Z. limonella is a common pest found throughout Asia. Its common names include "ma-kwaen" in Thailand, "kathit-pyu" in Burma, "chuan hua jiao" in Chinese, and "ivy-rue" in India. Z. limonella is used in traditional medicine and to flavour food. This species' varied parts are used to cure a variety of illnesses, such as rheumatic, heart, respiratory, and stomach infections.[9-10] The plant is officially named "Winged prickly ash" in English, however, it is more often called "Timur" or "Toothache tree." It can reach a height of 6 m in its natural environment and has dense foliage and armed branches with flattened prickles. Compound, imparipinnate, rachis-winged, serrate with gland spots, aromatic leaves with a flavour reminiscent of lime and mint is 4 to 20 cm long.[11] Due to its extensive biodiversity, India possesses the most advanced traditional system of plant-based medicine. Similar to India, most developing nations' national resources in the health sector heavily rely on herbal plants. Due to their affordability, effectiveness, and lack of negative side effects on human health, these herbal medications are primarily used for healthcare (Sekar et al., 2010). Therefore, plant material affects the pharmaceutical industries either directly or indirectly.[11] Numerous compounds have been identified and extracted in significant amounts from Z. armatum essential oil, including various alkaloids, flavonoids, flavonol glycosides, lignins, phenolics, sterols, terpenoids, fatty acids, alkenicacids, amino acids, various aromatic and volatile, and several others. Essential seed oil (EO) examination using gas chromatography-mass spectrometry (GC-MS) showed that there are 22 distinct components.[11] An essential member of this genus is Zanthoxylum armatum DC. (syn. Z. alatum Roxb.), is also known as toothache.[12]

Many of the components in the essential oil that this plant produces are volatile. Monoterpenes and sesquiterpenes, which give the essential oil its distinctive aroma and are part of the structurally varied class of natural chemicals known as isoprenes, make up the majority of the essential oil.[13]

In various places of the world, plants have served as beneficial sources of nutrients and therapeutic preparations for treating a variety of medical ailments. Most people who take plant extracts as medicine believe they are safer than synthetic pharmaceuticals.[14] Additionally, it has been demonstrated that herbal remedies can effectively treat a variety of infections, parasite disorders, and malignancies that are resistant to some synthetic pharmaceuticals.[15] This genus has a variety of plant species, the majority of which are found in Asia, America, and Africa.[20] Numerous Z. species have been traditionally utilized as medicinal herbs to treat a variety of illnesses. This genus of plants' secondary metabolites has shown a variety of pharmacological activity, including antioxidant, analgesic, anti-inflammatory, and modulatory properties against diabetes, dementia, and obesity.[25]

TAXONOMIC CLASSIFICATION[29]

Botanical name	Zanthoxylum armatum
Family	Rutaceae
KIngdom	Plantae
Sub kingdom	Viridaeplantae
Domaim	Eukaryote
Phylum	Tracheophyta
Sub phylum	Euphyllophytin
Infra phylum	Radiatopses
Class	Magnoliopsida
Sub class	Rosidae
super order	Rutanae
Order	Spindale
Sub order	Rutineae
Genus	Zanthoxylum

GEOGRAPHICAL DISTRIBUTION

Zanthoxylum Species (armatum) trees are widely dispersed around the world. Zanthoxylum armatum is also grown in nations including China, Japan, Korea, Taiwan, Bangladesh, Bhutan, Nepal, Pakistan, Laos, Myanmar, Thailand, Vietnam, and Indonesia. There are numerous kinds of tree in the Indian states of Andhra Pradesh, Jammu & Kashmir, Assam, Manipur, Meghalaya, Nagaland, Orissa, and Uttar Pradesh[31] At an altitude of about 2500 m, Zanthoxylum armatum is mainly found in North-East India but may also be found from Jammu and Kashmir to Bhutan. The main habitats of the species include wastelands, mountains, valleys, and forests.[30]

MAJOR SPECIES[11]

There are about 250 species found all over world. And in india mainly 11 species are reported.

