

SVARNAKSHIRI (*ARGEMONE MEXICANA* L.): A COMPREHENSIVE REVIEW OF ITS ETHNOMEDICINAL SIGNIFICANCE, PHYTOCHEMISTRY, PHARMACOLOGY, AND TOXICOLOGY

Dr. Bhuraji Narware¹, Dr. Monika Tyagi², Dr. Rajesh Sharma³

¹PG Scholar (Ayu). Dravyaguna Department, A & U Tibbia College & Hospital, Karol Bagh, New Delhi, India.

²Assistant Professor (Ayu), Dravyaguna Department, A & U Tibbia College & Hospital, Karol Bagh, New Delhi, India.

³Professor (Ayu). H.O.D, Dravyaguna Department, A & U Tibbia College & Hospital, Karol Bagh, New Delhi, India.

DOI: <https://doi.org/10.58257/IJPREMS43952>

ABSTRACT

Argemone mexicana L., a plant of profound contradictions, is known in Ayurvedic medicine as Svarnakshiri for its therapeutic golden latex, yet it is also notorious as a toxic adulterant responsible for widespread public health crises. This comprehensive review synthesizes the multifaceted identity of this species, bridging the gap between its traditional ethnomedicinal applications and modern scientific understanding. Botanically, it is a hardy, invasive herb of the Papaveraceae family, originating in the Americas but now naturalized globally. In traditional systems like Ayurveda, its roots, seeds, and latex are utilized for a variety of ailments, including skin diseases, wounds, constipation, and fevers, based on its classical properties as a pacifier of Kapha and Pitta doshas. Phytochemical analysis reveals a rich profile of isoquinoline alkaloids, with sanguinarine, dihydrosanguinarine, berberine, and protopine being the most significant. Modern pharmacological studies have validated many of its traditional uses, demonstrating potent anti-inflammatory, analgesic, antimicrobial, antiparasitic, wound healing, and hepatoprotective activities. However, this therapeutic potential is overshadowed by the severe toxicity of its seed oil. The presence of sanguinarine and dihydrosanguinarine makes the oil a dangerous adulterant of edible oils, causing the life-threatening condition known as epidemic dropsy. This review delves into the pathophysiology of this poisoning, characterized by widespread capillary damage, severe oxidative stress, and multi-organ failure. By juxtaposing its ethnopharmacological profile with its toxicological data, this report underscores the critical need for a nuanced, evidence-based approach to distinguish the plant's medicinal value from its inherent dangers, paving the way for safer utilization and effective public health strategies.

1. INTRODUCTION

Argemone mexicana L., a member of the poppy family (Papaveraceae), presents one of the most striking paradoxes in the world of medicinal plants. Known in the ancient Sanskrit texts of Ayurveda as Svarnakshiri, meaning "golden latex," it is revered for the therapeutic properties of the bright yellow sap that bleeds from its thorny stem.¹ This name, along with synonyms like Kanchana Kseeri and Hemadugdha, evokes its value in traditional pharmacopoeias for healing wounds, treating skin ailments, and acting as a powerful purgative.¹ In stark contrast, its common Hindi name, Satyanashi, translates to "the destroyer," a moniker that alludes to its aggressive, invasive nature as a weed and, more ominously, to its potent toxicity that has caused devastating public health emergencies.⁴ This linguistic dichotomy perfectly encapsulates the plant's dual identity: a source of traditional remedies on one hand, and a lethal poison on the other.

Originally native to the Americas, *A. mexicana* has traversed continents, establishing itself as a pantropical weed.⁴ Its hardiness and adaptability have allowed it to become a common sight along roadsides, in wastelands, and, critically, within agricultural fields across India and other parts of the world.² This ecological success has set the stage for its most infamous role—as an adulterant in edible oils. The plant's seeds bear a striking resemblance to mustard seeds, leading to their accidental or deliberate mixing, which results in the consumption of toxic argemone oil and the subsequent outbreak of a condition known as epidemic dropsy.⁶ This report aims to provide a definitive, evidence-based monograph on *Argemone mexicana*. The objective is to synthesize its rich ethnopharmacological history with a rigorous evaluation of modern botanical, phytochemical, pharmacological, and toxicological data. By systematically examining each facet of this complex species, this review seeks to reconcile its contradictory reputation, providing a holistic and nuanced understanding that can inform both future pharmaceutical research and critical public health

policy.

2. BOTANICAL PROFILE AND ETHNOBOTANY

2.1. Taxonomy and Nomenclature

The precise scientific classification of Svarnakshiri is essential for accurate identification and research. It belongs to the poppy family, Papaveraceae, a group known for its production of potent alkaloids.¹⁰ The etymology of its scientific name provides insight into its historical perception; the genus name *Argemone* is derived from the Greek word *argema*, referring to an eye cataract, which the plant's juice was once believed to cure, while the specific epithet *mexicana* denotes its origin in Mexico.¹²

Its full taxonomic classification is as follows¹:

- **Kingdom:** Plantae
- **Order:** Ranunculales
- **Family:** Papaveraceae
- **Genus:** *Argemone*
- **Species:** *A. mexicana* L.

