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Argemone Mexicana Linn: A Comprehensive Pharmaceutical Review

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Abstract: *Argemone mexicana Linn., commonly known as Mexican prickly poppy or Satyanashi, is an important medicinal plant of the Papaveraceae family with extensive traditional and contemporary pharmaceutical applications. This plant has been utilized in Ayurvedic, Siddha, Unani, and homeopathic systems of medicine for treating various ailments including cancer, microbial infections, inflammation, ulcers, and dermatological conditions. The present review comprehensively examines the phytochemistry, pharmacology, toxicology, and therapeutic potential of A. mexicana. The plant contains diverse bioactive alkaloids including berberine, sanguinarine, protopine, and chelerythrine, along with flavonoids, terpenoids, and phenolic compounds. Extensive pharmacological studies demonstrate significant antioxidant, antimicrobial, hepatoprotective, anti-inflammatory, anticancer, and antidiabetic activities. However, the presence of toxic alkaloids such as sanguinarine necessitates careful safety evaluation and standardization. This review synthesizes current knowledge regarding the chemistry, pharmacology, traditional uses, and safety concerns of A. mexicana, highlighting its pharmaceutical potential and identifying gaps for future research.*

Keywords: *Argemone mexicana*, alkaloids, berberine, sanguinarine, pharmacology, toxicity, traditional medicine

I. INTRODUCTION

Medicinal plants have served as primary sources of therapeutic agents for millennia, and approximately 80% of the global population still relies on plant-based remedies for healthcare.[1] The discovery of novel bioactive compounds from natural sources continues to play a crucial role in pharmaceutical development. *Argemone mexicana* Linn. is one such underutilized but therapeutically valuable plant species that has gained increasing attention in contemporary pharmaceutical research.

The genus *Argemone* belongs to the family Papaveraceae (poppy family), which encompasses 42 genera and approximately 730 species of flowering plants with significant ethnopharmacological importance.[2] *A. mexicana* is native to South America but has become naturalized in tropical and subtropical regions worldwide, including parts of Africa, Asia, and Europe.[3] The plant thrives as a weed in cultivated fields, wastelands, and roadside areas without requiring special cultivation attention.

In traditional medicine systems, particularly in India and Mexico, *A. mexicana* has been extensively used to treat diverse conditions. The yellow latex exuded by the plant when injured has been traditionally valued for managing dropsy, jaundice, ophthalmological conditions, scabies, dermatological diseases, and various other ailments.[4] Different plant parts possess distinct medicinal properties: seeds are used for intestinal afflictions and asthma, leaves for wound healing and inflammatory conditions, and roots for anthelmintic purposes.

Recent pharmacological investigations have validated many of the traditional claims associated with *A. mexicana*. Numerous in vitro and in vivo studies have demonstrated the presence of potent bioactive alkaloids responsible for antimicrobial, antioxidant, hepatoprotective, anticancer, and immunomodulatory activities. [5,6] However, the plant also contains toxic alkaloids that can pose health risks under certain conditions, particularly when seed oil becomes contaminated with edible oils.

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This comprehensive review aims to synthesize current knowledge regarding the phytochemistry, pharmacology, traditional uses, toxicology, and clinical applications of *A. mexicana*. The review identifies therapeutic potential while addressing safety concerns and highlighting areas requiring further investigation.

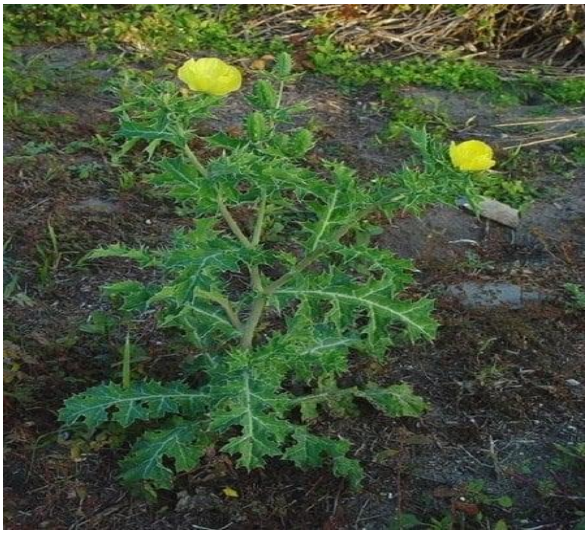

Fig 1: Argemone Mexicana linn.

