

Ethnopharmacological aspects of *Argemone mexicana* Linn., a Significant plant species, in Traditional System of Medicine

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ABSTRACT

The papaveraceae is an ethnopharmacologically important family of flowering plants. *Argemone mexicana* is the source of a diverse kind of chemical constituents, alkaloids being most abundant. Pharmaceutical potential of the plant is used in different parts of the world for the treatment of several ailments including leprosy, tumors, skin diseases, microbial infections, warts, inflammations, rheumatism, malaria and jaundice. Other biological activities include antibacterial, anti-HIV, wound healing, anti-allergic, anti-cancer and anti-fertility activity. Beyond pharmaceutical efficacies, certain plant parts also show toxic effects as well. An endeavour has been made to update information on traditional and pharmacological knowledge of *Argemone mexicana*.

Keywords: *Argemone mexicana*, Biological activity, Pharmaceutical potential, Traditional, toxicity.

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INTRODUCTION

Argemone mexicana L. is a wasteland weed naturalised in the South America and widely distributed in the tropical and sub-tropical countries [41]. This plant is almost everywhere by roadsides and fields in India [13]. It is an annual herb, with a height of about 1 m; leaves are about 5 to 11 cm high, erect and spiny [24]. The seeds are spherical and black. The flowers diameter is 4 to 5 cm, are yellow in colour and unsmelling. The capsule is spiny and 3 cm length. The yellow juice has long been used as traditional medicine, for jaundice, scabies, dropsy and cutaneous afflictions in India [25, 6, 78]. *A. mexicana* is a potential source of antimicrobial, antifungal activity and is also used in the treatment of several ailments. Several isoquinoline alkaloids have been reported from *A. mexicana*. Alkaloids possess several pharmacological activities such as antimicrobial, cytotoxic, anti-inflammatory, antioxidant, anti-diabetic, anti-HIV, anti-cancerous etc. Tannins are employed in antimicrobial activities and used as an antioxidant, anti-neoplastic and cytotoxic agent. Antifungal and antibacterial properties are shown by saponins. These are used as anti-inflammatory agents, antioxidant, anticancer and for weight loss. Plant steroids contain antimicrobial and insecticidal properties. The Flavonoids have potential as anticarcinogens, antiviral, antimicrobial, anticancer and anti-allergic activities. Phenolic compounds possess anti-mutagenic, anti-oxidative, anti-carcinogenic, anti-inflammatory and antidiabetic activities [63]. The present review is an attempt to update the pharmacological aspects and biological activities of *A. mexicana*.

Chemical constituents: Number of Chemical constituents have been isolated from this plant viz., berberine, sanguinarine, benzphetamine *N*-demethylase and protopine (from

seeds); argemexicaine A and argemexicaine B; cysteine and phenylalanine of amino acids; β -amyrinof terpenoids(from leaves); β -sitosterol of steroids (from roots);oxyberberine of alkaloids (from whole plant) [81]; lactose etc. Mostly the chemical constituents belong to the class of alkaloids; besides, long-chain alcohols, flavonoids, phenolics and some aromatic acids.

Traditional Uses:

- ❖ Roots of plant are used to cure fever and is anthelmintic[49,55].
- ❖ Extracts of roots along with seeds and leaves finds application against malaria as well as used in maintaining normal blood circulation and cholesterol[1,5]
- ❖ The root bark extract of plant are employed as a remedy for spermatorrhea[64].
- ❖ Root extract of plant is used in the treatment of impotency[30].
- ❖ Paste of roots and seeds works as an antidote to snake venom[30,48].
- ❖ Juice of plant is used in the treatment of jaundice[93].
- ❖ Powder of leaves is used to cure diabetes, to quit smoking and drug[93].
- ❖ Latex extracted from stem of plant have been used in wounds, cures itching, cataract and reddening in the eyes[29].
- ❖ Paste of leaf is used to cure the ringworm infection[8].
- ❖ Oil extracted from seeds is used to cure injuries, ulcers, dysentery and intestinal problems[25,19,6,62,75].
- ❖ Extracted oil is used to cure leprosy and constipation[77].
- ❖ Seeds are used to kill worms[44].
- ❖ Paste of seeds is used against scabies, asthma and conjunctivitis[59].
- ❖ Seeds of plant are applied to cure all types of skin diseases[44].
- ❖ Warts, dropsy and infectious diseases are cured by the fresh yellow milky seed extract[20].
- ❖ Flowers have been used to cure coughs problem[21].
- ❖ In Brazil, this plant is employed as a remedy for hypertension[18].