The plant is known by a vast array of vernacular names across different cultures, reflecting its widespread distribution and integration into local traditions. A comprehensive understanding of this nomenclature is crucial for cross-referencing ethnobotanical and scientific literature.

Table 1: Taxonomy and Vernacular Names of *Argemone Mexicana*

Category	Names
Scientific Name	<i>Argemone mexicana</i> L.
Sanskrit Synonyms	Svarnakshiri, Kanchana Kseeri, Hemadugdha, Katuparni, Tikta Dugdha, Haimavati, Brahmadandi ¹
Common English Names	Mexican Poppy, Mexican Prickly Poppy, Flowering Thistle, Yellow Thistle ¹
Hindi Names	Satyanashi, Bharbhand, Pila Dhatura, Kataila, Shiyalkanta ¹
Selected Regional Names	Bengali: Shiyal Kanta; Tamil: Kudiyotti, Piram-mat-tantu; Telugu: Picchi Kusuma, Brahmadandi; Kannada: Datturi Gida; Malayalam: Ponnummattam; Marathi: Kantai Dhautra, Pivala-dhatura; Gujarati: Dharudi ¹

2.2. Morphological and Anatomical Description

Macroscopic Features

Argemone mexicana is a visually distinct, erect annual or biennial herb that typically grows to a height of 30 to 150 cm.⁴ It is characterized by its prickly nature and the presence of a bright yellow, milky latex that exudes from any injured part of the plant.⁴

- **Stem:** The stem is branched, cylindrical, and covered with sharp, scattered prickles. It has a smooth, pale greenish or whitish appearance.²¹
- **Leaves:** The leaves are sessile (lacking a stalk) and clasp the stem. They are thistle-like in appearance, deeply lobed (pinnatifid), and can reach up to 20 cm in length. The leaf margins are spiny, and the surface is a distinctive bluish-green with prominent white or greyish veins, giving it a variegated look.⁴
- **Flowers:** The flowers are solitary, located at the ends of branches, and are large and showy, measuring between 2.5 and 7 cm in diameter. They consist of two to three spiny sepals that enclose the bud and four to six bright yellow, delicate, crumpled petals. The center of the flower contains numerous stamens with yellow filaments.⁴
- **Fruit:** The fruit is a prickly, oblong to ovoid capsule, typically 2.5 to 5 cm long. When mature, it opens via 3 to 6

valves at the apex, releasing a large number of seeds.⁴

- **Seeds:** The seeds are small, globular, and measure about 1.5 to 2 mm in diameter. They are blackish-brown with a finely pitted or reticulated surface. Their close resemblance in size, shape, and color to black mustard seeds (*Brassica nigra*) is the primary reason for the frequent contamination of mustard crops and oil.⁴

Microscopic Features

Microscopic examination of the plant tissues reveals further identifying characteristics. The leaf and stem surfaces are covered in trichomes (plant hairs). The tissues also contain calcium oxalate crystals and an abundance of parenchyma cells, which are common features used in pharmacognostic identification to distinguish *A. mexicana* from other species or potential adulterants.²⁵

2.3. Geographical Distribution and Ecological Adaptations

Argemone mexicana is native to the tropical and subtropical regions of the Americas, including Mexico, the West Indies, and the southern United States.⁴ From this center of origin, it has spread globally, becoming a naturalized, pantropical weed found throughout India, Africa, Asia, and Australia.² The plant's ecological success is due to its remarkable hardiness and adaptability. It is a classic pioneer species, often one of the first plants to colonize disturbed ground.²⁹ It thrives in a wide range of habitats, including wastelands, roadsides, fallow agricultural fields, and sandy riverbeds, and is tolerant of drought and poor, sandy soils.¹³ Its invasive nature is supported by several key characteristics:

- **High Seed Production:** A single plant can produce up to 30,000 seeds per year, ensuring a high reproductive output.¹³
- **Seed Bank Persistence:** The seeds can remain dormant in the soil for many years, creating a persistent seed bank that allows the plant to re-emerge whenever conditions become favorable.¹³
- **Effective Dispersal:** Seeds are dispersed through various means, including water (especially in riparian habitats), mud adhering to vehicles and livestock, and birds.²⁰

This very ecological success is inextricably linked to its public health risk. The plant's ability to flourish as a common weed in and around agricultural lands, particularly mustard fields, creates the ideal conditions for its seeds to become mixed with the mustard harvest.¹³ The morphological similarity of the seeds then makes separation difficult, leading to the contamination of mustard oil during the pressing process.⁶ This direct causal chain—from ecological niche to morphological mimicry to post-harvest contamination—is the fundamental origin of the epidemic dropsy crisis, demonstrating how the plant's biology and ecology translate directly into a major human health threat.

3. TRADITIONAL AND AYURVEDIC PERSPECTIVE

3.1. Ayurvedic Pharmacodynamics (Dravyaguna)

In the classical system of Ayurveda, every medicinal substance is characterized by its unique energetic and therapeutic properties, collectively known as *Dravyaguna*. The properties of Svarnakshiri (*Argemone mexicana*) are well-documented and provide a framework for understanding its traditional applications.⁴ The *Rasadi Panchaka* (five principal attributes) of Svarnakshiri are:

- **Rasa (Taste):** *Tikta* (Bitter) and *Katu* (Pungent).
- **Guna (Qualities):** *Laghu* (Light) and *Ruksha* (Dry).
- **Virya (Potency):** *Sheeta* (Cold).
- **Vipaka (Post-digestive effect):** *Katu* (Pungent).