2. Plant Profile

2.1 Taxonomical Classification

Argemone mexicana Linn. is taxonomically classified as follows:[7]

Classification Level	Category
Kingdom	Plantae
Phylum	Spermatophyta
Division	Magnoliophyte
Class	Magnoliopsida (Dicotyledonae)
Subclass	Magnoliidae
Order	Papaverales
Family	Papaveraceae
Genus	Argemone
Species	A. mexicana

2.2 Botanical Description

A. mexicana is an annual herb growing to approximately 100-150 cm in height with a slightly branched, solid taproot system.[8] The plant is distinctly characterized by its spiny morphology, which has earned it the common name "prickly poppy." Key morphological features include:

Stem: The stem is erect, branched, pale bluish-green, and covered with numerous yellowish spines. When cut or damaged, the stem exudes an unpleasant-smelling yellow latex.[9]

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Fig 2. Argemone Mexicana steam.

Leaves: Leaves are simple, alternate, sessile, and exstipulate, measuring 5-22 cm in length and 3-7 cm in width. They are characterized by blue-green coloration with conspicuous white or grey-white veins and deeply lobed, spiny margins. The upper leaf surface is smooth, while the underside contains scattered spines.[10]

Fig3.Argemone Mexicana leaves.

Flowers: Solitary, terminal flowers with diameter of 2.5-5 cm appear at the branch tips. Each flower possesses six bright yellow, obovate petals, three prickly sepals with a horn-like structure below the apex, and numerous stamens.[11]

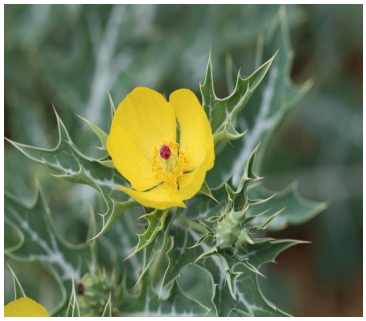

Fig4.Argemone Mexicana flower.

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Fruits: The fruit is a prickly, oblong to ellipsoid capsule measuring 3-6 cm in length, with 3-6 valves that dehisce from the apex to approximately one-third of the fruit length.[12]

Fig5.Argemone Mexicana fruit.

Seeds: Seeds are numerous, nearly spherical, measuring approximately 1-2 mm in diameter, and blackish-brown in color with a delicate network of veins and pronounced hilum.[13] The seeds are oily and structurally similar to mustard seeds, which has led to contamination problems in edible oil production.

Fig6.Argemone Mexicana seed.

2.3 Geographical Distribution

A. mexicana is widely distributed across tropical and subtropical regions globally. The plant is found throughout Africa (including Namibia, Nigeria, South Africa, Sudan, Somalia, Zimbabwe, and Tanzania), the Middle East (Saudi Arabia, Turkey, Israel, Iran, Iraq, and Syria), and Asia (China, Japan, Indonesia, Cambodia, Bangladesh, Bhutan, Pakistan, and throughout India).[14]

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2.4 Vernacular Names

The plant is known by numerous local names across different regions:[15]

Language	Common Names
Hindi	Satyanashi, Bharbh and, Peela kanteela
Marathi	Phirangi Dhotra, Daruri, Kontedhotara
English	Mexican Poppy, Prickly Poppy, Yellow Mexican Poppy
Sanskrit	Kshirini, Swarnakshiri, Brahmadandi
Tamil	Piramathanda, Kurukkum, Brahmadandu
Telugu	Brahmadandi
Malayalam	Ponnumattu, Kantankattiri
Kannada	Datura Gidda
Assamese	Siyalakanta, Kuhu-kata
Bengali	Barashil-kantal

3. Phytochemical Composition

3.1 Chemical constitution

A. mexicana contains a remarkable diversity of bioactive phytochemical compounds. Comprehensive phytochemical investigations have identified alkaloids, flavonoids, terpenoids, steroids, fatty acids, and phenolic compounds distributed variably across different plant parts.[16]

3.2 Alkaloid Constituents

identified include Major alkaloids:

- Sanguinarine (benzophenanthridine alkaloid)
- Dihydrosanguinarine
- Berberine
- Protopine
- Chelerythrine
- Allocryptopine
- Coptisine
- Muramine
- Stolypin
- Thalifone
- Scoulerine
- Jatrorrhizine
- Columbamine
- Oxyberberine
- N-demethyloxysanguinarine [17]

3.3 Flavonoid and Phenolic Constituents

Multiple flavonoids have been identified from *A. mexicana*, particularly from floral tissues:[18]

