Indian J. Applied & Pure Bio. Vol. 41(1), 46-56 (2026). **ISSN: 0970-2091**

Phytochemical Composition, Pharmacological activities and Traditional Therapeutic Significance of *Argemone mexicana* L: A Comprehensive Review

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Abstract

Argemone mexicana L. (also referred to as Mexican prickly poppy or Satyanashi) is a highly significant phytho-ethnopharmaceutical species of the Papaveraceae containing several very significant ethnopharmacological products. Conventionally, seeds, roots, leaves, and latex of the plant have been used in Ayurveda, Siddha, Unani, and Homeopathy in the treatment of jaundice, skin infections, diabetes, inflammation, ulcers, and hepatic ailments. Different bioactive compounds have been found in phytochemical studies which include: isoquinoline alkaloids (berberine, chelerythrine, sanguinarine, and protopine), flavonoids, phenolics, terpenoids, sterols and fatty acids that make it have a wide range of pharmacological activities. The contemporary pharmacological research has shown that *A. mexicana* has strong antimicrobial, antioxidant, antidiabetic, anticancer, hepatoprotective, antirenal, anti-inflammatory, analgesic, and antiulcer effects. Mechanistically, it is said to have these effects due to its free radical scavenging properties, effects on enzyme activities and pro-inflammatory pathway suppression. Although this has a tremendous therapeutic potential, some of the toxic alkaloids that are found in the seeds require controlled and standardized use. More studies on its safety and bioavailability in the context of clinical use should be conducted to determine *A. mexicana* as a promising natural source of drug.

Key words: *Argemone mexicana*, phytochemicals, isoquinoline alkaloids, pharmacological activity, traditional medicine, antioxidant, hepatoprotective, anticancer.

The country has long history of using herbal remedies in the traditional therapies. Chemicals of plant origin are now finding use in a host of disorders. The ecological and therapeutic properties of herbs are also very many and therefore they provide a good source of organic chemicals with a possible pharmaceutical application. *Argemona mexicana* L. is a medicinal plant[24]. One type of a species of poppy in Mexico and which is now widely growing wild in various parts of the globe is *Argemone mexicana* (Mexican poppy, Mexican prickly poppy, flowering thistle)[15]. In India, *Argemone mexicana* is referred to as Satyanashi or Bhatkatiya[18]. It is a prickly, herbaceous plant, which is a member of Papaveraceae family[22]. The plant is an exotic species that was introduced in South America and has started spreading to most of the tropical and subtropical countries including West Africa[7]. It is usually present in the paths and farms in India[1]. It is a thorny herb which grows periodically up to 1 m tall. It has leaf lengths of between 5 and 11 cm, which are a combination of green and white blotches. They are glaucous, broad at the base, partly envelop the stem, and have large sinuate lobes and spiny edges[23].The flowers become terminal, yellow and odorless and have a diameter of 4 to 5 cm. The capsule has a cavity which is spiny, oval, or elliptic-oblong, and approximately 3 cm long. The seeds are round, shiny, black and pitted[4].The plant has a number of alkaloids, flavonoids, tannins, sterols, and terpenes[8]. The plant exhibits a wide range of biological activities, including antibacterial, anti-inflammatory, antioxidant, anticancer, antidiabetic, and wound-healing properties. It has also been reported to show anti-HIV, anti-stress, anti-allergic, vasoconstrictive and vasorelaxant, antifertility, cytotoxic, nematicidal, antifeedant, fungitoxic, and hepatoprotective effects[9,20].

Fig. 1. *Argemone mexicana*

Taxonomical Description[15]

Fig. 2. Taxonomic Classification of *Argemone mexicana* L.