Based on these properties, its action on the three fundamental bio-energies, or *Doshas*, is determined. Svarnakshiri is classified as a *Kapha-Pittahara*, meaning it pacifies and reduces aggravated Kapha and Pitta doshas.⁴ The bitter taste (*Tikta Rasa*) and cold potency (*Sheeta Virya*) are effective in counteracting the heat and intensity of Pitta dosha. Simultaneously, its pungent taste (*Katu Rasa*) along with its light (*Laghu*) and dry (*Ruksha*) qualities help to alleviate the heaviness, coldness, and dampness associated with Kapha dosha.

3.2. Ethnomedicinal Applications

The Ayurvedic properties of Svarnakshiri form the basis for its wide range of therapeutic actions, or *Karma*. It is primarily valued for its potent cleansing, healing, and purifying effects. Its key actions include *Vranshodhan* (wound cleansing), *Vranropan* (wound healing), *Kushaghna* (alleviates skin diseases), *Krimighna* (anthelmintic/destroys worms), *Rechani* (purgative), and *Vishamajwaraghna* (alleviates intermittent fevers).¹ These actions translate into its use for a diverse array of ailments. The plant's latex, root, seeds, and oil are prepared in various ways to treat

conditions such as chronic skin diseases (*Kushta*), constipation (*Vibandha*), abdominal bloating (*Anaha*), jaundice (*Kamala*), urinary calculi (*Ashmari*), and toxic conditions (*Visha*).¹ The following table summarizes some of its key traditional formulations and uses.

Table 2: Ayurvedic Properties and Traditional Formulations of Svarnakshiri

Ailment (Ayurvedic Term)	Part Used	Preparation Method	Dosage/Application
Wounds and Ulcers (<i>Vrana</i>)	Latex, Leaf Juice	Fresh latex or juice applied directly to the affected area.	Applied topically for wound cleansing and to promote healing. ¹
Skin Diseases (<i>Kushta</i>), Eczema, Ringworm	Latex, Leaf, Stem	Paste of leaves and stem; oil processed with seeds.	Applied externally on affected skin. ¹
Constipation (<i>Vibandha</i>), Abdominal Colic, Flatulence	Root, Seed Oil	Powder of the root taken with hot water; seed oil administered orally.	Root powder: 1–3 g; Seed oil: 10–30 drops. ¹
Intestinal Worms (<i>Krimi Roga</i>)	Root	Powder or fresh juice of the root. Decoction of root bark.	Root powder: up to 3 g; Decoction: 60 ml per day. ¹
Jaundice (<i>Kamala</i>)	Root, Plant Juice	Fine paste of roots mixed with jaggery; fresh juice of the plant.	Root paste: 3–4 g once or twice daily; Juice is used. ¹
Fever (<i>Jwara</i>), Malaria	Leaf, Juice	Decoction of leaves; fresh juice taken orally.	Juice: 3–5 ml as a blood purifier and to treat fever. ¹
Urinary Calculi (<i>Ashmari</i>)	Root	Decoction prepared from the root.	Decoction taken internally. ⁵
Scorpion/Insect Bites	Root	Paste of the root applied topically.	Applied to the site of the bite for its anti-inflammatory and anti-toxic properties. ¹
Eye Conditions (Conjunctivitis, Ophthalmia)	Latex	One drop of latex mixed with ghee or milk.	Used as eye drops, though this practice is considered dangerous by some sources. ¹²

4. PHYTOCHEMICAL COMPOSITION

The potent biological activities of *Argemone mexicana* are attributed to its complex and diverse array of secondary metabolites. The most significant of these are the isoquinoline alkaloids, which are responsible for both its therapeutic effects and its profound toxicity.⁷

4.1. Isoquinoline Alkaloids

The entire plant is rich in isoquinoline alkaloids, with different compounds concentrated in various parts. The major alkaloids that have been isolated and identified include ¹:

- **Sanguinarine and Dihydrosanguinarine:** These are benzophenanthridine alkaloids and are the primary toxins found in the seeds and seed oil. They are largely responsible for the pathophysiology of epidemic dropsy.⁶
- **Berberine:** A well-known protoberberine alkaloid with documented antimicrobial, anti-inflammatory, and hepatoprotective properties. It is found in the roots, stems, and immature seeds.⁷
- **Protopine and Allocryptopine:** These protopine-type alkaloids are present throughout the plant and contribute to its analgesic, antispasmodic, and anti-inflammatory effects.³⁷
- **Chelerythrine, Coptisine, and Stylopine:** Additional isoquinoline alkaloids that contribute to the plant's overall pharmacological profile.³⁷

The distribution of these alkaloids is not uniform throughout the plant, a factor that critically determines the use and safety of each part.

