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Review article

On poisonous plant but medicinally active- *argemone mexicana*

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ABSTRACT

Argemone mexicana Linn (Papaveracea) is commonly known as 'Mexican prickly poppy' and 'Satyanashi' is a common name, it is a well-known weed in the agricultural and waste lands. It is a widely distributed plant throughout the subtropical and tropical regions of the world. Argemone mexicana Linn has been reported to possess Anti-malarial, Antibacterial, Wound healing, Antiasthma tic, Hepatoprotective, Anti-HIV, Vasorelaxant activities. The present article reviews the pharmacological and phytochemical work done on the plant and determines a scientific base for novel study for future research to establish toxin free response of plant or its phytoconstituents.

Keywords: *Argemone Mexicana*, Poisonous plant, Agricultural weed, Toxicity study.

INTRODUCTION

Argemone mexicana Linn (Papaveracea) is commonly known as 'Mexican prickly poppy' and 'Satyanashi'. It occurs as wasteland weed in almost every part of India. In many parts it is repoorted as crop weed also. The genus Argemone includes 12 species. According to Ayurveda the plant is used as diuretic, purgative and destroys worms. In Homoeopathic system of medicine, the drug prepared from this herb is used to treat the problem caused by tape- worm. The plant contains alkaloids as berberine, protopine, sarguinarine, optisine, chelerytherine etc [1].

Taxonomical classification:

Kingdom: Plantae Divison: Angiosperm Sub division: Eudicots Order: Ranunculales Family: Papaveraceae Genus: *Argemon* Species: *A. mexicana*

Vernacular names:

Hindi: Shialkanta, Satyanashi

Gujrati: Darudi

Danarese: Balurakkisa, Datturi, Pirangi, datturi

Marathi: Daruri, Firangi-kote-pavola, dhotara.

Sanskrit: Brahmadandi, Pitopushpa, Srigalkanta, Svarnakshiri.

Malyalam: Ponnummattu, Kantankattiri Tamil: Kutiyotti, Ponnummuttai

Telugu: Brahmadandicettu

English name: Mexican prickly poppy

Morphological description

It is a prickly, glabrous, branching herb with yellow juice and showy yellow flowers, The Sanskrit name svarnakshiri is given because of the yellow juice (Svarna - Gold; Kshiri - Juice). The height of this plant varies between 0.3 to 0.12 meters, Leaves are thistle like. Stem clasping; Oblong, sinuately pinnatifid, spinous and viens are white. Flowers are terminal, yellow and of 2.5–5.0 cm diameter. Fruits are capsule. Prickly and oblong ovoid. Seeds numerous, globose, netted and brownish black. Flowering time is all round the year in Indian conditions.

Useful Parts: Roots, leaves, seeds and yellow juice.

Chemical Constituents

The seed oil contains myristic, palmitic, oleic, linoleic acids etc. The yellow juice containing small quantities of berberine, potassium nitrate was identified among the salts naturally existing in the plant.

.Two aliphatic compounds; mexicanol and mexicanic acid have been isolated from leaves. Three isoquinoline alkaloids have been isolated as dihydropalmitine hydroxide; berberine and protopine from the seeds. Oil contain up to 40% free glycerides of fatty acids.

A. mexicana seeds contain 22 - 36% of pale yellow non-edible oil, called argemone oil or katkar oil, which contains the toxic alkaloids sanguinarine and dihydrosanguinarine. Four quaternary isoquinoline alkaloids, dehydrocorydalmine, jatrorrhizine, columbamine, and oxyberberine, have been isolated from the whole plant of *Argemone Mexicana*.

Traditional Uses

According to Ayurveda the plant is diuretic, purgative and destroys worms. It cures lepsory, skin-diseases, inflammations and bilious fevers. Roots are anthelmintic. Juice is used to cure ophthalmia and opacity of cornea. Seeds are purgative and sedative. Seeds resemble mustard seeds and in India it is used to adulterate mustard seed. Seed yield non edible toxic oil and causes lethal dropsy when used with mustard oil for cooking. In Homoeopathic system of medicine, the drug prepared from this herb is used to treat the problem caused by tape- worm.

Other uses

The plant is found suitable for the reclamation of alkaline soils. Oil cake is used as manure. Dried and powdered plants are recommended as green manure as it contain sufficient amount of Nitrogen, Phosphorus and Potassium. Biodiesel production from *A. mexicana* seed oil using crystalline manganese carbonate has been demonstrated. Seed oil, popularly known as Satyanashi oil is used as an illuminant, lubricant, in soap making, and for protection from termites [2].

