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Review

# A review on *Zanthoxylum Armatum*: Traditional Uses, Phytochemistry, Pharmacological Activities

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**Abstract:**

***Background:*** *Zanthoxylum armatum*, a versatile plant known for its extensive pharmacological and phytochemical properties, has been traditionally utilized in various cultures for medicinal purposes. It is a well-known medicinal plant from the Rutaceae family that is native to Korea, China, Japan, and Pakistan. ***Objective:*** The current review provides the necessary data for collecting descriptive information on the organoleptic, microscopical, ethnobotanical, phytochemicals, and pharmacological properties of *Z. armatum*; thus it may aid in bridging research gaps and future findings for the majority of studies. ***Materials & Methods:*** The current investigation seeks to assess the extant body of research pertaining to the biological evaluation of *Z. armatum* derivatives. Specifically, this analysis will concentrate on the approaches, and findings employed by scholars in this field. ***Results:*** The majority of bioactive metabolites have been identified and described, such as monoterpenes in essential oils and lignan components in herbs. Several in vitro and in vivo pharmacological bioassays indicated *Z. armatum* potential for antimicrobial, antifungal, antibacterial, and hepatoprotective properties, among others. ***Conclusions:*** The present study focuses on the phytochemical analysis of *Z. armatum*, to investigate its pharmacological characteristics and potential therapeutic applications. It is imperative to conduct additional studies in order to fully understand its biological mechanism of action and explore its potential therapeutic applications. ***Significance:*** It is widely recognized for its medicinal properties in treating dental cavities, stomach aches, rheumatism, and other ailments. The plant fruits stem barks and stems contain several bioactive secondary metabolites such as alkaloids, amides, lignin's, and terpenoids. These entities potential applications in pharmaceutical research and beyond are being considered, emphasizing their importance in a variety of fields of study.

**Keywords:** *Zanthoxylum Armatum, taxonomy, geographical distribution, ethnopharmacological, phytochemical constituents, pharmacological aspects.*



## 1. Introduction:

The utilization of medicinal plants can be traced back to ancient civilizations, as exemplified by the Rigveda and Atharveda, and remains a prominent component of healthcare on a global scale [1-3]. Medicinal plants are being studied as a possible way to fight many diseases, including AIDS, malaria, tuberculosis, conditions causing

inflammation, and cancer [4-8]. The desire to find therapeutic options with reduced side effects motivates this exploration. The utilisation of medicinal plants in the search for novel pharmaceutical agents is rooted in the presence of bioactive compounds within them, which can be harnessed for the purpose of drug development and exploration [9-10]. Traditional medical systems such as unani and ayurveda have significantly impacted the healthcare sector in India. Several studies have highlighted the significant contributions made by these systems [11-15]. The family Rutaceae, specifically the subkingdom viridaeplantae, classifies the genus *Zanthoxylum* as its belong to the Phylum Tracheophyta, Subclass Rosidae, Order Spindale, and Superorder Rutanae [16]. *Z. armatum*, commonly known as prickly ash or toothache tree, is a species of flowering plant in the Rutaceae family, native to the Himalayan region; it thrives in subtropical and temperate zones, such as India, Nepal, and Bhutan. The plant is a deciduous shrub or small tree, characterized by its aromatic leaves, sharp thorns, small red to brown fruits the fruits are valued for their distinct pungent lemon flavor, often used as a spice in local cuisines. It is also known for its medicinal properties, traditionally used to treat various ailments such as toothaches, digestive disorders, and rheumatism they contains essential oils which are utilized in aromatherapy or as an natural insect repellent its plays a significant role in both culinary and traditional medicine practices in its native regions [17].

**2. Indigenous uses of *Zanthoxylum armatum*:**

*Z. armatum* has been extensively used in indigenous practices for its medicinal properties, bark and seeds are commonly used to alleviate pain and inflammation, while the leaves, fruits serve as stimulants and carminatives. Himalayan communities, utilize plants as essential oils for natural remedy in skin infections the fruits are utilized as folk medicine to treat digestive issues such as diarrhea and dysentery, for their antimicrobial properties. Additionally, the extract of plant is used in traditional remedies for their perceived effectiveness in managing skin disorders. *Z. armatum* thus holds a significant role in indigenous medicinal practices, contributing to both gastronomical and therapeutic traditions in the regions India, Nepal, and Bhutan[18] as shows in table 1.

