REVIEW OF LITERATURE
**Argemone mexicana** Linn. (Fam. Papaveraceae)

*A. mexicana* is a common weed found in cultivated and waste land. It is a native of Mexico ([Shivraj and Balchandran, 1994](#)), a tropical American plant, which has naturalized in India and grows wild all over the country up to 5,000 ft. It is also found in several other countries. It favors dry soil and appears predominantly in cold season. It has been collected wild from Maharashtra and Madhya Pradesh, states of India.

It is known by different names in different geographical regions:

- **Hindi:** Satyanashi, Bharbhand, Brahmadundi, Piladhatura
- **Sanskrit:** Satyanasi, Bhrahmadandi
- **Bangla:** Shialkanta
- **Kannada:** Datturigidda
- **Malyalam:** Bhrahmadanti
- **Marathi:** Pivia dhotra
- **Oriya:** Kantakusham
- **Tamil:** Kurukkum, Kudy tupoodu
- **Telegu:** Brahmadandi
- **Urdu:** Baramdandi
- **Mundari:** Bakulajanum
- **Punjab:** Bhatkateya
- **Santal:** Gokhulajanum
- **English:** Yellow thistle, Mexican poppy, Prickly poppy
- **Nepalese:** Thakal
- **Sinhalese:** Rankirgokatu
- **Japanese:** Azamigeshi
- **German:** Stachel Mohn
- **Unani:** Satiyanası
- **Arabian:** Shajzatyssoom
- **Persian:** Badanjane Dashti
- **Burmese:** Khyoa
A. *mexicana* is a robust erect prickly herbaceous annual 1 to 4 ft high with spreading branches. Leaves are thistle-like 3-7 cm, sessile, alternate, semiamplexicaule, sinuate-pinnatified, variegate green, spiny on margins, with veins beneath. Flowers are 1-3 inches across, yellow and terminal on short leafy branches. Three sepals are present which are horned at the top and prickly. Six petals are present and ovary is prickly and 1-celled. Stigma is sessile 4-6 lobed and numerous ovules are present. Capsules are ⅓ to 1½ in. long, elliptic or oblong, prickly. Seeds are numerous, blackish-brown, round, reticulate-scrobiculate.

**HISTORY OF USE (ETHNO-PHARMACOLOGICAL ACTIVITY)**

*A. mexicana* is well known for its usage in herbal medicine. The plant has a bitter sharp taste, is an expectorant and an aphrodisiac. The juice of the plant is diuretic and alterative [Shivraj and Balchandran, 1994]. It is given in dropsy, jaundice, skin diseases and gonorrhea [Nadkarni, 2002]. The juice is also applied to blisters, rheumatic pains, ulcers, scabies, herpetic eruptions and warts [Shivraj and Balchandran, 1994]. It is applied externally to the eyelid in conjunctivitis [Kirtikar and Basu (1999)]. Mixed with milk it is given in the treatment of leprosy. It is also useful in low chronic type malarial fevers.

The root is alterative, stimulant [Shivraj and Balchandran, 1994] and anthelmintic; its decoction is given in gonorrhea, gleet, vascular calculous and skin diseases. It is also given for treatment of tapeworm. A decoction of the root is an eyewash, a mouthwash and a lotion for inflammatory swellings [Shivraj and Balchandran, 1994]. Seeds are given in cough, catarrhal affections, pulmonary diseases, asthma and whooping cough.

The oil extracted from seeds is purgative, narcotic and demulcent. In syphilis, it is used as an alterative. It is applied locally over skin diseases. Alcoholic extract of the whole plant showed antiviral activity against Ranikhet disease virus [Dhar et al, 1968].
CHEMICAL COMPONENTS