Vernacular names :

Language	Vernacular names
Hindi	Satyanasi, Kataila
English	Mexican prickly poppy, flowering thistle, cardo or cardosanto
French	Argemone
German	Doppelklappen
Sanskrit	Swarna ksheeri, Kanchani, Karshani, Hemadugdha, Tikta Dugdha
Urdu	Baramdaandi
Bengali	Siyal Kanta; Bharband
Kannada	Datturigidda
Konkani	Phirangi dhutro
Malayalam	Ponnummattu
Tamil	Piramathanda
Telugu	Brahmadandi
Irula	Mulluumathai
Punjabi	Bhataiktheya
Manipuri	Khomthongpee
Marathi	Firangi dhotra

Habitat :

Argemone mexicana typically grows on floodplains, riverbanks, disturbed regions, roadsides, and fallow and farmed soils. It is a major crop weed that occasionally competes with and replaces natural plants[2].

Traditional uses[2] :

A. mexicana is extensively used in traditional system of medicine in the treatment of numerous diseases. Various parts of the plant were extensively using in Ayurveda, Siddha, Unani and Homeopathic medicines.

In Ayurveda medicine :

The whole plant of *A. mexicana* is effective in guinea-worm infestations, purgative and diuretic. Seeds of the plant are used as an antidote in snake poisoning and also

acts as an emetic, expectorant, demulcent and laxative. The protein-dissolving substances containing seed extract is used to cure warts, cold sores, cutaneous infections, itches, jaundice and dropsy. Seeds are effective against skin infection, sores, dropsy and jaundice. Juice of the plant cures ophthalmic and opacity of cornea. Oil of the seed is used to treat skin diseases. Roots are anti-helmentic and also used in, skin diseases, leprosy and inflammations.

In siddha medicine :

This plant is widely used to cure venereal sores, photophobia, scorpion bite, leucorrhoea. Leaves along with black pepper are used to cure diabetes. The latex of *A. mexicana* used to treat boils by topical application on the site of boils. Whole plant is used to treat dental disorders. Leaf decoction is used in the treatment of malarial fever and ulcers. Juice of the plant is applied on scorpion sting. Seeds are effective against leprosy, jaundice and dropsy.

In Unani medicine :

A. mexicana helps in the enrichment of blood which acts as an expectorant and aphrodisiac. It is also used in treating skin diseases and leukoderma.

In Homeopathic medicine :

The drug prepared from this plant is very effective in treating the problem caused by tape worm. The whole plant is reported to be used for the treatment of whooping cough and bronchitis.

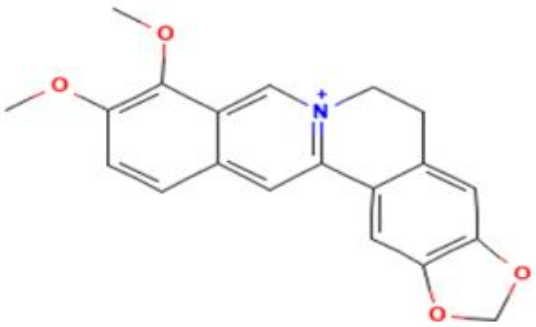
Phytochemistry :

Argemone mexicana Linn. (Mexican poppy) has been known to have a strong phytochemical profile, comprising of alkaloids (berberine, chelerythrine, protopine, and sanguinarine), flavonoids, phenolics, terpenoids, tannins, steroids, saponins and fatty acids, that are found all through its seeds, leaves, roots and latex. Isoquinoline alkaloids (berberine, chelerythrine, and protopine) are major in the plant, particularly in the latex, roots, and aerial parts and have been found to be the contributors of the antimicrobial, cytotoxic, and wound-healing effects of the plant. Notable properties of seeds are the presence of toxic alkaloids, e.g. sanguinarine and dihydrosanguinarine, and fixed oils with fatty acids, e.g. myristic, palmitic, stearic, linoleic and oleic acids[19].