Ayurvedic Formulations: Svarnakshiri churna and tail

Pharmacological Activities

Neuropharmacological study

In the present study methanolic and ethyl acetate extracts of *Argemone mexicana* whole plant (Papaveraceae) were tested orally in swiss albino mice at doses of 100 mg/kg, 200 mg/kg and 400 mg/kg b.w. for CNS related activities. Papaveraceae family is known to have CNS depressant activity, so *A. mexicana* was evaluated for CNS activities. Significant central and peripheral nociceptive activity was observed for both extracts. Methanolic and ethyl acetate extract have also showed significant decrease in motor activity and fall off time of animals on rotating rod, along with sedative effect by potentiating phenobarbitone-induced sleeping time. In the acute toxicity study, both extracts was found to be safe upto 2500 mg/kg b.w. These results suggested that methanolic and ethyl acetate extracts of *Argemone mexicana* show analgesic, anxiolytic and sedative effects.

Antipyretic Activity

Leaves of *Argemone mexicana* L. (Papaveraceae) are used in the folk medicine of Burkina Faso (West Africa) to treat a variety of illness. The aqueous decoction is indicated in the treatment of malaria fever, abdominal pains, and jaundice. A preliminary study led by the authors showed a good anti-hepatotoxic activity of leaves extracts against CCl4-induced hepatic injury in Wistar rats. The present survey projects to determine the antipyretic activity of a lyophilized water decoction (of *Argemone mexicana* powdered leaf). The plant extract was tested at 250 and 500 mg/kg p.o. for its antipyretic potential by using yeast induced pyrexia method in mice. Both the lyophilized extract (aqueous decoction) was found to exhibit significant ($p<0,05$) dose- dependent antipyretic activity in tested model when compared to control group. These results support the traditional use of *Argemone mexicana* Linn. in pain and febrile disorders in the south werstern area of Burkina Fas.

Toxicity of *argemone mexicana* seed, seed oil and their extracts

Albino rats received *A. mexicana* seed, seed oil and ethanolic seed extracts in different dosages and routes of administration suffered hyperae-sthesia, inappetence, intermittent diarrhea, emaciation and decrease in body weight. Hepatorenal lesions accompanied with increase in serum GOT activity and urea concentration were the pathological findings in rats.

Wound healing activity

The petroleum ether, chloroform, methanol and aqueous extracts of the leaves of Argemone mexicana Linn. (Family: Papaveraceae) were evaluated for their wound healing activity in ratsusing excision (normal and infected), incision and dead space wound models respectively. The effects of test samples on the rate of wound healing were assessed by the rate of wound closure, period of epithelialisation, wound breaking strength, weights of the granulation tissue,determination of hydroxyproline, super oxide dismutase (SOD), catalase and histopathology of the granulation tissues. Nitrofurazone (0.2% w/w) in Simple ointment I. P. was used as reference standard for the activity comparison. The results of the study revealed that the animals treated with methanol and aqueous extracts of A. mexicana showed faster rate of wound healing compared to other extracts under study. The chloroform extract of the selected plants also produced promising results but the effects are seen to be of lesser extent than the corresponding methanol and aqueous extracts. The petroleum ether extract did not produce significant results.The wound healing effects of the chloroform, methanol and aqueous extracts may be attributed to the presence of phytoconstituents like alkaloids, triterpenoids, tannins and flavonoids in the extracts which are known to promote the wound healing process mainly due to their astringent, antioxidant and antimicrobial properties. The present work justifies the use of the leaves of A. mexicana for wound healing activity as claimed in the folklore literature.

Anti-inflammatory and analgesic activities

The present study deals with evaluation of the anti-inflammatory and analgesic properties of a lyophilized leafextract of *Argemone mexicana* Linn. on laboratory animal. The anti-

inflammatory study was done by usingcarrageenan-induced paw edema method. It was found that lyophilized extract can be effective in acuteinflammatory disorders and in that case, it showed significant anti- inflammatory dose-dependent effect(p<0,001) at the dose level of 250 mg/kg and 500 mg/kg.The plant extract was equally tested for its analgesic potential by using the hot plate test method and acetic acid Writhing method. The lyophilized extract was found to exhibit significant (p<0,01; p<0,001) analgesic activity in tested model. By the hot plate method, the drug extract showed significant (p<0,001) increased latency periodthan the control group at oral dose of 250 and 500 mg/kg.In acetic acid induced writhing test, the lyophilized extract (250 & 500mg/kg) presented reduced number of writhes at the two dose levels, which were found significant (p<0,05; p<0,001) if compared to control group.These results support the use of *Argemone mexicana* Linn. for the treatment of pain and inflammation sickness [3].