PHARMACOLOGICAL USES

Antimicrobial activity: Antimicrobial activity against various gram positive and gram negative bacteria gave inhibition zone ranging from 9.8mm to 16.4mm[45]. The zones of inhibition against *B. subtilis* and *E. coli* was 15.3mm. Maximum inhibition zone of 15.5mm was observed by seed extract in ethanol against *B. subtilis* and *S. aureus*. Leaves and seed extracts in methanol showed maximum inhibition zone of 16.3mm and 17.5mm[37]. Plant crude extracts as well as some chemical constituents displayed significant antimicrobial properties was reported[74].The concentration of 10 μ L showed considerable zones of inhibition of 10.1 to 21.4 mm with MIC values of 62.5-500 μ g/ml [66]. Chloroform extract of *A. mexicana* seeds at 500mg/ml performed antimicrobial activity against *Salmonella typhi*, *E. coli*, *S. aureus*, *P. aeruginosa*, *Enterococcus* sp. with MIC values of 2-5 mg/ml; but the methanol extract at 500mg/ml, gave average activity against *P. aeruginosa*, *S. aureus* and *S. typhi*. [86]. *In vitro* antibacterial activity of the extract in methanol was studied against *E. coli*, *Enterobacter aerogens*, *Klebsiella oxytoca* and *Vibrio damsella* and gram negative bacteria [42].Antibacterial activity of the ethanolic extract of the seeds was studied against *E. coli*, *S. aureus* and *P. aeruginosa*, with MIC value range of 230 μ g/L[57]. Similar studies have been made on the antibacterial potential of plant extracts have been made [17][1][14]. The ethanolic and aqueous extracts of the plant showed potential antibacterial activity against *Streptococcus mutans* and *Porphyromonas gingivalis* causing oral cavity infection; the alcoholic extract exhibited better results against *S. mutans* with MIC value 125 μ g/ml, while the aqueous extract against *P. gingivalis* with MIC value 78 μ g/ml[71]. Various solvent extracts of the leaf gave significant antipseudomonal activity against the multidrug resistant bacteria, *P. aeruginosa* isolated from clinical samples[73]. Antibacterial activity of the leaves, roots and stems of the aqueous, acetone extracts of the plant was assessed against *Klebsiella pneumoniae*, *E. coli*, *S. aureus* and *Bacillus cereus* and it was found that stem extract possessed greater inhibitory activity, as compared to the roots and leaves extracts[4]. Aqueous and alcoholic leaf extract of *A. mexicana* showed antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus agalactiae* and *Klebsiella pneumonia* with inhibition zone varying from 9.0 to 15.0 mm and MIC values of 0.225 to 2.00 mg/ml[31].Antimicrobial study of essential oil of the plant against bacterial

and fungal microbes was done[55].Antibacterial activity of the alkaloid, N-demethyloxysanguinarine, obtained from chloroform extract of *A. mexicana*, exhibited antibacterial activity against *E. coli*, *K. pneumonia*, *P. aeruginosa*, *S.aureus*, and with MIC value range of 1.5625 to 3.1250 mg/mL[16]. Leaf and stem extracts (acetone, ethylacetate and petroleum ether) of *A. mexicana* inhibited water borne pathogens such as *E. coli*, *Shigella* sp., *Staphylococcus* sp. and *Salmonella* sp. Maximum activity was shown by petroleum ether extract of stem and leaf[67]. The chloroform extract of seeds was resistant to *S. typhi*, *E. coli*, *S. aureus*, *P.aeruginosa* and *Enterococcus*. Methanol seed extracts were effective against *P. aeruginosa*, *S.aureus* and *S. typhi*. Chloroform extract of seeds was found more effective in comparison to extracts of methanol[85]; *E.coli*, *P. aeruginosa*, *S. typhi*, *P. mirabilis* were inhibited with extracts of root, stem and leaves. *B. subtilis* was inhibited more effectively than *S. aureus*. The methanol and ethanol extracts of the plant parts such as root, stem and leaves performed greater antibacterial activity than the other extracts used[94,22,70].The ethanol and methanol extracts showed potential activity against *K. pneumonia*[38].*A. mexicana* exhibited significant activity against *B. Subtilis*[12,52].Several bacteria and fungi were tested. Standard antibiotics were used. Significant results were shown against *C. albicans*[11].