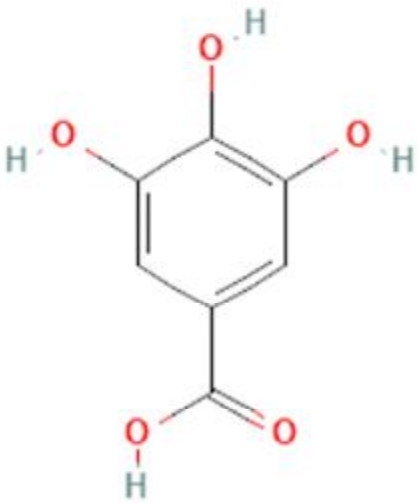
The leaves and flowers contain flavonoids (*i.e.*, quercetin, kaempferol) and phenolic compounds (*i.e.*, gallic acid, ferulic acid), which can effectively deliver anti-oxidant and anti-inflammatory effects, whereas the roots and latex contain berberine and chelerythrine, which can play a beneficial role in antimicrobial and cytotoxic activity. Phytosterols, fatty acids and terpenes (such limonene and 2-pinene) found in essential oils of the aerial parts may play a role in anti-inflammatory and analgesic activity. Recent reports validate the extensive pharmacological properties of the plant (antioxidant, antimicrobial, anti-inflammatory, antidiabetic and anticancer) but indicate that more clinical and toxicological studies are required to confirm the safety and efficacy of the plant when used by humans[12].

Table-1. Major Phytochemical Constituents of *Argemone mexicana*

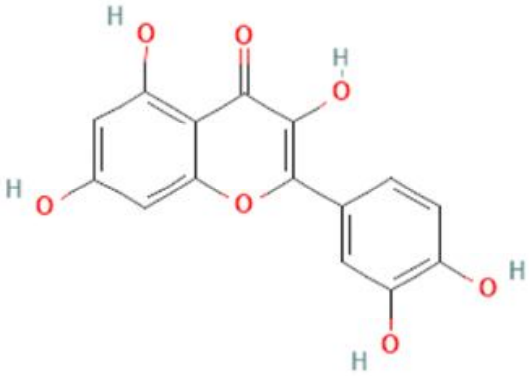
Phytochemical Class	Major Constituents	Plant Parts
Alkaloids	Berberine, Sanguinarine, Chelerythrine, Allocryptopine, Protopine, Coptisine	Latex, seeds, roots
Flavonoids	Quercetin, Kaempferol, Isorhamnetin	Leaves, flowers
Phenolics & Tannins	Gallic acid, Ferulic acid, Caffeic acid	Whole plant
Terpenoids & Sterols	β-sitosterol, Caryophyllene, Limonene	Roots, leaves
Fatty acids & Fixed oils	Linoleic, Oleic, Palmitic, Stearic acids	Seeds



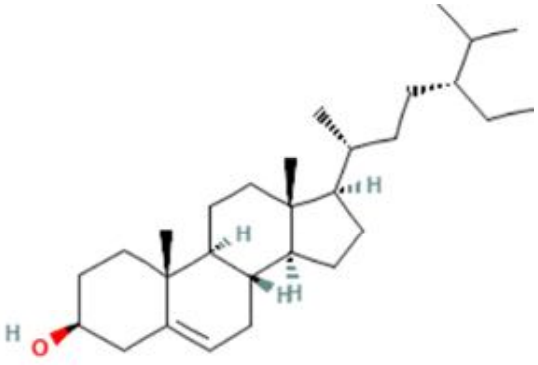
Berberine



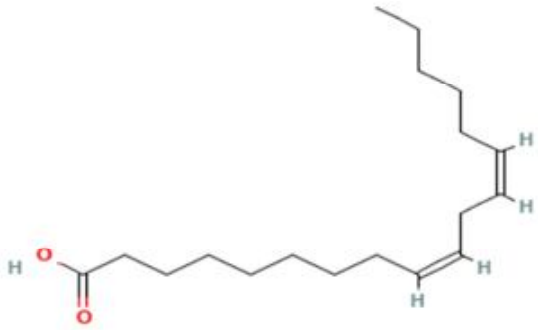
Gallic acid



Quercetin



β-sitosterol



Linoleic

Fig. 3. Major phytochemical of *Argemone mexicana*

Pharmacological Activities :

Antimicrobial Activity :