Anti-*candida* activity

In-vivo anti-candidiasis efficacy of GE. The results indicate that GE exhibits inhibitory effects against candidiasis in both control and diabetic rats. The anti-candidial effects of garlic attributed mainly to allicin. Allicin one of the active principles of freshly crushed garlichomogenates, has a variety of anti-bacterial, antifungal (particularly against *C. albicans*), anti-parasitic and anti- viral activities. It has been reported that blockage of lipid synthesis, enhancement of phagocytosis and increase in natural killer cell activity may be important components of the anti-candidal activity of garlic. It has been reported that the use of fresh garlic is more effective for antimicrobial activity than that from old garlic. These results indicate that GE exhibits inhibitory effects against candidiasis and therefore validates the traditional use of the plant in fungal infections in diabetic patients. A study on in vitro antimicrobial properties of aqueous GE against multidrug-resistant (MDR) bacteria and *Candida* species from Nigeria reported that the anticandidal effect of aqueous garlic extract (AGE) resulted in a growth inhibition zone of 27.4 ± 3.7 mm with no significant difference ($P > .05$) in MIC values at 24 and 48 hours. MFC were found to be 14.9 and 15.5 mg/mL, at these incubation periods. The observed zone of inhibition on agar of gram-positive and gramnegative bacteria and *Candida* isolates were comparable to those elicited by ciprofloxacin and FLU, showing that the isolates exhibitedsusceptibility. This indicates that AGE has a broad spectrum.

Inhibition of mild steel corrosion in sulfuric acid solutions

Inhibition potential of *Argemone mexicana* leaf extract (AMLE) for corrosion inhibition of mild steel in 0.5 M H_2SO_4 has been determined by weight loss, Tafel polarization and electrochemical impedance spectroscopy techniques. It is found from the results of weight loss method that inhibition efficiency of AMLE increases in concentration dependent manner which is also supported by the results of electrochemical techniques. Maximum inhibition efficiency of 87% has been achieved using 600 mg L-1 of inhibitor. Adsorption behavior of AMLE has been studied and it is found to be described most suitably by Langmuir isotherm. Organic moieties present in extract are found responsible for effective performance of inhibitor which is well supported by optical microscopy and FTIR studies [4].

Antidiabetic activity

Argemone mexicana L. (Papaveraceae) commonly known as prickly poppy is an indigenous herb used as a medicinal plant in several countries.The investigation was carried out to study the effects of chloroform and aqueous soluble fractions from hydroalcoholic extract of *Argemone mexicana* in normoglycemic and alloxan induced diabetic rats. It was also intended to establishcorrelation between the marker antioxidant enzymes and diabetes. Hyperglycemia was induced in rats by alloxan monohydrate (150mg/kg body weight i.p.). After alloxan induction diabetic rats received chloroform and aqueous fractions orally at 150 mg/kg body weight daily for 21days. The parameters studied were blood glucose, creatinine and urea, serum lipid profile, serum enzymes (serum glutamate pyruvate transaminases and serum glutamate oxaloacetate transaminases, lipid peroxidation, antioxidant enzymes (catalase (CAT), superoxide dismutase and reduced glutathione. The results of test drug were compared with standard hypoglycaemic drug-glibenclamide (5 mg/kg). All data were expressed as means ± SEM. Dunnet's t-test and one-way ANOVA test was used to compare the mean values of test groups and control.Experimental findings showed that the chloroform and aqueous soluble fractions significantly ($P < 0.01$)normalized blood glucose levels, serum biochemical parameters; decreased LPO and recovered glutathione-S-tranferase (GST) and CAT as compared with those of alloxan controls.. From this study it may be concluded that the potential anti-diabetic action of chloroform and aqueous fractions of *A.Mexicana* is plausibly due to its modulation of endogenous antioxidant status

Bacteriostatic potential

Bacterostatic efficacy of 16 crude extracts derived from different parts of *Argemone Mexicana* (Papaveraceae) has been analyzed on enteropathogenic bacteria such as Klebsiella oxytoca, vibrio damsella, Enterobacter aerogenes and Escherichia coli. The bacteriostatic efficacy was elucidated using single disc diffusion method. The minimum inhibitory concentration of the extracts showing higher efficacy against the test organism was determined. The MIC of acetone extract of seed and aqueous extract of leaf on different bacteria tested were found to be between 0.0005-0.02 mg/disc [5].