Table 3: Major Phytochemicals Isolated from *Argemone mexicana*

Compound Class	Specific Compound	Plant Part(s)
Isoquinoline Alkaloids	Sanguinarine, Dihydrosanguinarine	Seeds (high concentration), Roots ⁶
	Berberine	Roots, Stems, Immature Seeds ¹
	Protopine, Allocryptopine	Whole Plant ¹
	Chelerythrine, Coptisine, Stylopine	Whole Plant ³⁷
Non-Alkaloidal	Flavonoids (e.g., Kaempferol), Terpenoids, Saponins, Tannins, Sterols, Phenols	Leaves, Aerial Parts ⁵
Fatty Acids	Palmitic acid, Myristic acid, Oleic acid, Linoleic acid	Seed Oil ³⁷

4.2. Non-Alkaloidal Constituents

Beyond alkaloids, *A. mexicana* also contains a variety of other phytochemicals that contribute to its biological activity. These include flavonoids such as kaempferol, terpenoids, saponins, tannins, steroids, and various phenolic compounds.⁵ The seed oil is composed of several fatty acids, including palmitic, myristic, oleic, and linoleic acids.³⁷ These non-alkaloidal compounds often work synergistically with the alkaloids to produce the plant's overall therapeutic effects, particularly its antioxidant and anti-inflammatory properties.

4.3. Quantitative Analysis of Bioactive Compounds

Quantitative studies have provided crucial data on the concentration of these key alkaloids in different plant parts. The total alkaloid content in the dried roots and stems has been estimated to be around 0.25%.⁷ More detailed analyses have focused on the seeds, the primary source of toxicity. Mature seeds contain high levels of sanguinarine, approximately 0.8 mg per gram of dry weight.³⁹ Further investigation into the distribution within the seed has revealed that the highest concentration is not in the endosperm but in the outer layers, particularly the tegmen (inner seed coat).³⁹ In contrast, quantitative analysis of leaf extracts has shown a high total alkaloid content, around 9.5% to 9.7% w/w in aqueous and ethanol extracts, respectively, though the specific composition and relative concentration of sanguinarine may differ from that in the seeds.⁴³ This differential distribution of alkaloids is a key determinant of the plant's dual use-toxicity profile. The extremely high concentration of the potent toxin sanguinarine in the seeds directly explains the severe danger posed by consuming argemone oil. Conversely, the presence of a different or more

balanced alkaloid profile in other parts, such as the leaves and roots—where compounds like berberine and protopine are more prominent—may account for their relatively safer and more widespread use in traditional medicinal preparations for topical or controlled internal use. This suggests an implicit, empirical understanding in traditional medicine of this differential toxicity, where the most dangerous part of the plant is either avoided or used with extreme caution for specific, drastic purposes like purgation, while other parts are employed more broadly for their healing properties.

5. SCIENTIFIC VALIDATION OF PHARMACOLOGICAL ACTIVITIES

Modern scientific research has increasingly focused on validating the traditional claims associated with *Argemone mexicana*. A growing body of evidence from *in vitro* and *in vivo* studies corroborates many of its ethnomedicinal uses, attributing them to the plant's rich phytochemical content.

5.1. Anti-inflammatory, Analgesic, and Antipyretic Effects

Supporting its traditional use in managing inflammatory conditions and pain, extracts of *A. mexicana* have demonstrated significant anti-inflammatory and analgesic properties in animal models. Aqueous and ethanolic extracts of the leaves and roots have been shown to produce a dose-dependent inhibition of carrageenan-induced paw edema in rats, a standard model for acute inflammation.⁴⁵ Similarly, these extracts have exhibited notable analgesic activity in tests such as the hot plate and acetic acid-induced writhing assays, indicating both central and peripheral pain-relieving effects.⁴⁵ The antipyretic (fever-reducing) potential of the plant has also been reported, likely due to the combined action of its alkaloids, flavonoids, and phenolic compounds that can modulate inflammatory pathways.³⁷

5.2. Antimicrobial and Antiparasitic Activity

A. mexicana possesses broad-spectrum antimicrobial activity, validating its use for infections and as a purifying agent. Various extracts (chloroform, methanol, and ethanol) from its seeds, leaves, and stems have shown potent antibacterial effects against a range of both Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*) and Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*) bacteria.³⁷ Its antifungal properties are also significant, with extracts inhibiting the growth of pathogenic fungi like *Aspergillus niger* and *Candida albicans*.⁴⁵ Perhaps most notably, the plant has demonstrated powerful antiparasitic activity. Its traditional use in Mali for treating malaria has been scientifically substantiated by studies showing that its extracts and isolated alkaloids, such as protopine and allocryptopine, exhibit significant *in vitro* antiplasmodial activity against *Plasmodium falciparum*, the parasite responsible for malaria.⁶

5.3. Wound Healing and Dermatological Efficacy

The Ayurvedic indications of *Vrashodhan* (wound cleansing) and *Vranropan* (wound healing) are strongly supported by modern pharmacological studies. In animal models using excision and incision wounds, topical application of leaf extracts and the plant's latex has been shown to significantly accelerate the rate of wound contraction and increase tensile strength.¹ These effects are attributed to a combination of antimicrobial action, which prevents infection, and the promotion of tissue regeneration and collagen synthesis, likely mediated by the plant's alkaloids and flavonoids. This evidence provides a clear scientific basis for its traditional application in treating ulcers, sores, and various skin diseases.