**Table 1.** Indigenous uses of *Z. armatum* [19].

| S.N. | Pharmacological Activity | Active Parts | Preparation/Extract | Effects |
|---|---|---|---|---|
| **1** | Hepatoprotective | Leaves | Ethanolic extract | Restores elevated hepatic enzymes; protects liver cells from toxins. |
| **2** | Anti-diabetic | Bark | Hydro-methanolic extract | Reduces blood sugar, cholesterol, and triglycerides; increases HDL in diabetic rats. |
| **3** | Antidepressant | Seeds | Hexane and hydroalcoholic extracts | Significant antidepressant effects in depression models (rodents) |
| **4** | Memory Enhancer | Leaves | hydroalcoholic extracts | Improves memory, reverses scopolamine-induced amnesia in mice. |
| **5** | Cytotoxic | Stem | Ethyl acetate extract | Cytotoxic effects on cancer cells (pancreatic, lung cancer). |
| **6** | Anti-inflammatory and Antioxidant | Stem bark | Ethanolic extract | Significant anti-inflammatory and antioxidant effects. |
| **7** | Antimicrobial | Seeds, leaves | Essential oil, chloroform, methanol, acetone extracts | Effective against bacteria like Memory-enhancing aureus, E. coli, P. vulgaris, P. aeruginosa. |
| **8** | Larvicidal | Seeds | Essential oil | Potent larvicidal effects against mosquito species (Aedes aegypti, Anopheles |

| | | | | |
|---|---|---|---|---|
| | | | | stephensi, Culex quinquefasciatus) |
| **9** | Antitumor | Leaves, Fruits | Crude extract | Shows cytotoxicity against cancer cells, particularly due to lupeol |

**3. Taxonomy Classification:** [20]

| | |
|---|---|
| **Botanical Name** | *Zanthoxylum armatum* |
| **Family** | Rutaceae |
| **Kingdom** | Plantae |
| **Subkingdom** | Viridaeplantae |
| **Phylum** | Tracheophyta |
| **Subphylum** | Euphyllophytin |
| **Class** | Magnoliopsida |
| **Subclass** | Rosidae |
| **Order** | Spindale |
| **Suborder** | Rutineae |
| **Superorder** | Rutanae |
| **Genus** | *Zanthoxylum* |

**3.1 Geographical Distribution:**

The geographical distribution of *Z. armatum* is quite broad, with the species found across various parts of the world it is grown in the regions of Asia. In **India** it is predominantly found in the Northeast, extending from Jammu and Kashmir to Bhutan, specific states where it is commonly found are Andhra Pradesh, Assam, Manipur, Meghalaya, Nagaland, Orissa [21].

**Fig 1.** *Z. armatum* Plant with fruits

**Fig 2.** *Z. armatum* fruits

**4. Phytochemical Constituents:**

The phytochemical analysis of different parts of *Z. armatum* has shown that it contains a wide range of metabolites these include alkaloids, such as nitidine and chelerythrine, glycosides, resins, carbohydrates, tannins, flavones, carnosic acids, ursolic acid, limonene, citronellal, and geraniol so the *Z. armatum* a valuable resource in traditional medicine and modern pharmacological applications [22-25].

**5. Pharmacological activity of *Z. armatum*:**

It exhibits a wide range of pharmacological activities various parts, including the fruits, leaves, bark, and seeds, are rich in bioactive compounds such as alkaloids, flavonoids, and essential oils, which contribute to its therapeutic properties.

**5.1 Analgesic and Anti-inflammatory:**

Currently available drug for management of analgesic & anti-inflammatory have certain drawbacks therefore, there is a need a new safer and more effective choice of drugs. Studies have demonstrated that the analgesic and anti-inflammatory effects of *Z. armatum* extracts, alcoholic and petroleum ether-based, are comparable across various models of pain and inflammation. The result obtained in the present investigation suggests that the alcoholic extract of root *Z. armatum* has protective effect against the pain and inflammation activity than the petroleum ether extract [26]. The anti-inflammatory properties of the extract and crude alkaloids were effective at higher doses, though they did not outperform the conventional drug, diclofenac. In this study, both the extract and alkaloids demonstrated significant anti-inflammatory effects when compared to the standard pharmaceutical reference. The impact of *Z. armatum* fruit extract (ZAF) and its isolated alkaloids (ZAFA) on the writhing response in mice was evaluated, with results indicating a dose-dependent inhibition within 10 minutes. Pain reduction was notable, with a 300 mg/kg dose of ZAF reducing pain by 40.99% ($p > 0.05$), and a 100 mg/kg dose of ZAFA reducing pain by 45.91% ($p > 0.001$), closely matching the pain relief provided by Paracetamol, which achieved a 46.33% reduction [27].

**5.2 Actinociceptive:**

The study of pain modulation often includes exploring actinociceptive mechanisms, which refer to the processes that inhibit sensation of pain this mechanisms is crucial in understanding how the body responds to harmful stimuli. The reference drug morphine hydrochloride (10 mg/kg), significantly suppressed the formalin response in the first and second phases by 82.03% and 75.30%, respectively. Pretreatment with EAF at doses of 800 mg/kg caused 18% and 60.42% inhibition of the licking times in both phases, while EAF at doses of 100, 200, and 400 mg/kg only caused 11.03%, 36.81%, and 59.82% reduction in licking times in the second phase respectively. This suggested that the mechanisms of antinociceptive activity might be mainly involved in the periphery inflammatory analgesic [28].