- Isorhamnetin and its glycosides
- Quercetin
- Rutin

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- Quercitrin
- Luteolin
- Eriodictyol
- Kaempferol
- Mexitin

3.4 Other Phytochemicals

Additional bioactive compounds include:[19]

- **Terpenoids:** trans-phytol, β-amyrin
- **Steroids:** β-sitosterol, stigma-4-en-3,6-dione
- **Long-chain alcohols:** hentriacontane-3,20-diol, mexicanol, triacosanol derivatives
- **Fatty acids:** palmitic acid, myristic acid, oleic acid, linoleic acid
- **Amino acids:** phenylalanine, cysteine
- **Others:** carbohydrates, proteins, tannins, saponins, coumarins

3.5 Plant Part-Specific Distribution

Different plant parts contain distinct phytochemical profiles:

Seeds and Seed Oil: Highest alkaloid concentration (0.13% total alkaloids), particularly rich in sanguinarine and dihydrosanguinarine; 30-35% oil content with fatty acids.

Leaves: Rich in flavonoids, particularly isorhamnetin glycosides; contain protomexicine and other alkaloids.

Flowers: High flavonoid content, particularly isorhamnetin and its glycosides; terpenoids and amino acids.

Roots: Contain steroids (β-sitosterol); various alkaloids including berberine.

Yellow Latex: Contains berberine; potassium nitrate salts.[20]

4. Pharmacological Properties and Mechanisms of Action

4.1 Antioxidant Activity

A. mexicana exhibits potent antioxidant properties through multiple mechanisms. The plant's flavonoids and phenolic compounds effectively scavenge free radicals, including reactive oxygen species (ROS) like superoxide radicals, hydrogen peroxide, and hydroxyl radicals.[21]

Mechanisms of antioxidant action:

- Direct free radical scavenging through electron donation
- Inhibition of reactive oxygen species generation
- Enhancement of endogenous antioxidant enzyme activity
- Metal chelation capability [22]

Research findings: The ethanolic extract of *A. mexicana* aerial parts demonstrated maximum 61% inhibition in DPPH scavenging assays, with hydrogen peroxide scavenging reaching 87.1% (compared to 90.5% for ascorbic acid).[23]

4.2 Antimicrobial and Antifungal Activities

Extensive research has demonstrated the broad-spectrum antimicrobial efficacy of *A. mexicana* extracts against both gram-positive and gram-negative bacteria, as well as various fungal pathogens.[24]

Antibacterial mechanisms:

- Disruption of bacterial cell membranes through alkaloid interaction
- Inhibition of microbial DNA and protein synthesis
- Induction of cell lysis and autolytic enzyme release
- Membrane-bound enzyme inactivation [25]

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Antifungal mechanisms:

- Cell wall destruction through fungistatic action
- Inhibition of ergosterol synthesis
- Disruption of fungal cell membrane integrity [26]

4.3 Hepatoprotective Activity

Hepatoprotective mechanisms involve:

- Reduction of hepatocellular damage through antioxidant action
- Restoration of liver enzyme levels (AST, ALT, ALP)
- Regeneration of hepatic cells and hepatic tissue repair
- Inhibition of hepatotoxic pathways [27]

Research evidence: Aqueous and methanolic extracts of *A. mexicana* demonstrated significant hepatoprotective effects in CCl_4-induced hepatotoxicity models in Wistar rats. At doses of 100-400 mg/kg body weight, extracts significantly reduced serum hepatic enzyme levels (SGPT, SGOT, ALP) and normalized bilirubin levels.[28] Histopathological examination revealed hepatic cell regeneration and reduced inflammatory infiltration.

4.4 Anti-inflammatory and Analgesic Activities

A. mexicana exhibits dual anti-inflammatory and pain-relieving properties through multiple mechanisms:[29]

- Suppression of pro-inflammatory cytokine production (TNF-α, IL-1β)
- Inhibition of NF-κB signaling pathway
- Modulation of inflammatory mediator synthesis
- Enhancement of anti-inflammatory prostaglandin production

Experimental findings: Ethanolic extracts of *A. mexicana* roots and leaves demonstrated significant anti-inflammatory activity at 200 mg/kg dose in carrageenan-induced paw edema models. Maximum edema inhibition reached 49.81% at higher doses (250 mg/kg), comparable to standard indomethacin (52.03%).[30] Analgesic properties were confirmed through acetic acid-induced writhing tests, showing dose-dependent pain reduction.