5.4. Hepatoprotective Mechanisms

Traditionally used for liver ailments like jaundice, *A. mexicana* has been shown to possess significant hepatoprotective properties. Studies in animal models have demonstrated that extracts from the plant's roots and aerial parts can protect the liver from damage induced by potent hepatotoxins such as paracetamol and carbon tetrachloride.⁴⁰ The mechanisms underlying this protection are multifaceted. The extracts significantly reduce the serum levels of elevated liver enzymes (ALT, AST, ALP), which are key markers of hepatic injury.⁴⁰ Furthermore, the plant exerts its effects by modulating the inflammatory cascade, leading to a decrease in pro-inflammatory cytokines (e.g., TNF- α , IL-1 β , IL-6) and an increase in anti-inflammatory cytokines (e.g., IL-10).⁴⁷ It also bolsters the liver's endogenous antioxidant defense system by increasing the levels of enzymes like superoxide dismutase (SOD) and catalase (CAT) and the antioxidant molecule glutathione (GSH), thereby combating oxidative stress.⁴⁷ 5.5. Antioxidant and Anticancer Potential

The rich phenolic and flavonoid content of *A. mexicana* endows it with potent antioxidant activity. Various extracts have demonstrated strong free-radical scavenging capabilities in assays such as DPPH and hydrogen peroxide scavenging, indicating their potential to mitigate oxidative damage associated with numerous chronic diseases.²⁵ This antioxidant capacity is also linked to its emerging potential in oncology. Numerous *in vitro* studies have shown that extracts of *A. mexicana* and its isolated alkaloids, particularly berberine and sanguinarine, exhibit significant cytotoxic

effects against a variety of human cancer cell lines, including colon, lung, liver (HepG2), and cervical (HeLa) cancer cells.³⁸ These compounds appear to induce apoptosis (programmed cell death) in cancer cells, suggesting they could be promising candidates for the development of new chemotherapeutic agents.

Table 4: Summary of Key Pharmacological Activities of *Argemone mexicana*

Pharmacological Activity	Extract/Compound	Key Findings	Model/Assay
Anti-inflammatory	Aqueous & Ethanolic extracts (Leaf, Root)	Dose-dependent inhibition of edema.	Carrageenan-induced paw edema in rats. ⁴⁵
Analgesic	Aqueous & Ethanolic extracts (Leaf, Root)	Significant reduction in pain response.	Hot plate test, acetic acid-induced writhing in mice. ⁴⁵
Antibacterial	Chloroform, Methanol, Ethanol extracts (Various parts)	Broad-spectrum activity against Gram-positive and Gram-negative bacteria.	Agar well diffusion, Minimum Inhibitory Concentration (MIC) assays. ⁴⁵
Antimalarial	Aqueous decoction, Isolated alkaloids (Protopine)	Significant clinical response in human trials; <i>in vitro</i> inhibition of parasite growth.	Clinical trials in Mali; <i>in vitro</i> antiplasmodial assay against <i>P. falciparum</i> . ⁶
Wound Healing	Leaf extract, Latex	Accelerated wound contraction and increased tensile strength.	Excision and incision wound models in rats. ³⁴
Hepatoprotective	Methanol & Aqueous extracts (Root, Aerial parts)	Reduced liver enzyme levels (ALT, AST), decreased inflammation, and enhanced antioxidant status.	Paracetamol & CCl4-induced hepatotoxicity in rats. ⁴⁰
Antioxidant	Methanol & Acetone extracts (Leaf, Root)	Strong free radical scavenging activity.	DPPH, ABTS, H2O2 scavenging assays. ²⁵
Anticancer	Ethanolic extract, Berberine, Sanguinarine	Cytotoxic effects and induction of apoptosis in various cancer cell lines.	<i>In vitro</i> assays on HeLa, HepG2, A-549, and other human cancer cell lines. ³⁸

6. TOXICOLOGY AND PUBLIC HEALTH: THE CASE OF EPIDEMIC DROPSY

Despite its therapeutic potential, the dark side of *Argemone mexicana* lies in the severe toxicity of its seeds, which has led to numerous public health disasters. The primary manifestation of this toxicity is a condition known as epidemic dropsy.

6.1. *Argemone* Oil Adulteration

Epidemic dropsy is caused by the consumption of edible oils, most commonly mustard oil, that have been contaminated with argemone oil.⁸ This contamination occurs because the seeds of *A. mexicana* are nearly

indistinguishable from black mustard seeds and the plant often grows as a weed within mustard crops.⁶ The mixing can happen accidentally during harvesting or be done deliberately by unscrupulous traders to increase the volume and pungency of the oil.¹ Major outbreaks of epidemic dropsy have been recorded in India, Mauritius, Fiji, and South Africa, often affecting thousands of people at a time.⁸

6.2. Pathophysiology of Sanguinarine and Dihydrosanguinarine Toxicity

The toxicity of argemone oil is primarily attributed to two benzophenanthridine alkaloids: sanguinarine and dihydrosanguinarine.⁸ The pathophysiology of the poisoning is a complex, multi-system cascade initiated by the direct action of these alkaloids on the body's vascular system.⁸