1. Z.budrunga
2.Z.oxyphyllum
3. Z.ovalifolium
4. Z.acanthopodium
5.Z.planispinum
6. Z.armatum
7. Z.nitidium
8. Z.rhesta
9. Z.simulans
10.Z.avicennae
11. Z.limonella

Out of these 4 species are mainly distributed in Uttarakhand

1.Z.armatum DC
2.Z.acanthopodium DC
3.Z.oxyphyllum edgew
4.Z.budrunga

MORPHOLOGICAL CHARACTERSTICS

Up to 8 m tall shrubs or small trees with incurved reddish brown prickles and scabrous, grey-brownish bark. Leaves are compound, imparipinnate, and about 20 cm long. The rachis is glabrous or rust-colored pubescent, and the petiolules are about 2-4 mm long. The lamina is about 3-8 x 1-3 cm, ovate-lanceolate or elliptic to oblong, oblique at the base, acuminate at the apex, glandular-crenate along the margins, chart Cymes terminal on brief lateral branchlets, paniculate, pubescent, and 4–10 cm long; Male flowers are approximately 0.5 mm long, pubescent; perianths are uni- or irregularly biseriate, segments 6-8, approximately 1 mm long, yellowish, ovate-lanceolate, acute or acuminate, glabrous; stamens are 6-8, exserted; filaments are approximately 1.5–2.5 mm long; anthers are approximately 1 mm long, yellowish or reddish-purple, ovoid–oblong; 2 mm long; ovary 1 to 3 or occasionally 4 carpellate, about 1.5 mm long; style 0.5 mm long; stigma capitate; fruiting pedicels 1-3 mm long. Follicles 1-3 are postular, ovoid-subglobose, apiculate, and have 2, 1, or 0 caducous abortive carpels. They measure 3–4 mm in length. Around 3 mm wide, smooth, ovoid, and black seeds.[32]

Fig no-1 leaf of zanthoxylum.[32]

Fig no-2 fruit of zanthoxylum.[33]

Fig no-4 steam of zanthoxylum

Fig no-4 Tree of zanthoxylum

Fruits: Round Zanthoxylum fruits, or follicles as they are formally known, burst open to release blue to black, lustrous seeds that are held to the open fruit by a thin, short thread. The fruits are frequently coated in oil-filled warts. It is believed that birds spread the seeds.[34] When ingested, zanthoxylum fruits have a strong, pepper-like flavour with citrus undertones that numbs the mouth. The Sichuan pepper, which is produced from a number of species in the genus, is its most well-known product.[34]

Leaves: When crushed, the leaves of Zanthoxylum species, which have leaflets grouped pinnately or in triplets, emit a potent scent and are prickly. Zanthoxylum leaves have translucent, oil-filled glands, just like those of all citrus plants. Another characteristic of the genus is the presence of prickles on the young stems or sharp-pointed, corky knobs on the trunks and primary branches.[34] The leaves are imparipinnate, 4–20 cm long, aromatic, pungent, and have two stipular prickles at the base of the glabrous, slightly winged petiole. There are two to six pairs of lanceolate, glabrous-underside leaflets. The plant can be identified by its shrubby habit, dense leaves, prickly trunk and branches, and little red, sub globose fruits. It also has a pungent aromatic taste.[35]

Flowers: There are six to eight subacute lobes on the calyx. There are roughly six to eight stamens per flower. Typically solitary, pale red, and tuberculated, ripe carpels or follicles. The seeds are round, shiny, and dark. While fruiting happens from July to August, flowering takes place from March to May.[35]

TRADITIONAL USE

Thai traditional medicine has utilized several Z. limonella components for various purposes. While the essential oil from the fruit is used to treat dental cavities,

the bark also has febrifugal, sudorific, and diuretic qualities.[38,39] The bark has been used in traditional Indian medicine to treat rheumatism, dental infections, respiratory illnesses, and infections of the stomach and mouth.[36,37] It is beneficial in traditional medicine because of its stomachic, carminative, and anthelmintic qualities. Timur seeds are a key component in Zuroor-eQula, a powdered polyherbal Unani preparation with antibacterial and anti-inflammatory properties. Younger twigs from this plant are used as toothbrushes, and the fruits are added to traditional recipes as spices and flavourings. The bark is used as a traditional resource for producing dye.[11]

PHYTOCONSTIUENT

Previous phytochemical studies on the various Z. species sections revealed a vast array of chemical compounds. This plant has been shown to contain a variety of secondary metabolites, including phenylpropanoid-lignans, coumarins, alkaloids, aromatic and aliphatic amides, terpenes, and sterols.[40-41]

Table 1: Chemical constituents found in Z. SPECIES.