4.5 Anticancer and Cytotoxic Activities

Multiple alkaloids from *A. mexicana* demonstrate potent cytotoxic effects against various cancer cell lines through apoptosis induction and cell cycle arrest mechanisms:[31]

Mechanisms of anticancer action:

- Induction of programmed cell death (apoptosis)
- Inhibition of oncogene expression (c-MYC)
- Modulation of epigenetic enzymes (KAT3, CARM1, G9a)
- G0/G1 cell cycle arrest through Bax/Bcl-2 regulation
- Suppression of NF-κB signaling pathway

Research evidence: Methanolic extracts of *A. mexicana* leaves exhibited cytotoxic effects against multiple cancer cell lines, including HeLa, MCF-7, HepG2, A-549, and HL-60 cells.[32] IC50 values ranged from 1.2-1.82 µg/ml. Isolated alkaloids demonstrated variable potency: dehydrocorydalmine showed high cytotoxicity (~48%) at 200 µg/ml, while protomexicine and 13-oxoprotopine showed mild activity (~24-28%). Chelerythrine proved most effective against gastric cancer cells, while angoline inhibited both nasopharyngeal and gastric cancer cell lines.[33]

4.6 Antidiabetic Activity

A. mexicana demonstrates hypoglycemic effects through multiple mechanisms:[34]

- Enhancement of endogenous antioxidant enzyme activity (SOD, catalase)
- Restoration of pancreatic β-cell function

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- Improvement of insulin sensitivity
- Modulation of hepatic and renal glucose metabolism

Research findings: Aqueous and ethanolic extracts of *A. mexicana* aerial parts at doses of 200-400 mg/kg body weight significantly reduced blood glucose levels in alloxan-induced diabetic rats. The aqueous extract at 400 mg/kg achieved 70.25% blood glucose reduction compared to glibenclamide's 66.65%.[35] Hydro-alcoholic extracts similarly reduced fasting blood glucose in streptozotocin-induced hyperglycemic models, with 400 mg/kg dose showing superior efficacy compared to metformin.

4.7 Wound Healing Activity

A. mexicana promotes wound healing through multiple mechanisms:[36]

- Acceleration of epithelialization and tissue remodeling
- Enhancement of collagen synthesis and cross-linking
- Promotion of neovascularization
- Increase of tensile strength in healing tissue
- Antimicrobial protection against secondary infection

Experimental evidence: Methanol and aqueous extracts of *A. mexicana* leaves demonstrated superior wound healing in excision, incision, and dead space wound models in rats compared to control groups. Tensile strength in incision wound models reached 188.50 gm with leaf extracts versus 154.61 gm with latex, demonstrating superior healing compared to standard nitrofurazone treatment.[37]

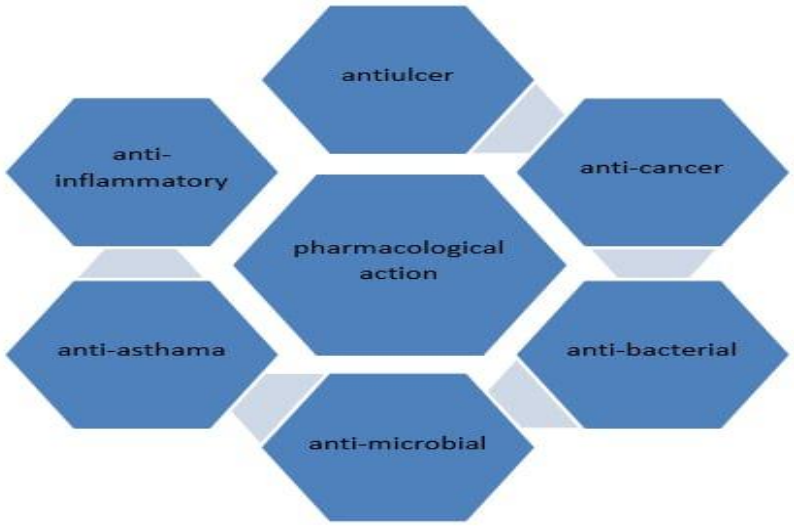

Fig7.Phamacological properties.