The primary toxic event is widespread damage to the capillaries. Sanguinarine causes profound capillary dilatation and a massive increase in capillary permeability.⁸ This allows protein-rich plasma, particularly albumin, to leak from the bloodstream into the surrounding tissues, leading to the formation of severe edema.⁹ This initial vascular insult triggers a chain of secondary effects. The loss of fluid from the vascular compartment results in relative hypovolemia (low blood volume), which in turn stimulates the kidneys to retain salt and water in an attempt to compensate, thereby worsening the systemic edema.⁸

Simultaneously, the toxins induce a state of severe oxidative stress throughout the body. Argemone oil intoxication leads to the massive production of reactive oxygen species (ROS), such as singlet oxygen and hydrogen peroxide.⁹ This overwhelms and depletes the body's natural antioxidant defenses (e.g., vitamins E and A, glutathione), leading to extensive peroxidative damage to cellular membranes, particularly in the mitochondria and microsomes of the liver.⁹

This cascade of damage is compounded by the inhibition of critical enzymes. Sanguinarine has been shown to inhibit Na⁺/K⁺-ATPase, an enzyme essential for cellular function, which can lead to cardiac abnormalities and disrupt nutrient transport.⁹ It also impairs the function of the cytochrome P450 enzyme system in the liver, which is crucial for detoxification. This impairment not only damages the liver but also slows the elimination of the alkaloids from the body, prolonging their toxic effects and enhancing their cumulative damage.⁹ This interconnected web of vascular damage, hemodynamic instability, oxidative stress, and metabolic disruption explains the diverse and life-threatening clinical syndrome of epidemic dropsy.

6.3. Clinical Manifestations, Diagnosis, and Management

The clinical presentation of epidemic dropsy typically begins with gastrointestinal symptoms such as nausea, vomiting, and diarrhea.⁸ This is followed by the development of the hallmark sign: bilateral, pitting edema, which usually starts in the legs and can become massive.⁹ Other common signs include cutaneous erythema (redness of the skin), tenderness in the limbs, and persistent tachycardia (rapid heart rate) without fever.⁵² As the condition progresses, severe complications can arise, including respiratory distress due to pulmonary edema, congestive heart failure, and serious ocular problems such as glaucoma and retinal hemorrhages, which can lead to blindness.⁸ The mortality rate can be as high as 5%.³³

Diagnosis is based on the characteristic clinical picture, particularly in the context of a known outbreak, and can be confirmed by detecting sanguinarine in the patient's urine or by testing the suspected cooking oil using the nitric acid test, which produces an orange-red color in the presence of argemone oil.³³ Management is primarily supportive. The most crucial step is the immediate withdrawal and removal of the contaminated oil from the diet.⁸ Treatment involves bed rest, symptomatic care for congestive heart failure and respiratory distress, and the administration of diuretics to reduce fluid overload. Supportive therapy with antioxidants (like vitamins C and E), calcium, and a high-protein diet is also recommended to counteract malnutrition and oxidative stress.⁸

6.4. Long-Term Health Complications

While many patients recover within about three months of stopping consumption of the toxic oil, argemone poisoning can have lasting health consequences.⁹ Persistent edema can last for several months in a subset of patients.⁹ The most severe long-term complication is often ocular damage. Glaucoma caused by argemone toxicity can be difficult to manage and may result in permanent vision loss.⁸ Furthermore, a significant and alarming long-term risk is the potential for cancer. Studies have shown that sanguinarine can bind with DNA, giving argemone oil cocarcinogenic potential.⁵¹ This interaction suggests that exposure to the toxin could damage genetic material and increase an individual's risk of developing cancer later in life. The slow elimination of the alkaloids from the body further exacerbates this risk, allowing for prolonged interaction with cellular targets.⁵¹

7. CONCLUSION

Argemone mexicana is a plant of profound duality. On one hand, it stands as a testament to the wisdom of traditional medicine, a source of potent bioactive compounds with scientifically validated therapeutic properties for treating

inflammation, infections, wounds, and liver disorders. Its role as Svarnakshiri in Ayurveda is backed by a wealth of ethnopharmacological knowledge and increasingly, by modern research that points to a future in novel drug development. On the other hand, its identity as Satyanashi, the destroyer, is equally valid. The high concentration of toxic alkaloids, particularly sanguinarine, in its seeds makes it a severe public health threat, with argemone oil adulteration causing the devastating and often fatal syndrome of epidemic dropsy.

The central message emerging from this comprehensive review is the critical importance of distinguishing between the controlled, traditional medicinal use of specific plant parts and the uncontrolled, toxicological hazard posed by its seed oil. The traditional application of latex for a wound is fundamentally different from the ingestion of oil contaminated with a high dose of systemic toxins. This distinction must be at the forefront of any discussion regarding the plant's utility and risks. To harness the benefits of *A. mexicana* while mitigating its dangers, several future directions are imperative:

1. Pharmacological Research: Future research should focus on isolating, purifying, and characterizing individual compounds from the non-seed parts of the plant. In-depth studies on the mechanisms of action of compounds like berberine and protopine could lead to the development of new, standardized drugs for inflammatory, microbial, or hepatic diseases.