Chemical investigations reported in literature show that leaves and stems contain alkaloids (protopine, berberine, cryptopine, norchelerythrine, norsanguinarine, (-)-β-scoulerine methohydroxide, (-) α and β stylopine methohydroxides and (-)-chelanthifoline), sugars (glucose and fructose), organic acids (sucinic acid, citric acid, tartaric acid and maleic acid), amino acids (phenylalanine, glycine, alanine, leucine, valine, tyrosine, threonine, arginine, serine, lysine, asparagine, cysteine, tryptophan, methionine, proline, histidine, aspartic acid and glutamic acid) [Dinda and Bandhopadhyay, 1986] and phytosterol namely β-sitosterol. Flowers contain flavonoids (isorhamnetin, isorhamnetin-3-O-glucoside, isorhamnetin-3,7-diglucoside, 3-methoxy quercetin and quercetin 5, 3',4' trimethyl ether) [Krishnamurti et al, 1965]. Roots contain protopine, berberine, sanguinarine, dihydrosanguinarine, norsanguinarine, allocryptopine, coptisine, dihydrochelerythrine and chelerythrine. Seeds contain sanguinarine, dihydrosanguinarine, dihydrochelerythrine, chelerythrine, coptisine, and norargemonine in addition to fatty acids like myristic, palmitic, stearic, arachidic, oleic, linoleic, [Wealth of India, 1985] 11-oxo-tricontanoic, 11-hydroxycontanoic, [Mahto et al, 1975] (+)-6 hydroxy-6-methyl-9-oxooctacosanoic acid (argemonic acid), [Rukmini, 1975] flavonoids like luteolin, argemexitin [Bharadwaj et al, 1982] and eriodictyol [Harborne and Williams]. The latex contains alkaloids like protopine, berberine and amino acids like glutamine, hydroxyproline, threonine, β-alanine and methionine. [Santra and Saoji, 1971]. The following compounds have been reported from the whole plant: protopine, berberine, sanguinarine, norsanguinarine [Tripathi et al, 1999], 6-acetonyldihydrosanguinarine, 6-acetonyldihydrochelerythrine, cryptopine, allocryptopine, (-)-chelanthifoline, (+)-chelanthifoline, coptisine, reticuline, thalifoline, muramine, chelerythrine, norchelerythrine, β-scoulerine methohydroxide, (-) α and β stylopine methohydroxides, oxyhydrastinine, [Hussain et al. 1983] argemexicaine A, argemexicaine B, [Chang et al, 2003] N-demethyloxyxsanguinarine and (+)-1,2,3,4-tetrahydro-1-(2-hydroxymethyl-3,4-dimethoxyphenylmethyl)-6,7-methyl-enedioxy-isoquinoline, [Naturforsch, 2003] helleritrine, argemonine and norargemonine, long chain diol like mexcanol and long
chain hydroxy acid named as mexicanic acid, longchain alcohol like ceryl alcohol and 6,11-triacontanediol and triacontane-11-ol

**PHARMACOLOGICAL ACTIVITY**

The chloroform-methanol and methanol extracts of A. mexicana reduced the electric contractions of the ileum (ECI) of guinea pig at 400, 200 and 100 μg/ml dose dependently. Further, the partially purified fractions of methanol extract also inhibited ECI (guinea pig ileum) at 200, 100 and 50 μg/ml. Similarly pure alkaloids protopine and allocryptopine reduced electric contraction of ileum in a dose dependent manner whereas berberine increased the same [Placente et al, 1997].

The aqueous extract of the leaves of A. mexicana containing isorhamnetin-3-glucoside, β-amyrin, cysteine and phenylalanine showed anti-inflammatory activity [Sukumar et al, 1984].

Oil of A. mexicana exhibited antibacterial activity in vitro [Patel and Trivedi, 1962].

The methanol extract, fractions and the pure components protopine and allocryptopine exhibited morphine withdrawal in guinea pig isolated ileum [Capasso et al 1997].

Berberine and sanguinarine at a concentration of 5 X 10^-6 M inhibited diamine oxidase from blood plasma in pregnancy [Vaidya et al, 1980].

Chelerythrine was found to exhibit significant activity against NUGC cell line, while angoline inhibited both types. (+)-Argenaxine showed moderate activity against the NUGC cell line [Naturforsch, 2003].

The known benzolchelintridine (+/-)-6-acetonyldihydrochelerythrine (S) exhibited significant anti-HIV activity in H9 lymphocytes with EC50 and TI (Therapeutic Index) values of 1.77 and 14.6 μg/mL, respectively [Chang et al, 2003].
OTHER BIOLOGICAL ACTIVITIES

The acetone fraction of the petroleum ether extract of seeds from *Argemone mexicana* exhibited larvicidal and growth inhibiting activity against the second instar larvae of *Aedes aegypti* (Linn). This activity was observed only at higher concentrations (200, 100, 50 and 25 ppm). Chemosterilant activity, including reduction in blood meal utilization (27.70%), reduction in fecundity (19.00%), formation of larval-pupal intermediates, formation of pupal-adult intermediates, adult mortality and sterility of first generation eggs (100%), occurred at low concentration (10 ppm) [Sakthivadivel and Thilagavathy, 2003]. Effects of extract of *Argemone mexicana* were studied on human breast cancer cell lines and found to be active on MCF7 cells, exhibiting low anti proliferative effects on MDA-MB-231 cells [Labertini et al, 2004].

Molluscicidal activity was shown by sanguinarine and protopine [Singh and Singh].

The nematicidic triglyceride from petroleum ether extract of *A. mexicana* seeds has been identified as sn-glycerol-1-eicosa-9, 12-dienoate-2-palmitoleate-3-linoleate [Saleh et al, 1987].

TOXICOLOGY

A detailed review on clinicoepidemiological, toxicological and safety evaluation studies on seed oil of *A. mexicana* has been published [Das and Khanna, 1997].

IN VIVO TESTING

Toxicolethal effects of seeds of *Argemone mexicana* were investigated in roof rat, (*Rattus rattus*) L. The seeds were fed at 100% as 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 hair, and edema of the hind legs and submandibular space 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: hepatocytolsis, nuclear degeneration, pyknosis, cloudy swelling and
dilatated sinusoids disturbing the lobular 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
(Palwa and Chatterjee, 1989).