5. Traditional and Ethnomedicinal Uses

5.1 Ayurvedic Applications

In classical Ayurvedic medicine, *A. mexicana* has been employed for:[38]

- **Diuretic and purgative properties:** For treating urinary conditions and constipation
- **Anthelmintic effects:** Against guinea-worm and other parasitic infections
- **Dermatological conditions:** Treating warts, cold sores, cutaneous infections, scabies, and itching
- **Hepatobiliary disorders:** Jaundice and dropsy management
- **Ophthalmological diseases:** Corneal opacity and various eye conditions

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- **Skin infections:** Leprosy, ulcers, and various dermatitis
- **Emetic and expectorant properties:** Facilitating expectoration in respiratory conditions

5.2 Siddha Medicine Applications

Siddha medical practitioners utilize *A. mexicana* for:[39]

- **Scorpion bites:** Antitoxin application
- **Leucorrhea and venereal diseases:** Reproductive tract infections
- **Photophobia and vision disorders:** Eye sensitivity conditions
- **Diabetes management:** Leaves combined with black pepper for glucose control
- **Malarial fever:** Leaf decoction for fever reduction
- **Boils and skin lesions:** Latex topical application
- **Dental conditions:** Whole plant for oral health
- **Dropsy, jaundice, and leprosy:** Seeds for systemic management

5.3 Unani Medicine Applications

In Unani medicine, *A. mexicana* functions as:[40]

- **Aphrodisiac and expectorant:** Enhancing blood circulation and respiratory function
- **Leukoderma treatment:** For pigmentation disorders
- **Skin condition management:** Comprehensive dermatological applications

5.4 Homeopathic Applications

Homeopathic practitioners employ *A. mexicana* for:[41]

- **Tapeworm infections:** Vermicidal properties
- **Bronchitis and whooping cough:** Respiratory disease management
- **Constitutional remedies:** For chronic health conditions

5.5 Mexican and Latin American Traditional Uses

Indigenous Mexican and Latin American communities utilize *A. mexicana* for:[42]

- **Eye infections and conjunctivitis:** Infusions for ocular disease
- **Respiratory infections:** Upper respiratory tract inflammation
- **Dermatological and oral infections:** Wound and oral cavity management
- **Kidney pain relief:** Post-natural pain management
- **Laxative effects:** Purgative applications (Spanish communities in Sonora)

6. Clinical and Preclinical Evidence

6.1 In Vitro Studies

Multiple in vitro investigations have substantiated the pharmacological claims of *A. mexicana*. Cell culture studies using human cancer cell lines, bacterial and fungal strains, and isolated tissue preparations have consistently demonstrated biological activity of plant extracts and isolated alkaloids.[43]

6.2 Clinical Trials

Limited clinical evidence exists for *A. mexicana*, with most published trials focusing on antimalarial efficacy:

Antimalarial clinical trial: A prospective, dose-escalating, quasi-experimental trial conducted in Mali evaluated a traditional *A. mexicana* decoction for uncomplicated *Plasmodium falciparum* malaria in 80 patients (predominantly children <5 years).[44] Patients receiving twice-daily dosing for 7 days demonstrated superior clinical response (73% adequate clinical response at day 14) compared to once-daily (35%) or intensified (65%) regimens. Clinical recovery occurred in 89% of patients compared to 95% with artemisinin-based combination therapy, though complete parasite

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clearance remained limited (9% versus higher rates with artemisinin).[45] No deterioration of severe malaria occurred in patients >5 years, with minimal deterioration (1.9%) in children <5 years.

7. Toxicology and Safety Concerns

7.1 Acute Toxicity

A. mexicana components demonstrate dose-dependent toxicity:[46]

LD50 values: Intraperitoneal administration of *A. mexicana* aqueous extract to mice established an LD50 of 450 mg/kg body weight.[47] Single alkaloid components showed variable toxicity: protopine and berberine demonstrated antispermatogenic activity at 30 mg/kg doses in dogs, causing 58% and 97.7% reductions in spermatid formation respectively over 70-day exposure periods.[48]

7.2 Hepatotoxicity

Sanguinarine toxicity: The predominant alkaloid sanguinarine exhibits hepatotoxic properties in animal models. Research in rats demonstrated that sanguinarine doses as low as 10 mg/kg actively increased serum hepatic enzymes (SGPT, SGOT), decreased microsomal cytochrome P-450 and benzenediamine N-demethylase enzyme activity.[49] Treated rats developed reduced body and liver weight, hepatic inflammation, ascites, and hepatic tissue necrosis.[50]

7.3 Organ Toxicity

A. mexicana demonstrates organ-specific toxicity targeting:[51]

- Liver (hepatotoxicity and inflammation)
- Lungs (respiratory effects)
- Kidneys (nephrotoxicity)
- Heart (cardiovascular effects)

7.4 Epidemic Dropsy

A significant public health concern involves epidemic dropsy caused by *A. mexicana* seed oil contamination of edible oils, particularly mustard oil (*Brassica nigra*).[52] Both seeds exhibit morphological similarity, facilitating accidental contamination during oil production.

