



Phytoconstituents and Pharmacological Activities of *Argemone mexicana*: A Comprehensive Review

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ABSTRACT

Argemone Mexicana belongs to *Papaveraceae* family show potential ethnopharmacological activities. In Ayurveda, Homeopathy, Siddha and Unani system, various parts of *Argemone Mexicana* are widely used as traditional medicine to treat various diseases. Numerous pharmacological activities like antimicrobial, antifungal, antipyretic, analgesic, anti-inflammatory, anticancer, antiviral, antidiabetic, antimalarial, wounds healing, antistress, antiplasmodial & antioxidants have reported. Diverse type of phytoconstituents like Alkaloids, terpenoids, steroids, carbohydrates, amino acids, flavonoids, long-chain aliphatic alcohols and carboxylic acids have revealed by chemical investigators. Along with this, plant also show toxicological effect. An up to date information on phytoconstituents revealed & its therapeutic uses are covered which may be helpful for researcher to investigate further chemical constituents along with their pharmacological activities.

Keywords: *Argemone Mexicana*, *Papaveraceae*, biological activity, phytoconstituents, anticancer activity.

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INTRODUCTION

Argemone Mexicana, also known as Mexican poppy or Mexican prickly poppy (kingdom: Plantae; division: Magnoliophyta; class: Magnoliopsida Dicotyledons; subclass: Magnoliidae; order: Papaverales; family: Papaveraceae) is indigenous of tropical America which has disseminated in tropical and subtropical areas of the World.[1][2][3][4]. It has widespread distribution throughout the India specially, in temperate region as a weed in roadsides, cultivating fields, and waste lands.[5][6]. The plant is an erect prickly, glabrous, branching annual herb of about 1 m high. Leaves are sessile, semi-amplexicaul, sinuately pinnatifid, and spiny on margins, mid-rib and veins beneath usually 5 to 11 cm long and more or less blotched with green and white. Flowers are yellow, terminal, and scentless about 4 to 5 cm in diameter. Capsules are about 3 cm in length and obovate or elliptic-oblong, and prickly. Seeds are small, spherical, shining, black, and pitted.[7][8][9]

In India, *A. mexicana* is an important medicinal plant. When the plant is injured it discharges the yellow juice which is used as traditional medicine for numerous diseases like ophthalmia, jaundice, dropsy, scabies and cutaneous fondness. The seeds and oil of this plant are used to treat ulcers, asthma, dysentery, and other intestinal maladies. Its various parts are employed as an expectorant, emetic, demulcent, diuretic, and in the treatment of chronic skin problems[7]. Leaves and seeds are used for maintaining cholesterol level and normal blood circulation in human.[10] Anti-venom activity is reported by parts of this plant.[11] Flowers are shown expectorant activity and therefore used in treatment of coughs.[12] Seeds are used as laxative, purgative and digestive while its latex is used to treat conjunctivitis.[13] In Brazil, the plant commonly termed as 'cardo-santo' and its infusion is used in treatment of hypertension.[7] Roots, Seeds and leaves are shown potential antibacterial activity.[14][15][16] It's roots shown potential analgesic and anti-inflammatory activity.[17] Aerial parts of plant shown anxiolytic-like effect in Wistar rats.[18] Leaves and stems of plant shown antifungal and

anticancer activity.[19]The present review emphasis on a variety of phytochemical constituents present in plant and its medicinal uses.

BIOLOGICAL ACTIVITIES

Both crude extract & isolated chemical constituents exhibit various biological activities as describe in below subsections.