Argemone mexicana has been found to possess a good antimicrobial potential due to its high content of bioactive phytochemicals including alkaloids namely chelerythrine and berberine. The extracts of methanol have shown to highly inhibit the Gram-positive bacteria such as *Staphylococcus aureus, Bacillus* cereus among others, but only moderate to low effect on Gram-negative strains and fungi, especially when it comes to the outer roots and leaves. Mechanisms of antimicrobial effect may include the obstruction of bacterial cell membrane permeability and the suppression of proteins and DNA production that are

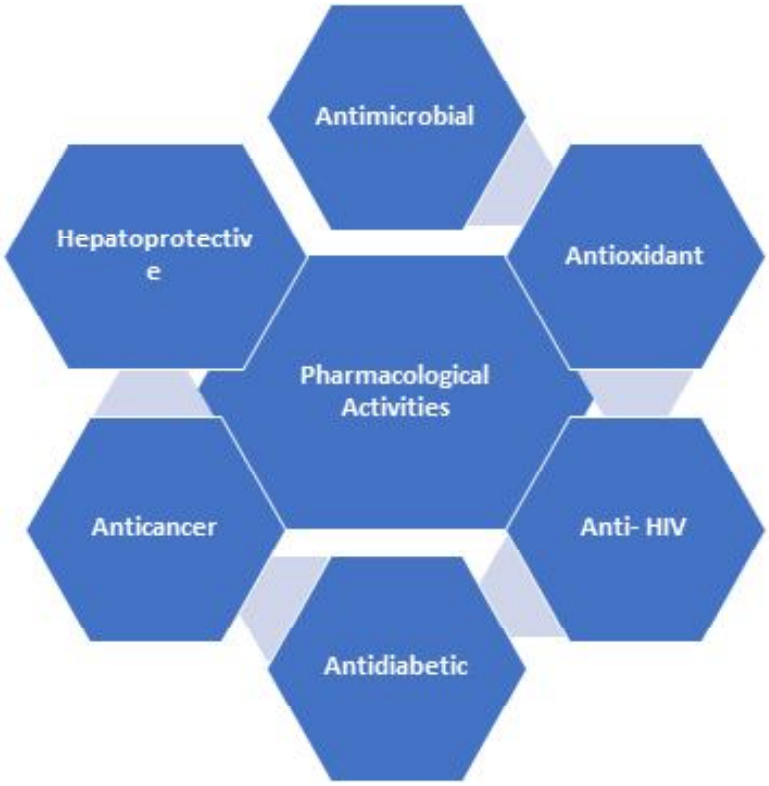


Fig. 4. Pharmacological Activities

associated with the bioactivity of the chelerythrine and berberine. Moreover, ethanol and methanol extract of different parts of plants have exhibited broad spectrum antibacterial effect against gastrointestinal pathogens such as *E. coli, S. typhi* and *K. pneumoniae* and inhibition zones were similar to those of conventional antibiotics such as ampicillin. The results justify the promise of *A. mexicana* exploitation as a rich source of phytotherapeutics in the development of antimicrobial drugs[17].

Antioxidant Activity :

A. mexicana root is said to have antioxidant activity with ethanol extract. It was found that high DPPH radical scavenging activity (85.17 %), ABTS radical scavenging activity (75.27 %) and H_2O_2 radical scavenging activity (84.25 %) was observed at 100. The concentration is in the range of 100 104 g/ml. Extract had high free radical scavenging activity which was dose dependent[3]. *A. mexicana* leaf solvents were found to have super oxide anion scavenging ability using the Nitro Blue Tetrazolium assay. At a dosage of 200 µg/ml, the greatest percentage of free radical scavenging was demonstrated by all extracts. With an IC50 value double that of L-ascorbic acid, acetone extract had the strongest radical scavenging activity[6].