PART	COMPOUND	CHEMICAL CATEGORY	REF.NO
Stem	Limonellone	Quinolone alkaloid	42
	Dihydroalatamide	Aromatic amide	42
	(-)-Tembamide	Aromatic amide	42
	Dictamnine	Furoquinoline alkaloid	42
	N-Nornitidine	Benzophenanthridine alkaloid	42
Stem bark	l Lupeol	Triterpene	42
	Xantoxyletin	Pyronocoumarin	42
	Osthol	O-methylated coumarin	42
	Scopoletin	Hydrooxy coumarin	42
	Rutaecapine	Quinazolinocarboline alkaloid	42
Fruits	Xanthoxyline	Phenolic compound	42
	Limonene	Monoterpene	42
	Terpinen-4-ol Terpinen-4-ol	Monoterpene	42
	Sabinene	Monoterpene	42
	3-Carene	Monoterpene	42
	α-Terpineol	Monoterpene alcohol	42
	β-Pinene α	Monoterpene	42
	α-Pinene	Monoterpene	42
	gamma-Terpinene	Monoterpene	42
	α-Terpinene	Monoterpene	42
	p-Cymene	Alkylbenzene	42

Table no. 2: Medicinal properties shown by different parts of Z.SPECIES [ARMANTUM].[11]

S.no	Activity	Active parts	Preparation
1.	Antioxidative activity	Fruits	Methanolic extract
		Fruits	Ethanolic extract
2.	Antitumor activity	Leaves/fruits	Ethanolic extract
3.	Antiinflammatory activity	Stem bark	Ethanolic extract
		Fruits	Methanolic extract
		Roots	Ether extract
4.	Analgesic activity	Leaves/stem	Ethanolic extract
5.	Antibacterial activity	Seeds/leaves	Essential oil
6.	Antifungal activity	Leaves	Essential oil
7.	Larvicidal activity	Fruits/seed	Essential oil
8.	Piscicide activity	Fruits	Ethanolic extract
9.	Hepatoprotective activity	Leaves/bark	Ethanolic extract

VERNACULAR NAME

Chinese Name	Majiao
Hindi Name	Timroo, Trimal, Tumru
Manipuri Name	Mukthrubi
English Name	Toothache Tree,Yellow wood, Suterberry
Nepali Name	Timur
Thai Name	Huigiao

PHARMACOLOGICAL ACTIVITY

1. Hepatoprotective: By bringing the increased levels of hepatic enzymes back to normal, Zanthoxylum armatum's ethanolic extract showed hepatoprotective effects against carbon tetrachloride-induced liver injury. In comparison to silymarin, which is said to have a protective effect on the plasma membrane of hepatocytes, Zanthoxylum armatum's ethanolic extract can condition the hepatocytes, protecting against membrane fragility and reducing the leakage of the marker enzymes into the circulation.[43]

2. Anti-diabetic Activity: In rats that had been given streptozotocin (60 mg/kg) to produce diabetes, the anti-diabetic effect of a hydro methanolic extract of the bark of Zanthoxylum armatum was examined. The normal reference medication was glibenclamide (5 mg/kg). The oral treatment of Zanthoxylum armatum hydro methanolic extract for 21 days (200 and 400 mg/kg) led to a substantial decrease in blood sugar, total cholesterol, triglycerides, LDL, and VLDL as well as a significant increase in HDLP.[44]

3. Anti-deppresent activity: Z. alatum's antidepressant qualities. To identify the component that acts as an antidepressant the most effectively, bioassay-guided fractionation was used. In several models of depression, including the forced swimming model in rats and mice and the tail suspension test in mice, its hexane extract demonstrated the highest effectiveness, followed by the hydroalcoholic extract. The plant's seed has a considerable antidepressant effect, according to behavioral, biochemical, and molecular research.[45]

4. Memory enhancing property

The impact of Z. alatum on neurological illnesses has not yet been investigated. Locals utilize it as a folk remedy for toothaches, as a stimulant or nerve tonic in weak, weakened patients. We conducted the first in-depth investigation on memory enhancement using different extracts, and its hydroalcoholic extract reversed scopolamine-induced amnesia in mice. These findings were later supported by biochemical, immunological, and molecular studies.[46]

5. Cytotoxicity

To test the cytotoxic and antioxidant activity of Zanthoxylum alatum stem bark, Mukhija et al. Using the MTT assay, the cytotoxicity of ethyl acetate extract was investigated in various malignant cell lines, including pancreatic, lung, breast, and colon cancer. A substantial cytotoxic capability has been demonstrated by the plant extract against pancreatic and lung cancer cell lines. The cytotoxic action of the ethyl acetate extract was caused by flavonoids that were extracted from the extract.[47]