Antibacterial activity

A. mexicana seeds chloroform extract significantly inhibited growth of gram positive and gram negative microorganism such as *E. coli*, *Enterococcus Sp.*, *P. aeruginosa*, *S. aureus*, and *S. typhi* with minimum inhibitory concentration (MIC) of 2 to 5 mg/mL. Whereas its methanolic extract showed moderate activity against *P. aeruginosa*, *S. aureus*, and *S. typhi*. While hexane and water extract of seeds do not show inhibitory activity.[20]An alkaloid- N-demethyloxysanguinarine, extracted in third fraction of chloroform by column chromatography showed MIC of 1.5625 to 3.125 mg/mL with potential antimicrobial activity against *E. coli*, *S. aureus*, *K. pneumonia*, and *P. aeruginosa* as compared to standard drug tetracycline. Formation of pores and subsequently leakage of cytoplasmic constituents may be the mechanism of action of active components collected in third fraction of chloroform.[21] *A. mexicana* leaves aqueous and ethanolic extracts inhibited growth of microbes responsible for oral cavity infection like *S. mutans* and *P. gingivalis*. Aqueous extract was found more potent against *S. mutans* with MIC value of 78 µg/mL while ethanolic extract have MIC value of 125 µg/mL. Both aqueous and ethanolic extract were found less active against *P. gingivalis*. [22] *A. mexicana* leaves ethanolic extract showed highest antimicrobial activity against *P. aeruginosa* followed by *E. coli*, *B. subtilis* and *S. aureus* compared to analogous water extracts.[23]Saranya et al extracted *A. mexicana* leaves in methanol, chloroform & petroleum ether and then its antimicrobial activity studied against *E. coli*, *P. aeruginosa*, *P. mirabilis*, *S. typhi*, *S. aureus*, and *K. pneumonia*. Methanolic extracts showed maximum antimicrobial activity followed by chloroform and petroleum ether extracts against all the bacterial strains used.[24] *A. mexicana* leaves were extracted in three organic solvents (ethanol, methanol, and acetone) and tested for antipseudomonad activity against multidrug resistant *P. aeruginosa* isolated from clinical samples. Methanolic extract was found to exhibit highest antipseudomonad activity.[25] *A. mexicana* fruits 50% v/v hydromethanolic extract exhibit potent antibacterial activity against both gram positive and gram negative bacteria but it was found more effective against gram negative bacteria. Antibacterial activities of *A. mexicana* fruits extract were against *K. oxytoca*, *V. damsella*, *E. aerogenes* and *E. coli* found. [26] Various parts of plant (Stem, leaves and fruits) were extracted in different organic solvents (acetone, benzene, chloroform, ethanol and methanol) and its antimicrobial activity was compared against numerous gram positive and gram negative strains like *E. coli*, *P. aeruginosa*, *B. subtilis*, *S. aureus*, *S. epidermidis*. *A. mexicana* parts extracted in acetone, benzene, chloroform, and ethanol exhibited considerable antimicrobial activity while methanol exhibited very little activity.[27] Similarly in another study *A. mexicana* root, stem and leaves extracts in water, acetone, ethanol and chloroform showed promising antimicrobial activity against various microbes.[28] An alkaloid, berberine was extracted and isolated from leaves of *A. mexicana* leaves in water and methanol and it's antimicrobial activity was determined in *B. subtilis*, *S.aureus*, *P. aeruginosa*, and *E.coli*. Structural elucidation was carried out by Nuclear Magnetic Resonance (NMR) and its retention time in High Performance Liquid Chromatography (HPLC) was compared with standard berberine chloride as sample.[29] Silver nanoparticles of yellow colored blooms of *A. mexicana* and *T. ulmifolia* were formulated. The blooms used as bioreducing agent who makes the method ecologically welcoming and cost effective. The formulated silver nanoparticle using bloom of *A. mexicana* shown effective antibacterial activity against *E. coli*, *K. aerogenes*, *P. aeruginosa* and *S. aureus*. [30] Recently extraction of *A. mexicana* flowers, berries and seeds was carried out in ethanol, methanol and chloroform and it's antibacterial activity was determined in gram positive and gram negative bacteria like *S. aureus*, *B. subtilis*, *E. coli*, *K. pneumonia*, *V. cholera* and *E. aerogenes*. Potent antibacterial activity was observed for ethanolic extract over chloroform and methanol extracts.[31]

Antifungal activity

A whole plant of *A. mexicana* was collected, dried, powdered and then extracted in methanol. The extracted quaternary alkaloids were dissolved in methanol: chloroform mixture (1:1) and then distilled water was added. The required concentrations of 1000 to 5000 ppm were prepared from stock solution by diluting with distilled water. Antifungal activity was performed against fungi such as *U. cynodontis*, *C. cajani*, *Sphaerotheca sp.*, *Cercospora sp.*, *A. solani*, *Bipolaris sp.*, *Helminthosporium sp.*, *Curvularia sp.*, *F. udum* and *A. cajani*. Spore germination was inhibited at concentrations of 2000, 3000, 4000 and 5000 ppm.³² At a concentration of 40 g extract (20 µL), the methanolic and cold aqueous extracts of *A. mexicana*'s stem and leaves have demonstrated to inhibit the growth of fungi such as *M. indicus*, *A. flavus*, *A. niger*, and *P. notatum*. [19] Hexane extracts of seeds of *A. mexicana* against superficial fungal pathogens

was tested. The degree to which the oil inhibited spore germination at concentrations of 156, 312, 625, 1250, 2500, and 5000 g/mL over a time span of 30 to 180 min was studied. Spore germination was inhibited by 60 to 80% by seed oil of *A. mexicana* on 180 min of exposure.[33] In another study, *A. mexicana* plant was dried and its powder was extracted in methanol. Antifungal activity was carried out using fungi like *A. niger*, *Mucor species*, and *A. fumigates* at concentrations 25, 50, 100 mg/mL. The zone of inhibition in mm is compared with a standard drug ketoconazole and it showed promising activity.[34] *A. mexicana* flowers, berries and seeds was extracted in ethanol, methanol and chloroform. Antifungal activity of extracts was performed using *A. niger* and *A. fumigates*. In bioassay, highest antifungal activity was found for ethanolic crude plant extract followed by the methanol and chloroform.[31]