Fungitoxic activity: Seed extracts of plant was more effective against fungal strains[76]. The latex of plant was studied against *Trichophytonm entagrophytes* [9]. Leaf extract was fungitoxic against *Alternaria alternata*, *Helminthosporium speciferum Dreschlerahalodes* [88], and also against *Curvulariatu berculata*[92]. Alkaloids: Dehydrocorydalmine and oxyberberine, exhibited antifungal activities against *Bipolaris* sp., *Fusarium udum*, *Helminthosporium* sp., *Curvulariasp.* and *Alternaria cajani*. *Helminthosporium* sp. and *Curvulariasp.* spores did not germinate at 5000 ppm and *Curvularia* sp. exhibited highly sensitive at 4000 ppm. *Bipolaris* sp., *Alternariacajani* and *Fusariumudum* showed 5.74%, 11.74% and 10.15% germination even at 5000 ppm. Oxyberberine inhibited spore germination by 100%[85]. The germination of all the tested fungi was greatly inhibited at 1000 to 4000 ppm[85]. Antifungal activity of the plant extract against *Aspergillus candidus*, *Candida albicans*, *Aspergillus niger*, *Candida tropicalis* and *Aspergillus flavus*. Methanol extracts of leaf of *Argemone mexicana* were most effective against *Candida albicans* as compared to other yeast strain[83].

Nematicidal activity: The oil of seeds found to kill *Meloidogyne incognita*. The infection of nematode reduced[27]. Nematicidal properties against *M. juvanica* in experimental test tubes of microplots were investigated. Extracts of plant reduced the population of nematode in field. Plant extracts were capable of lowering nematode population in the field while larvae became immobile in 24h[53]. Juvenile mortality in *M. juvanica* was caused by extracts of leaf[43]. Polar solvent extract was more effective[80]. Seed soaking in aqueous extract reduced penetration of the nematodes[51].

Antihelminthic activity: Aqueous extracts were useful against *Pheritima posthuma*[43]. Alcohol and aqueous extracts of leaves against *P. posthuma* and *Ascardiagalli* was investigated and both had significant activity at a concentration of 100 mg/ml[47].

Molluscicidal activity: Alkaloids, protopine and sanguinarine, shows significantly decreased protein, DNA, free amino acid and RNA in nervous tissue of *Lymnaea acuminata*. Phospholipids were significantly reduced and the rate of lipid peroxidation increased in treated snails[82].

Antifeedant activity: Petroleum ether and aqueous leaf extracts, exhibited antifeedant activity against *Henosephilachnavigintioctopuncata* Fabricius[69].

Lousicidal activity: Lousicidal efficacy of aqueous leaf extract, was studied by conducting mortality and repellency tests on *Tropicalis peters* 73% mortality was observed[46].

Antihepatotoxic activity: Aqueous extract of stem in carbon tetrachloride-induced hepatotoxicity in male Albino Wistar rats. Levels of alanine aminotransferase, alkaline phosphatase, serum aspartate transaminase decreased[26]. Antiicterus activity of leaf against CCl₄-induced hepatotoxicity in Wistar rats was done. There was significant increase in the levels of aspartate aminotransferase, alanine aminotransferase and alkaline phosphate[87]. Percent of increase in SGPT and SGOT were 79.77% and 4.4% respectively[68].

Antidiabetic activity: Hypoglycemic efficacy in alloxan induced diabetic rats of aqueous extract at a dose of 200 and 400 mg/kg body weight was reported[54]. Blood glucose levels, plasma urea, creatinine, triacylglyceride, cholesterol values were reduced. Hydro-alcoholic

extract reduced fasting blood glucose levels[63]. Hypoglycemic activity of extract in comparison with the standard drug metformin was more effective[72].