Antileishmanial activity

Infections caused by protozoa of the genus *Leishmania* are a major worldwide health problem, with high endemicity in developing countries. The incidence of the disease has increased since the emergence of AIDS. L.G. Rocha *et al* refered in a review

The MeOH extract, partially purified fraction (IV), and pure compounds from *Argemone mexicana* examined for its effect on the morphine withdrawal in guinea pig isolated ileum. The MeOH extract, the partially purified fraction (IV), and the pure compounds isolated from *A. mexicana* significantly and in a concentration- dependent manner reduced the morphine withdrawal. Since the pure compounds were identified as protopine and allocryptopine, the observed effects could be related to these compounds. The results of the present study suggest that isoquinoline alkaloids may be potential agents in the treatment of drug abuse.

Fungal spore germination inhibition

The alkaloids dehydrocorydalmine and oxyberberine isolated from *Argemone mexicana* were assessed against spore germination of some fungi, e.g., *Alternaria cajani*, *Bipolaris* sp.,*Helminthosporium* sp., *Fusarium udum* and *Curvularia* sp. While dehydrocorydalmineinhibited 100% spore germination of the fungi *Helminthosporium* sp. And *Curvularia* sp. at 5 000 ppm, oxyberberine showed similar activity against spore germination of *Bipolaris* sp. And *Curvularia* sp. All the five fungi were significantly inhibited at 1 000 to 5 000 ppm concentrations [6].

Toxicity and safety evaluation

The plants is toxic to animals and cattle avoid grazing this plant. Harmful allelopathic effects of Argemone mexicana on germination and seedling vigour of wheat, mustard, fenugreek, sorghum, fingermillet, tomato, cucumber etc. (important crops in India) have been reported. The allelochemicals cinnamic and benzoic acid are identified as harmful chemicals responsible for inhibition of germination and seedling vigor.The alkaloid sanguinarine isolated from seeds of *Argemone mexicana* was examined for its hepatotoxic potential in rats. The studies showed that a single i.p. dose (10 mg/kg) of sanguinarine not only increased the activity of SGPT and SGOT substantially but also caused a significant loss of microsomal cytochrome P-450 and benzphetamine N- methylase activity. Furthermore, the treated rats exhibited considerable loss of body and liver weight, peritoneal edema and slightly enlarged livers with fibrinous material. Microscopic examination of the liver tissue showed progressive cellular degeneration and necrosis further substantiating that sanguinarine is a potential hepatotoxic alkaloid 31. Toxicolethal effects of seeds of *Argemone mexicana* were investigated in to roof rat, (*Rattus rattus* L). The argemone seeds were fed at 100% of the diet up to the death or for a maximum of 10 days. Observed signs of poisoning were sedation, passiveness, sluggishness, feeble or no muscular jerks, abdominal contractions and increased defecation. Also black secretions from the eyes, corneal opacity, erection of hairs, and edema of the hind legs and submandibular space in were noted. Fourteen of 16 rats died. Significant reduction in the weights of the rats was observed. There were significant increases in blood glucose, BUN and SGOT. Major histopathological lesions were: hepatocytolysis, nuclear degeneration, pyknosis, cloudy swelling and dilatated sinusoids disturbing the lobulalar architecture of the liver; proliferated endothelium of glomeruli, hemorrhage in glomeruli and interstitium, and cloudy swelling of convoluted tubular epithelium in the kidney cortical region; erosion and atrophy of the upper stomach mucosa and calcification in the cardiac stomach, and; erosion and congestion of the upper mucosa of the duodenum. No change was noticed in the ileum 32. Safety evaluation studies on argemone oil through dietary exposure for 90 days in rats: Epidemic dropsy is a disease caused by the consumption of mustard oil contaminated with argemone oil (AO). During 1998 dropsy in New Delhi, which is so far the largest with more than 3000 victims and over 60 deaths, it was enquired at various scientific and regulatory meetings about the maximum tolerated dose of AO. Animals were given AO in diet at a dose of 0.001%, 0.01%, 0.1%, 0.5% and 1% daily for 90 days and the two control groups received the standard diet with and without 1% mustard oil. A decrease in body weight gain (28–31%) was observed in 0.5% and 1% AO groups; while significant increases in relative lungs and liver weight was noticed in respective doses of 0.01% and 0.1% AO groups as well as in higher dosage animals. Reduction in RBC count and haemoglobin content ($p < 0.05$) was noticed in 0.01% and 0.1% AO exposed animals. This effect was more pronounced in higher AO doses. Serum marker enzymes including alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) were found to be significantly elevated in 0.01– 1% AO groups. Further, a decrease in albumin/globulin ratio (42–78%) was observed in the serum of 0.01% to higher AO dose groups. The levels of serum animals. Histopathological changes in lung were observed at 0.01% dose of AO while liver, kidney and heart produced produced changes at 0.1% AO and above doses. None of the parameters were found to be affected in 0.001% AO treated animals. These results suggest that the no observed adverse effect level (NOAEL) dose of AO is 0.001% in rats and considering a factor of 100 for humans for highly toxic compound, the safe limit of 0.00001% (100 ppb or 100 ng AO/g oil) AO can be implicated which shall contain only 0.55% of sanguinarine equivalent to 0.6 ng sanguinarine per gram oil. However, the minimum detectable limit of AO is 5 ppm (equivalent to 5 ng sanguinarine per gram oil) with the present existing HPLC method, thereby suggesting that mustard oil should be absolutely free from AO contamination 33. *In vivo* DNA damaging potential of sanguinarine alkaloid, isolated from argemone oil, using alkaline Comet assay in mice: Consumption of mustard oil contaminated with