Analgesic, Anti-inflammatory activity and Antipyretic activity

Aqueous leaves extract of *A. mexicana* was collected by decoction followed by filtration, centrifugation and freeze drying. Anti-inflammatory activity was carried out in albino mice 30 minutes before carrageenan injection. Freeze dried aqueous extract exhibit considerable dose dependent anti-inflammatory activity and maximum inhibition (59.15%) of edema at 5 h after administering 500 mg/kg extract. Analgesic activity of same lyophilized aqueous extract of *A. mexicana* leaves also studied in albino rats. Analgesic activity also found to be dose dependent with maximum activity observed at 4 h at dose of 500 mg/kg.[35] Similarly antipyretic activity of aqueous extract of *A. mexicana* leaves was carried out in albino rat and results when compared with paracetamol. When an freeze dried aqueous extract administered orally at dose 250 mg/kg and 500 mg/kg, it showed significant reduction in yeast induced temperature.[36] *A. mexicana* roots was dried and extracted in ethanol, then analgesic and anti-inflammatory activity was studied in mice and rat respectively. An ethanolic extract of dried roots showed significant analgesic and anti-inflammatory activity.[17][37]

Anticancer activity

In vitro cytotoxicity against different human cancer cell lines was found for ethanolic extract of *A. mexicana* whole plant. The *in vitro* cytotoxicity was performed against five human cancer cell lines, plant extract showed maximum activity against colon 502713, lung-A-549 (83 %), liver of HT-29 (99 %) human cancer line and IMR-32 neuroblastoma (96%) cell lines.[38] Inhibition of cell viability towards different cancer cell lines HeLa-B75 (48.13 %), HL-60 (20.15 %), and PN-15 (58.11 %) was showed by ethanolic extract.[39] The anticancer activity may be due to presence of flavonoid in methanolic extract of leaves. Anticancer activity against HeLa and MCF-7 cancer cell lines with 50% inhibition of biological activity of cancer cells (IC_{50}) values ranging from 1.35 to 1.2 $\mu\text{g}/\mu\text{L}$ was observed. Cytotoxic activity of methanolic extract of *A. mexicana* is apoptotic rather than necrosis.[40] *A. mexicana* leaves and stems were extracted in water and methanol and its cytotoxicity were studied against lung carcinoma (A549), cervical cell (SiHa) and oral cancer cell (KB) taking Vinblastin 20 μg per well (24.5 nM) as a control. A concentration of both extract 50 μg to 300 μg per well were added and incubated. After 72 h incubation, an alkaloid berberine at 300 μg (μM) concentration per well cytotoxicity against A549 (leaf-67%, stem-70%), SiHa (leaf-23%, stem-36%) and KB (leaf-25%, stem-23%) were showed.¹⁹ A new flowers of *A. mexicana* was extracted firstly in ethanol, and then in ethyl acetate. Ethyl acetate fraction was collected and its cytotoxicity against human liver cancer (HEPG2) cell line was studied. It shown promising anticancer activity with IC_{50} about $72 \pm 1.7 \mu\text{g}/\text{mL}$ against liver cancer HepG2 cell line.[41]

Anti HIV activity

A methanolic extract was obtained from *A. mexicana* whole air-dried plant and from which the benzo[c]phenanthridine (+/-)-6-acetonyldihydrochelerythrine was isolated. This isolated compound exhibit significant anti-HIV activity with EC_{50} and therapeutic index value of 1.77 $\mu\text{g}/\text{mL}$ and 14.6 respectively in H9 lymphocytes.[42]

Antioxidant activity

A. mexicana roots methanolic extract was obtained and its antioxidant activity was determined by antioxidant assay such as 1, 1-diphenyl-2-picrylhydrazyl (DPPH), 2, 2'-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) (ABTS), and hydrogen peroxide (H_2O_2) scavenging method. High scavenging activity against DPPH (85.17%), ABTS (75.27%) and H_2O_2 (84.25%) radicals was showed by methanolic extract at 100 $\mu\text{g}/\text{mL}$ concentration.[43] *A. mexicana* fruits hydromethanolic extract also evaluated for antioxidant activity with IC_{50} of 49.38.[26] Silver nanoparticles synthesized using *A. mexicana* yellow bloom exhibited a highest DPPH scavenging activity of 87.06% at a concentration of 500 $\mu\text{g}/\text{mL}$. [14] Extracts of *A. mexicana* leaves in different solvents exhibited antioxidant activity by Nitro blue tetrazolium assay method. Maximum superoxide anion radicals scavenging responses about 84.0, 81.0 and 75.0 % observed at 200 $\mu\text{g}/\text{mL}$ concentrations in acetone, methanol and chloroform extracts respectively. IC_{50} value observed to be double over L-ascorbic acid for acetone extract.[44]