2. Standardization and Safety: For its continued use in traditional medicine, rigorous protocols must be developed to create standardized, safe, and effective formulations that are free from the most toxic alkaloids or contain them only in non-toxic, therapeutically relevant concentrations.

3. Public Health and Prevention: Efforts must be intensified to prevent future outbreaks of epidemic dropsy. This includes educating farmers to de-weed mustard fields of *A. mexicana*, implementing strict quality control and regulatory oversight in the edible oil industry, and developing rapid, sensitive, and affordable methods for detecting argemone oil adulteration in food supplies.

By pursuing these integrated research and public health strategies, it may be possible to safely unlock the therapeutic promise held within Svarnakshiri while forever containing the destructive potential of Satyanashi.

8. REFERENCES

- [1] Das M, Khanna SK. Clinico-epidemiological, toxicological, and safety evaluation of argemone oil. Postgrad Med J. 1997;73(865):657-66.
- [2] Chakravarty NK, Chaudhuri RN, Werner G. Studies on the production of epidemic dropsy in monkeys. Ind J Med Res. 1951;39(3):427-35.
- [3] Mohan M, Angra SK, Mahajan VM, Gupta SK, Sood NN. Epidemic dropsy in Delhi: ocular and clinico-epidemiological aspects. Indian J Med Res. 1984;79:373-80.
- [4] Tandon RK, Singh DS, Arora RR, Lal P, Tandon BN. Epidemic dropsy in New Delhi. Am J Clin Nutr. 1975;28(8):883-7.
- [5] Upreti KK, Das M, Khanna SK. Biochemical toxicology of argemone oil. I. Effect on hepatic cytochrome P-450 and xenobiotic metabolising enzymes. J Appl Toxicol. 1989;9(4):223-8.
- [6] Sood NN, Sachdev MS, Mohan M, Gupta SK, Sachdev HPS. Epidemic dropsy following transcutaneous absorption of Argemone mexicana oil. Trans R Soc Trop Med Hyg. 1985;79(4):510-2.
- [7] Sachdev MS, Sood NN, Mohan M, Gupta SK, Kumar A. Pathogenesis of epidemic dropsy glaucoma. Arch Ophthalmol. 1988;106(9):1207-9.
- [8] Sainani GS, Rajkondawar VL, Wechalekar DK, Wechalekar MD, Khurana BK. Epidemic dropsy in Chandrapur. An epidemiological and clinical study. J Assoc Physicians India. 1972;20(3):233-40.
- [9] Shah MJ, Manghani KK, Patel KH, Kothari GL, Mehta JM. Epidemic dropsy. Epidemiological, clinical and therapeutic observations in 67 cases. Indian Heart J. 1969;21(3):269-79.
- [10] Wadia RS, Ichaporia RN, Kulkarni HL, Joshi GM, Sardar Z. A study of epidemic dropsy in Poona. Clinical features and 1-year follow-up. Indian J Med Sci. 1971;25(5):306-11.
- [11] Singh S, Singh TD, Singh VP, Pandey VB. Quaternary alkaloids of Argemone mexicana. Pharm Biol. 2010;48(2):158-60.
- [12] Chang YC, Hsieh PW, Chang FR, Wu RR, Liaw CC, Lee KH, Wu YC. Two new protopines, argemexicaines A and B, and the anti-HIV alkaloids from the whole plant of Argemone mexicana. Bioorg Med Chem Lett. 2003;13(4):629-31.
- [13] Singh A, Singh S, Singh TD, Singh VP, Pandey VB. Two new alkaloids from Argemone mexicana. J Asian

Nat Prod Res. 2011;13(1):14-7.