6. Anti-inflammatory and anti-oxidant activities

Zanthoxylum armatum steam bark was extracted ethanolically to create Anti-inflammatory and antioxidant effects that have been researched. Carrageenan-induced in vivo anti-inflammatory effects in Wister rats paw edoema, DPPH performed in vitro antioxidant activity. use of free radicals. Significant anti-inflammatory and antioxidant effects were seen in the plant extract.[48]

7. Anti-microbial activities

Zanthoxylum armatum's antimicrobial effectiveness was assessed against four different bacterial strains, including S. aureus, E. coli, P. vulgaris, and P. aeruginosa. Zanthoxylum alatum bark extracts in chloroform, methanol, and acetone were used in the good diffusion method to examine the antibacterial activity. The highest activity was discovered in chloroform extract against P. vulgaris, whereas the highest zone of inhibition was identified in acetone extract against S. aureus (42.3mm), followed by methanolic extract against S. aureus (28.7mm) (28.3mm). The bark extracts in methanol, acetone, and chloroform were more effective at killing S. aureus and P. vulgaris, respectively.[49]

8. Larvicidal activities

The essential oil from the seeds of Zanthoxylum armatum has larvicidal efficacy against Aedesa egypti, Anopheles stephensi, and Culex quinquefasciatus, three medically significant species of mosquito vectors. At least 28 molecules, mostly oxygenated monoterpenes, were discovered through the study of essential oils. These mosquito species' larvae were sensitive to the essential oil composition, which offers hope for the creation of new plant-based larvicides. In this context, essential oils have drawn a lot of attention as potentially beneficial bioactive molecules against insects. These compounds exhibit a wide range of insect-specific activity, low mammalian toxicity, and quick environmental degradation.[50]

9. Mosquito and insect repellent

Z. armatum essential oil has leech or insect-repelling properties. Assam's evergreen and deciduous forests were used as test sites for the persistent repellent abilities 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 Results were compared with its volatile oil to determine the effectiveness of the substance as a leech deterrent. Z. armatum oil performed similarly to citronyl and showed superior outcomes against DMP and NBP, however DEPA and DEET were ultimately shown to be the most effective.[51]

10. Anthelminitic activity

The seeds' anthelmintic properties after being macerated in methanol and water. The testing was carried out using mature Indian earthworms called Pheretima posthuma because of their physiological and anatomical similarity to human intestinal roundworms. Different concentrations of the extract—10, 25, and 50 mg/ml—were examined. The standard reference medication was piperazine citrate (10 mg/ml). Results demonstrated that the aqueous extract is more potent than other extracts since it killed the earthworms more quickly than the standard reference medication did. Giardia lamblia and Plasmodium berghei were both resistant to the antiprotozoal effects of the leaves aqueous extract.[52]

11. Antinocecicептive and anti-convusant activity

Zanthoxylum alatum (ZEO) leaf essential oils were hydro steam distilled, and their acute toxicity, antinociceptive, and anticonvulsant properties were assessed. ZEO considerably reduces pain in formalin-induced noxious animals in both the neurogenic (first phase) and inflammatory (late phase) stages. It also shows anticonvulsant properties in pentylene tetrazole (PTZ)-induced convulsions.[53]

12. Piscicide activity

In the management of fish nurseries, the fruits of this plant can be utilized as an efficient piscicide. The air-breathing catfish, Heteropneustes fossilis, had its Mg2+ and Na+, K+-ATPase activity in various tissues assessed using an ethyl alcohol extract. According to kinetic investigations on Mg2+ -ATPase activity, piscicide is a non-competitive inhibitor.[11]

13. Anti-tumor activity

Because the crude extract of the leaves and fruits exhibits cytotoxicity, Z. armatum shows potential as an anticancer medication (Barkatullah et al., 2011). Lupeol, a monoterpene found in it, functions as a medicinal agent for the treatment of cancer and inflammation.[11]

CONCLUSION

Due to its vast medical use, Z. armatum has been found to possess antibacterial, insecticidal, larvicidal, anti-inflammatory, and analgesic qualities. Since there is little information on the plant's use as an anticarcinogenic agent, further research may be done to demonstrate its prospective applications. In this way, the plant has demonstrated its effectiveness in pharmacology and its potential for future studies. The collecting of this species has come under growing pressure because it is an IHR medicinal plant with great value. These plants are harvested by people from untamed areas for their economic value. Therefore, understanding the genetic diversity of this plant is useful for creating conservation plans and securing intellectual property. The in vitro method of propagation offers a very effective instrument for the bulk reproduction of many endangered plants. In order to multiply and conserve this plant, it is important to design a reproductive propagation procedure.

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