Antidiabetic activity

Hydroethanolic extract of aerial parts of *A. mexicana* was obtained and then various fractions of it were collected in petroleum ether, chloroform and water. The aqueous and chloroform extracts at a dose 150 mg/kg body weight were administered for 21 days and it exhibited hypoglycemic efficiency in alloxan induced diabetic Wistar rats. Significant reduction in blood glucose level, recovery in body weight, reduction in food and water intake, decrease in total Triglycerides (TGs), Low-density lipoprotein (LDL), Very Low-density lipoprotein (VLDL), and Total cholesterol (TC), were observed, while value of High-density lipoprotein (HDL) levels were remained normal. The levels of serum glutamate oxaloacetate transaminases (SGOT), serum glutamate pyruvate transaminases (SGPT), and total creatinine were fetched their levels near normal values. The Superoxides dismutase (SOD), Catalase (CAT), glutathione (GSH), glutathione-S-transferase (GST), lipid peroxidation (LPO) and total protein levels were appreciably elevated to almost normal values.[45] *A. mexicana* aerial parts hydroalcoholic extract was found to have hypoglycemic effect in Streptozotocin-induced diabetic Wistar albino rats at doses of 200 and 400 mg/kg body weight, according to another study. When compared to the normal dosage of 300 mg/kg body weight of metformin, the extract dose of 400 mg/kg body weight showed an effective hypoglycemic efficacy.[46]

Wound healing activity:

A. mexicana leaves extracts in petroleum ether, chloroform, methanol and aqueous were investigated for wound healing activity. Various models like excision, incision and dead space wound were adopted in Whistar albino rats. The results divulged that the treatment with methanol and aqueous extracts exhibited rapid wound healing activity.[47] In another similar research extracts of stem and leaves *A. mexicana* were extracted in petroleum ether, dichloromethane and methanol and wound healing activity was carried out in rabbits. All extracts then separately formulated as an ointment and wound healing activity was tested by excision wound model. Methanolic extract showed highest wound healing activity with 100 % & 93.57% wound healing in normal and infected wounds was reported.[48]

Antistress and Antiallergic activity

The stem of *A. mexicana* was extracted in petroleum ether, acetone, methanol and water. At a dose of 50 mg/kg, i.p., antistress and antiallergic effectiveness in asthma exacerbated by milk-induced leucocytosis and milk-induced eosinophilia was assessed in Wistar albino rats. Out of that, aqueous and methanolic extracts showed significant decrease in leucocytes and eosinophils.[5]

Antiplasmodial activity

When compared to the chloroquine-susceptible strain of *P. falciparum*, an ethanolic extract of *A. mexicana* immature fruit and root displayed considerable antiplasmodial activity with 35% and 87% *in vitro* inhibition, respectively, at a dose of 100 µg/mL. [49]

Antimalarial activity

A. mexicana's dried aerial portions were decocted in water, and the resulting decoction's antimalarial activity was determined. Aqueous decoction with different regimen was given to different age groups and 73% adequate clinical response (ACR) was noted for average dose regimen twice a day for 7 days. Overall ACR were low (45%) in age group less than 1 year and higher (81%) in patient aged more than 5 years.[50] The aqueous decoction used as effective traditional medicine to treat uncomplicated falciparum malaria in Mali, which is comparable to artesunate–amodiaquine. The two alkaloids, allocryptopine and protopine isolated through bioguided fractionation were selective antiparasitic activity towards *P. falciparum*. [51] *A. mexicana*'s whole plant was dried and extracted in methanol and Antitoxoplasmal study was carried put. Cytotoxic effects (CC₅₀) and IC₅₀ were found to be 63.64 µg/mL and 33.6 µg/mL respectively.[52]

DISCUSSION

The present article covered an up to date review on the phytoconstituents present *A. mexicana* & its pharmacological actions. Various parts as well as whole plant is used for treatment of several diseases like microbial & fungal infections, inflammations, cancer, HIV infections, diabetes, malaria, wounds, stress, plasmodial infections in different parts of the. Majorly it contains alkaloids along with terpenoids, steroids, carbohydrates, amino acids, flavonoids, long-chain aliphatic alcohols and carboxylic acids. In addition to therapeutic activity, toxic effects of certain parts of plant are reported, which required more careful studies. Therefore this up to date information on various phytoconstituents present & its pharmacological uses may be helpful for researchers to further explore on *A. Mexicana*. Further a more detail pharmacological & toxicological study along with chemical nature, mechanism of action, structure-activity relationship (SAR) of phytoconstituents is requisite.

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