**5.3 Antimicrobial and Antioxidant:**

Antimicrobial are the agent plays a crucial role inhibiting the growth of microorganisms [29-30] while antioxidants are the agents play a vital role in neutralizing free radicals, which can cause oxidative stress and damage to cells [31-32]. The study revealed that extracts from the leaves and fruits of Z. armatum exhibit antimicrobial properties against S. aureus. The methanolic extracts showed the strongest effect, creating an inhibition zone of 13.33 mm on average (±1.33 mm). Ethanolic leaf extracts also demonstrated a significant impact, with an average inhibition zone of 12.67 mm (±0.89 mm). In contrast, aqueous leaf extracts displayed minimal activity, with a much smaller inhibition zone of 3.66 mm (±3.67 mm). Among the fruit extracts, chloroform extracts were the most effective, producing an inhibition zone of 10 mm (±5.12 mm) [33-34]. The minimum bactericidal concentration (MBC) values varied between 0.78 mg/mL and 50 mg/ml the fruit extracts showed the lowest MBC value of 0.78 mg/mL against MRSA, while the highest MBC value of 50 mg/mL was observed for wild seed and fruit extracts against S. epidermidis [35].

**5.4 Antidiabetic**:

The extract of Z. armatum demonstrated a reduction in blood sugar levels starting two hours after administration across all tested doses. This hypoglycemic effect suggests that ZAE contains compounds capable of lowering blood glucose levels in normoglycemic mice compared to the control group, Alloxan, a chemical that induces diabetes by destroying pancreatic beta cells, leads to decreased insulin production and a subsequent rise in blood glucose levels [36]. *Z. armatum* leaf and bark extracts showed significant inhibition of α-glucosidase, with inhibition rates of 96.61 ± 2.13% and 93.58 ± 2.31% [37]. The methanolic extract of *Z. armatum* leaves demonstrated significant antidiabetic and antioxidant properties in vitro. The concentration required to inhibit

50% of alpha-amylase activity (IC50) was determined to be 89.37±4.68 µg/ml, which is higher compared to the standard reference [38].

**5.5 Anticancer:**

Anticancer agents are substances that help in preventing, inhibiting cancer [39-40]. They work through various mechanisms, such as inducing apoptosis in cancer cells, inhibiting cell proliferation, or blocking the pathways that allow tumors to grow and spread [41-42]. The leaf extract of *Zanthoxyllum armatum* (ZALE) has shown potential to enhance the effectiveness of chemotherapeutic drugs such as camptothecin, mitomycin C, and cisplatin. In a study involving HeLa cells, treatment with 80 µg/ml of ZALE for 48 hours resulted in noticeable morphological changes and cytotoxic effects in a dose-dependent manner, with apoptosis characterized by membrane blebbing. To explore the molecular mechanism behind ZALE-induced apoptosis, the activation of caspase-3 and cleavage of PARP (Poly ADP-ribose polymerase) were assessed through immunoblotting. Interestingly, ZALE-treated cells did not exhibit caspase-3 activation or PARP cleavage, indicating apoptosis can occur without these typical markers. HeLa cells were treated with a lower dose of ZALE (approximately 15 µg/ml) for 16 hours, followed by exposure to cisplatin for 48 hours. The results from the cell proliferation assay indicated that the combination treatment led to greater cell death compared to treatment with the extract alone [43].

**6. Conclusion:**

The primary aim of conducting research on *Z. armatum* is to identify and analyse its pharmacological characteristics and evaluate its potential therapeutic applications. The potential optimization of the pharmacological properties of *Z. armatum* may require structural modifications which will influence the pharmacological effects the primary goal of investigating *Z. armatum* is to develop novel modified compounds with enhanced therapeutic efficacy and reduced side effects for the treatment of various diseases, fungal infections, cancer, and inflammatory disorders. These modified agents aim to surpass the effectiveness of currently available treatments. Thus, through the optimization of alkaloid such as nitidine and chelerythrine, derivatives from *Z. armatum*, scientists have been able to enhance activity against specific targets, minimise toxicity, and expand pharmacokinetics. This has led to the creation of more reliable and safer individuals for human use by examining *Z. armatum*, researchers are focusing on understanding its molecular-level mechanisms, its interactions with tissues, proteins, and amino acids, and how it can be further improved for therapeutic purposes.

**Credit authorship contribution statement:**

**Anchal Singh:** Conceptualization, Methodology, Investigation, Data curation, Writing- Original draft, Supervision; **Shourya Pratap:** Writing-reviewing and editing.

**Declaration of competing interest:**

The authors assert that no competing interests exist.

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