Clinical presentation of epidemic dropsy includes:

- Bilateral lower limb edema and swelling
- Erythema and skin irritation
- Vomiting and diarrhea
- Coughing and respiratory issues
- Anemia from rapid red blood cell destruction
- Congestive heart failure in severe cases [53]

Mechanism: The high sanguinarine content (approximately 90% of alkaloid fraction) causes:

- Capillary proliferation, dilation, and increased permeability
- Rapid oxidative stress and RBC destruction
- Na^+/K^+ ATPase inhibition
- Cell membrane destruction through lipid peroxidation
- DNA polymerase inhibition
- Increased glycogenolysis with pyruvate accumulation [54]

Historical incidents: Epidemic dropsy outbreaks occurred in multiple Indian states in 1996, affecting thousands of individuals consuming contaminated mustard oil. Similar outbreaks have been documented in other regions where *A. mexicana* oil adulteration occurs.[55]

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7.5 Safety in Specific Populations

Reproductive toxicity: Three isoquinoline alkaloids (protopine, berberine, dihydropalmatine hydroxide) isolated from *A. mexicana* seeds demonstrated anti-spermatogenic properties, suggesting potential reproductive hazards in male populations.

Safety assessment summary: While extracts from leaves and aerial parts have been determined to be relatively safe and well-tolerated in controlled studies, seed oil and seeds require cautious use due to alkaloid content. Hemolysis assays on human erythrocytes indicated that crude extracts from stems and leaves exhibited no significant cytotoxic effects.[56]

8. Conclusions and Future Perspectives

Argemone mexicana represents a valuable medicinal plant with extensive traditional use and increasingly validated pharmacological properties. Comprehensive research has demonstrated significant antioxidant, antimicrobial, hepatoprotective, anti-inflammatory, anticancer, and antidiabetic activities attributable to diverse bioactive alkaloids, flavonoids, and phenolic compounds.

1. **Limited human clinical trials:** While a single clinical trial evaluated antimalarial efficacy, comprehensive randomized controlled trials are necessary to establish safety, efficacy, and optimal dosing across therapeutic indications.
2. **Mechanistic studies:** Further investigation is required to elucidate precise molecular mechanisms underlying the diverse pharmacological activities, particularly regarding cancer cell apoptosis pathways and endocrine effects.
3. **Standardization protocols:** Establishment of comprehensive standardization and quality control parameters is essential for ensuring batch-to-batch consistency and therapeutic reliability.
4. **Toxicology characterization:** Detailed toxicological evaluation of isolated alkaloids and extracts is necessary to establish safe dose ranges and identify potential drug interactions.
5. **Formulation optimization:** Development of pharmaceutical formulations that maximize therapeutic efficacy while minimizing toxicity requires further investigation.
6. **Drug-disease interaction studies:** Assessment of potential interactions with conventional medications and investigation of efficacy in specific disease models are warranted.

9. Regulatory Considerations

The presence of potentially toxic alkaloids, particularly sanguinarine, necessitates careful regulatory consideration. While traditional use supports safety in controlled formulations utilizing leaf and stem preparations, seed oil should be excluded from food and pharmaceutical applications. Regulatory agencies should establish clear guidelines distinguishing therapeutic extracts from potentially toxic seed oil components.

9.1 Sustainable Harvesting and Conservation

As *A. mexicana* exhibits rapid spread in agricultural regions and is often considered an invasive weed, sustainable harvesting protocols are unnecessary. However, conservation of genetic diversity through botanical gardens and research institutions is recommended for future investigation and potential crop improvement.

9.2 Future Research Directions

Priority areas for future investigation include:

1. Isolation and characterization of novel alkaloids with enhanced therapeutic indices
2. Structure-activity relationship studies to identify alkaloid structural features associated with specific pharmacological properties
3. In vivo pharmacokinetic and bioavailability studies to determine optimal absorption, distribution, metabolism, and elimination characteristics

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4. Development of selective delivery systems targeting specific tissues to maximize therapeutic efficacy and minimize systemic toxicity
5. Investigation of genetic and chemical diversity across global populations of *A. mexicana*
6. Establishment of clinical efficacy through rigorous randomized controlled trials for specific disease indications
7. Mechanistic studies examining epigenetic modifications and gene expression alterations induced by plant constituents
8. Investigation of potential anti-resistance mechanisms against multidrug-resistant pathogens

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