Anti- HIV Activity :

After the entire A. mexicana plant was allowed to air dry, a meth anol extract was made. After being extracted from the extract, the alkaloid compounds (±)-6-acetonyl dihydrochelerythrine and benzo[c] phenanthridine may exhibit effective anti-HIV activity in the H9 lymphocyte assay, with an EC50 value of 1.77 µg/ml. Selected 23 plants with comparable anti-HIV chemical constituents and 92 extracts were made using Soxhlet extraction and liquid-liquid partitioning. The extracts' anti-HIV properties were examined in a human CD4+ T-cell line, CEM-GFP cells, infected with HIV-1NL4.3. *Argemone mexicana*, *Aegle marmelos, Asparagus racemosus, Rubia cordifolia*, and *Coleus forskohlii* were the eight plant species that significantly decreased viral production in CEM-GFP cells infected with HIV-1NL4.3 and demonstrated encouraging anti- HIV activity. Their research provided support for their long- standing use as immunomodulators[5].

Antidiabetic Activity :

Different fractions of the hydroethanolic extract of *A. mexicana* aerial parts were gathered in water, petroleum ether, and chloroform. In alloxan-induced diabetic Wistar rats, the aqueous and chloroform extracts demonstrated hypoglycemic efficacy throughout a 21-day period at a dose of 150 mg/kg body weight. Significantly lower blood glucose levels, weight recovery, decreased food and water intake, lower levels of total triglycerides (TGs), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and total cholesterol (TC) were also noted, but high-density lipoprotein (HDL) levels stayed normal. Total creatinine, serum glutamate pyruvate transaminases (SGPT), and serum glutamate oxaloacetate transaminases (SGOT) all had levels that were close to normal. The levels of glutathione (GSH), glutathione-S-transferase (GST), lipid peroxidation (LPO), superoxide dismutase (SOD), catalase (CAT), and total protein were significantly raised to nearly normal levels[16].In another investigation,

Streptozotocin-induced diabetic Wistar albino rats treated with hydroalcoholic extract from the aerial portions of *A. mexicana* showed a hypoglycemic effect at 200 and 400 mg/kg body weight. The 400 mg/kg body weight extract dose demonstrated a significant hypoglycemic impact in comparison to the standard dosage of 300 mg/kg body weight of metformin[21].

Anticancer/Cytotoxic Activity :

According to review papers included in significant scientific databases, *Argemone mexicana* has encouraging anticancer pharmacological efficacy. Many extracts from its leaves, flowers, and entire plant, particularly the methanolic and ethanolic fractions, have demonstrated cytotoxicity both in vitro and in vivo against chemically produced tumor models and several cancer cell lines, including HepG2 and MCF-7. Its abundance in bioactive phytochemicals, including argemonine, protopine, and berberine, which cause apoptosis and block important pathways like NF-κB and TNF-α that contribute to the development of cancer, is largely responsible for its anticancer impact. Extracts from *Argemone mexicana* have been shown in numerous animal experiments to exhibit benefits similar to those of conventional chemotherapeutics in reducing tumor incidence, delaying the start of tumors, and reducing tumor burden. Histopathological, molecular, and cellular studies have confirmed these results, indicating that *A. mexicana* may be developed into new anticancer drugs. To prove safety and effectiveness in humans, more clinical trials are necessary[10,11,13].

Hepatoprotective Activity :

The hepatoprotective and anti-icterus property of *Argemone mexicana* has been justified in different experimental and ethnobotanical investigations. The whole plant in aqueous extract at 150 and 250mg/kg, given over a period of 7 days, exhibited dose dependent protective effect on hepatic failure as evidenced by a significant attenuation of the high liver enzymes (AST, ALT, ALP) and a rise in body weights in Wistar rats induced by CCl 4 ($P< 0.001$). In another experiment, methanol and aqueous extracts of aerial part of plant were obtained through Soxhlet and rotary evaporation followed by freeze drying whereas the doses used were 100, 200 and 400 mg/kg. The methanol extract at the dose of 100 mg/kg produced prominent hepatoprotective effect ($p<0.05$) by decreasing the concentrations of serum enzymes (SGOT, SGPT, ALP) and this was evident as shown by histopathological analysis implying regenerative capacity of the liver. Moreover, at 125, 250, and 500 mg/kg, there was also evidence of crude leaf powder having anti-icterus due to a decrease in the levels of total bilirubin as well as direct bilirubin. Traditional healing of *Argemone mexicana* in the treatment of jaundice is confirmed by ethnobotanical reports of people in Sub-Himalayan regions where the people of Bhoxa rim latex sugar mixture and Gujjar consume dried whole plant powder mixed with curd. The results present the therapeutic potential of *Argemone mexicana* but additional studies are required to prove by science the conventional evidence[15].