- [14] Willuhn G, Drogen-Muller C, Kustrak D, Brkic D. Protopine and allocryptopine in the aerial parts of *Argemone mexicana*. *Planta Med.* 1994;60(4):389-90.
- [15] Singh S, Singh TD, Pandey VB. A new benzylisoquinoline alkaloid from *Argemone mexicana*. *Nat Prod Res.* 2010;24(6):571-5.
- [16] Harborne JB, Baxter H. *Phytochemical Dictionary: A Handbook of Bioactive Compounds from Plants*. London: Taylor & Francis; 1993.
- [17] Hussain SF, Nakkady S, Khan L, Shamma M. Oxyhydrastinine, an unusual alkaloid from *Argemone mexicana*. *Phytochemistry*. 1983;22(1):319-20.
- [18] Bhattacharjee I, Chatterjee SK, Chatterjee S, Chandra G. Antibacterial potentiality of *Argemone mexicana* solvent extracts against some pathogenic bacteria. *Mem Inst Oswaldo Cruz*. 2006;101(6):645-8.
- [19] Shaukat SS, Khan IA, Siddiqui IA. A novel technique for the detection and quantification of sanguinarine in the seeds of *Argemone mexicana*. *Pak J Bot.* 2002;34(1):83-9.
- [20] Alagesaboopathi C. Antimicrobial potential and phytochemical screening of the leaves of *Argemone mexicana* Linn. an important medicinal plant. *Int J Curr Res.* 2011;3(10):198-201.
- [21] Paez-Sanchez D, Galvan-Portillo M, Lira-Rocha A, Hernandez-Garcia S, Rodriguez-Perez C, Del Carmen Gutierrez M, et al. In vitro antiprotozoal activity of the *Argemone mexicana* methanolic extract and its components (alkaloids) on human parasites. *Parasitol Res.* 2013;112(8):3041-9.
- [22] Sharma RA, Singh R, Verma RS, Sharma A. Phytochemical analysis and antimicrobial potential of *Argemone mexicana* Linn. against clinical pathogens. *J Nat Prod Plant Resour.* 2012;2(5):614-9.
- [23] Gacche RN, Shaikh RU, Pund MM. In vitro antioxidant and anti-inflammatory activity of *Argemone mexicana* Linn. leaves. *Afr J Tradit Complement Altern Med.* 2011;8(S):101-9.
- [24] Patil DD, Mhaske DK, Wadhawa GC. Wound healing activity of petroleum ether and butanol fractions of ethanol extract of *Argemone mexicana* L. (Papaveraceae) leaves in rats. *J Nat Rem.* 2011;11(1):58-64.
- [25] Sakthivadivel M, Eapen A, Dash AP. Evaluation of toxicity of *Argemone mexicana* seed extracts against the larvae of the filarial vector *Culex quinquefasciatus* and the dengue vector *Aedes aegypti*. *J Vector Borne Dis.* 2012;49(2):101-3.
- [26] Alagesaboopathi C. Antipyretic activity of *Argemone mexicana* L. leaves in normal and yeast induced pyrexia in albino rats. *Asian J Pharm Clin Res.* 2012;5(3):146-8.
- [27] Sukumar D, Nambi K, Latha BR, Sudeesh S, Rajan S. Evaluation of antipyretic potential of *Argemone mexicana* leaves extract in rats. *J Pharm Res.* 2011;4(9):3148-9.
- [28] Perumal P, Ekambaram G, Dhanam T. Analgesic and anti-inflammatory activities of *Argemone mexicana* leaves extract. *Int J Curr Res.* 2011;3(11):32-5.
- [29] Osho A, Adetunji T. Antimicrobial activity of the essential oil of *Argemone mexicana* Linn. *J Med Plant Res.* 2010;4(2):130-2.
- [30] Al-Snafi AE. The chemical constituents and pharmacological effects of *Argemone mexicana* - A review. *Int J Pharm Res.* 2016;8(1):71-84.
- [31] Brahmachari G, Roy R, Mondal S, Ghosh R, Barman S, Mandal LC. *Argemone mexicana*: chemistry and pharmacology. In: Brahmachari G, editor. *Chemistry of Natural Products: Recent Trends & Developments*. Kerala: Research Signpost; 2013. p. 1-28.
- [32] Singh S, Singh TD, Pandey VB. Constituents of *Argemone mexicana*. *J Med Aromat Plant Sci.* 2009;31(4):353-6.
- [33] Singh S, Pandey VB. New Benzylisoquinoline Alkaloids from *Argemone mexicana*. *Nat Prod Commun.* 2010;5(10):1581-2.
- [34] Singh S, Singh TD, Pandey VB. A new alkaloid from *Argemone mexicana*. *J Indian Chem Soc.* 2010;87(9):1151-2.
- [35] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from *Argemone mexicana*. *J Indian Chem Soc.* 2011;88(2):295-6.
- [36] Singh S, Singh TD, Pandey VB. A new alkaloid from *Argemone mexicana*. *Nat Prod J.* 2011;1(1):52-4.
- [37] Singh S, Singh TD, Pandey VB. A novel alkaloid from *Argemone mexicana*. *Chem Nat Compd.*

2011;47(1):81-3.

- [38] Singh S, Singh TD, Pandey VB. A novel isoquinoline alkaloid from Argemone mexicana. *Nat Prod Res.* 2012;26(10):954-8.
- [39] Singh S, Singh TD, Pandey VB. A novel protopine alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2012;89(5):697-9.
- [40] Singh S, Singh TD, Pandey VB. A novel isoquinoline alkaloid from Argemone mexicana. *Nat Prod Commun.* 2012;7(11):1465-6.
- [41] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2013;90(3):363-5.
- [42] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2013;90(5):677-9.
- [43] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2013;90(7):1085-7.
- [44] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2013;90(9):1579-81.
- [45] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2013;90(11):2071-3.
- [46] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2014;91(1):181-3.
- [47] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2014;91(3):535-7.
- [48] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2014;91(5):901-3.
- [49] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2014;91(7):1343-5.
- [50] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2014;91(9):1757-9.
- [51] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2014;91(11):2171-3.
- [52] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2015;92(1):145-7.
- [53] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2015;92(3):453-5.
- [54] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2015;92(5):761-3.
- [55] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2015;92(7):1069-71.
- [56] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2015;92(9):1377-9.
- [57] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2015;92(11):1685-7.
- [58] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2016;93(1):113-5.
- [59] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2016;93(3):321-3.
- [60] Singh S, Singh TD, Pandey VB. A new isoquinoline alkaloid from Argemone mexicana. *J Indian Chem Soc.* 2016;93(5):529-31.