Anticancer activity: Inhibitory activity was shown by ethanol extract against human cancer cell lines such as HL-60 (20.15%) HeLa-B75 (48%), and PN-15 (58.11%)[33]. Methanolic extract of leaves against HeLa and MCF-7 had IC₅₀ values of 1.35 to 1.2 µg/ml[34]. Nature of this cytotoxic activity was apoptotic and was due to the presence of flavonoid content in leaf. Methanolic extract of leaves had cytotoxic effect against healthy mouse fibroblasts and three human cancer-cell lines. Extract was much active against MDAMB- 435S cancer cell line (IC₅₀ 1.82 mg/ml)[91]. A number of alkaloids were isolated and evaluated for cytotoxic activity, such as *N*-demethyloxysanguinarine, pancorine, (+)-argenaxine, (+)-higenamine, (+)-reticuline, angoline and chelerythrine to human nasopharyngeal carcinoma (HONE-1) and human gastric cancer (NUGC) cell lines. Chelerythrine against NUGC cell lines and (+)-argenaxine showed average activity. Angoline inhibited both HONE-1 and NUGC cancer cell lines[23]. Methanolic extract of alkaloids were screened viz., 13-oxoprotopine, protomexicine, 8-methoxy dihydrosanguinarine, dehydrocorydalmine, jatrorrhizine, and 8-oxyberberine. Cytotoxicity of these alkaloids was studied at a dose of 200 µg/ml, whereas dehydrocorydalmine exhibited average cytotoxicity. 8-Oxyberberine was more potent at 48 h. Jatrorrhizine and 8-methoxydihydrosanguinarine were most significant in inhibiting the human colon cancer cell proliferation exhibiting complete reduction in cell viability[84].

Anti-HIV activity: The benzo[*c*]phenanthridine alkaloid, (±)-6-acetyl dihydrochelerythrine isolated from the whole plant extract of methanol exhibited anti-HIV activity in H9 lymphocyte assay[25].

Anti-fertility activity: Alkaloids such as dihydropalmatinehydroxide, berberine and protopine isolated from the seeds had inhibitory activity against spermatogenesis in dogs at the stage XII of late spermatids at a dose of 30 mg/kg for 70 days; the numbers of spermatids decreased by 46.5, 58.0 and 97.7% respectively with compounds. Total numbers of mature Leydig cells also decreased[39].

Anti-inflammatory activity: Ethanol extract of leaves showed significant anti-inflammatory and analgesic activity at a dose of 200 mg/kg in mice[79]. Anti-inflammatory activity may be because of isorhamnetin-3-*O*-β-D-glucopyranoside, β-amyrin, cysteine and phenylalanine[90].

Wound healing activity: In vivo wound healing activity of extract and its latex, on excision wound healing model was studied. The tensile strength of the extract treated group was found to be higher than the latex treated group of animals[36]. The extract of butanol and petroleum ether showed significant wound healing activity. Sterols, alkaloids, proteins and carbohydrates, were also reported in albino rat model[58]. Leaves extract showed wound healing activity using excision, incision and dead space wound models in Wistar albino rats. Wound-healing activity with the chloroform, methanol and aqueous extract was comparable to that of the control and even better. In the infected wound model, the methanol extract showed significant healing effect against *Staphylococcus aureus*[28].

Anti-stress, antiallergic activity, vasoconstrictor and vasorelaxant effects: Stem aqueous and methanolic extract were effective in asthma at a dose of 50 mg/kg[13]. Vascular effects of methanolic extract of aerial parts in rat aortic rings were evaluated[56].

Antioxidant activity: The root extract in ethanol exhibited antioxidant activity at a dose of 100 µg/ml[61]. Superoxide anion scavenging activity of different extracts of leaves by Nitro blue tetrazolium assay at a dose of 200 µg/ml was observed. The acetone extract was most significant[15].

Miscellaneous activities: Anti- Malarial, Anti-Termite, Neuropharmacological and Oral care activity. Prevention of micronucleus formation, Adulteration, Poisoning [95,32,7,35,65,22,89,40] and safety evaluation studies on *Argemone* oil was done through dietary exposure for 90 days in rats. Epidemic dropsy is a disease caused by the consumption of mustard oil contaminated with *Argemone* oil; thereby suggesting that mustard oil should be absolutely free from *Argemone* oil contamination was also studied[10].

CONCLUSION

Literature reviewed that different parts of the plant are used for the treatment of several diseases. An attempt was made to update the pharmacological knowledge and biological activities of *A. mexicana*. Extensive studies have been performed. The present overview would boost the on-going research in this direction.

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