Antiulcer/anti-urolithiatic activity :

Historically, ulcers and related conditions have been treated with the plant *A. mexicana*. Both methanolic and aqueous

extracts of the plant demonstrated substantial effectiveness against duodenal ulcers caused by cysteamine hydrochloride in a rat investigation. Compared to the methanolic extract, the aqueous extract exhibited stronger action. The precise components and method of this reduction are still unknown, though. In a different study, albino wistar rats were given 90% ethanol (5 ml/kg) and indomethacin (IND; 5 mg/kg) for five days, which caused stomach ulcers. When compared to reference medications misoprostol and ranitidine, the ethanolic extract of the aerial portion of A. mexicana demonstrated a considerable dose-dependent reduction in the animal pretreated with the extract, yielding gastroprotection of 68.51% and 70.38%, respectively. Additionally, the 70% hydro-ethanolic leaf extract of *A. mexicana* L. showed anti-ulcer action in models of stomach ulcers caused by water immersion stress, aspirin-induced mucosal injury, and pylorus ligation. Maximum ulcer protection at the highest investigated extract dose of 400 mg/kg b.w.p.o. was 39.9%, 43.6%, and 54.7%. It's possible that the extract's astringent flavonoids are what cause the anti-ulcer effect. *A. mexicana* also has anti-urolithiasis and diuretic properties. Calcifications known as urolithiasis develop in the urinary system, usually in the kidney or ureter, although they can also begin in the bladder or urethra or spread to other parts of the lower urinary system. Side effects from contemporary urolithiasis therapies include peripheral vasodilation, weakness, itching, internal bleeding, urinary tract infections, and weight loss. Significant inhibition against calcium oxalate crystal was demonstrated in vitro using petroleum ether, chloroform, methanol, and aqueous extracts of *A. mexicana* leaves[18].

Anti-inflammatory, Analgesic and Antipyretic Activity :

Argemone mexicana Linn leaves have been shown in both popular and scientific research to have valuable analgesic (pain-killing) and anti-inflammatory properties. The phytochemical profiles indicate that the leaves have flavonoids, phenolic compounds and alkaloids which are said to introduce these pharmacological effects. *A. mexicana* extracts have been shown to have these effects through experimental research which demonstrates that extracts of *A. mexicana* can inhibit inflammation and pain in animal models, including carrageenan induced paw edema and writhing tests induced by acetic acid, and confirm its use in traditional medicine to treat pain and inflammation. This effect can be explained by the fact that the plant stabilizes cell membranes and prevents protein denaturation and the occurrence of certain bioactive compounds, such as β-amyrin and isorhamnetin derivatives. Although these findings have scientific support to the use of the *A. mexicana* leaves traditionally, other studies, such as a clinical trial and toxicological studies, should be done to prove its full efficiency and safety in humans. All in all, the current literature demonstrates the perspectives regarding the *A. mexicana* Linn leaves as a source of natural analgesic and anti-inflammatory properties, particularly in areas where the access to conventional medicine is restricted[14].

Argemone mexicana has a great medicinal potential due to its great phytochemical composition and a tremendous impact on pharmacological activities. Modern pharmacological evidence has been helpful in

supporting its traditional uses which have reinforced its therapeutic versatility. Nevertheless, the toxicity profile of the plant and the absence of thorough clinical validation is still a major weakness. *A. mexicana* could yield safe, plant-derived therapeutic agents in the future with future studies possible concentrating on dosage standardization, toxicity, and molecular studies.

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