argemone oil is well known to cause clinical manifestation referred to as ‘‘Epidemic Dropsy’’. Our prior studies have shown that argemone oil produces genotoxic effects in mice30Since, sanguinarine alkaloid is the major component of argemone oil, the in vivo DNA damaging potential of the isolated alkaloid was investigated in blood and bone marrow cells of mice using alkaline Comet assay. Swiss albino male mice were given single intraperitoneal administration of 1.35, 2.70, 5.40, 10.80 and 21.60 mg sanguinarine alkaloid/kg bwt., while controls were treated with saline in the same manner. The results revealed a dose dependent increase in DNA damage in blood and bone marrow cells following 24h treatment of sanguinarine alkaloid. All the three parameters of Comet assay including olive tail moment (OTM), tail length and tail DNA showed significant ($p < 0.05$) increases in blood and bone marrow cells at respective doses of 10.80 and 5.40 mg alkaloid/kg bwt. However, some of the parameters were significantly increased even at lower doses of sanguinarine alkaloid (2.70 mg/kg bwt.). The frequency of cells exhibiting greater DNA damage was found to be increased by sanguinarine alkaloid in a concentration dependent manner. These results indicate that single exposure of sanguinarine alkaloid causes DNA damage in blood and bone marrow cells of mice, which could be responsible for the genotoxicity of argemone oil. The present study clearly indicates that sanguinarine alkaloid, an active ingredient of argemone oil possesses DNA damaging potential in blood and bone marrow cells using alkaline Comet assay. These results fully support the earlier observation that in vivo argemone oil caused genotoxicity by enhancing the frequencies of chromosomal aberrations, micronuclei formation and development of Comets resulting in DNA damage 30. In this regard studies have shown that sanguinarine forms DNA adducts following metabolism by cytochrome P-450 system under in vitro conditions 34. It has been suggested that sanguinarine may undergo N-demethylation by cytochrome P-450.32 Since, sanguinarine has been shown to cause inactivation of cytochrome P-450, it can be argued that the N-demethylated product of sanguinarine or any other electrophilic metabolite, could be responsible for this effect. The decrease in cytochrome P-450 thereby impairs the elimination of a metabolite of sanguinarine, identified as benzacridine, in urine and feces. Although, minimum group of sanguinarine has been shown to have affinity with b-form duplex DNA by intercalation with a high preference to G–C base pairs nonetheless, it could not reveal genotoxicity in SOS chromtest using *E. coli* PQ37 in the absence and presence of metabolic activation system. However, it raised the possibility of usage of Sanguinaria extract in toothpaste in the development of oral leukoplakia [7, 8].

CONCLUSION

The extensive survey literature reviewed that *Argemone mexicana Linn*, has some important medicinal activity but also cause considerable toxicity. Further evaluation need to be carried out on *Argemone mexicana* in order to explore concealed areas and their practical clinical application, which can be used for the welfare of the mankind. There is a scope to identify new compound and check claimed pharmacological activity by eliminating toxic effect. And identify new mean for elimination of toxic effect to get toxic free as well as significant response on claimed pharmacological activity.

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