Seeds of Argemone mexicana produced growth depression, oedema and
death when fed at 1% and 3% of a basal ration to day-old, layer strain,
cockerel chickens. Mortality rate was increased by raising the sodium
chloride content of basal ration, from 0.18% to 1.68%. Clinical signs
consisted of subcutaneous oedema, a high pitched chirp and terminal
gasping. Hydropericardium, oedema of the lungs, and subcutaneous
oedema of the thorax, abdomen, wings, neck and throat were the major
lesions. Foci of calcificaton were present in the ventricular myocardium of
some chickens fed with 3% of seeds (Norton and O’Rourke, 1980).

Consumption of edible oils contaminated with Argemone mexicana seed
oil causes various toxic manifestations. In this investigation the in vivo
effect of argemone oil on NADPH-dependent enzymatic and Fe2+,
Fe2+/ADP- or ascorbic acid-dependent non-enzymatic hepatosubcellular
lipid peroxidation was studied. Parenteral administration of argemone oil
(5 ml/kg body weight) daily for 3 days produced a significant increase in
both non-enzymatic and NADPH-supported enzymatic lipid peroxidation in
whole homogenate, mitochondria, and microsomes. Lipid peroxidation
aided by various pro-oxidants, namely Fe2+, Fe2+/ADP and ascorbic acid
also revealed a significant enhancement in the whole homogenate,
mitochondria and microsomes of argemone oil-treated rats. Further, when
compared with whole homogenate, the hepatic mitochondria and
microsomes of either control or argemone oil-treated rats showed a 4- and
6-fold increase in non-enzymatic, and a 5- and 18-fold increase in NADPH-
dependent enzymatic lipid peroxidation, respectively. Similarly, both
mitochondrial and microsomal fractions showed a 5- and 7-fold increase in
Fe2+-, and a 12- and 15-fold increase in either Fe2+/ADP- or ascorbic acid-
aided lipid peroxidation, respectively. These results suggest that the
hepatic microsomal as well as the mitochondrial membrane is vulnerable to 
the peroxidative attack of argemone oil and may be instrumental in 
leading to the hepatotoxicity symptoms noted in argemone poisoning 
victims [Upreti et al, 1988].

TOXIC PRINCIPLE

The alkaloid sanguinarine reported to be responsible for several outbreaks 
of epidemic dropsy in the tropics 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-demethylase 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 
进一步 substantiating that sanguinarine is a potential hepatotoxic alkaloid 
[Dalvi, 1985].

CASE STUDIES

Epidemic dropsy results from the consumption of edible oils adulterated 
with oil of seeds of Argemone mexicana by unscrupulous traders. Twenty 
consecutive 'in-door' patients of dropsy were intensively studied during 
the recent Delhi epidemic. Samples of edible oil used by them, their urine 
and their serum samples tested positive for sanguinarine on thin layer 
chromatography. The illness starts as a gastro-enteric illness followed by 
oliguria and pedal oedema. The following are often observed: cutaneous 
erythema with blanching and tenderness on pressure; violaceous 
pigmentation of the skin; shortness of breath with orthopnoea; right-sided 
heart failure with normal left ventricle (LV) functions; as well as severe 
anaemia and hypalbuminaemia. Renal function tests showed: bland 
urinary sediments; decreased glomerular filtration rate (GFR); mild to 
moderate azotaemia; acute tubular necrosis; patchy pneumonitis; 
moderate hypoxia with respiratory alkalosis; and restrictive ventilatory 
defects on blood gas analysis; and spirometry suggestive of interstitial 
pulmonary oedema of non-cardiogenic origin. 99mTc colloid sulphur liver 
scans showed colloid shift. There was marked dilatation and proliferation
of dermal capillaries in the absence of significant inflammation in the biopsy specimens. Toxic alkaloids of seed oil induced widespread capillary dilatation and permeability causing leakage of protein rich plasma into the interstitial tissues of various organs. A hypovolaemic state is thus induced producing renal hypoperfusion which may progress to acute tubular necrosis. Interstitial fluid in alveoli causes restrictive ventilatory dysfunction with hypertension and right-sided failure with well-preserved LV function. The hepatic venous congestion induces Kupffer's cell dysfunction, which results in colloid shift on a radionuclide liver scan [Sharma et al, 2002].

Another study on twenty-six persons from five families comprising 34 members residing in different areas of Saptari district of the Eastern region of Nepal developed symptoms of epidemic dropsy over 6-8 weeks. Seventeen patients were studied during July-August 1996. The age of affected individuals varied from 3 to 75 years. Members who had not consumed food cooked in mustard oil or who were not residing with the family were spared. Mustard oil, which was used for cooking was found contaminated with oil of Argeome mexicana seeds. Sanguinarine was detected in all mustard oil samples collected from the homes of affected families. Gastrointestinal symptoms were present in 82 per cent of cases a week or so prior to the onset of pedal oedema. Pitting oedema of the lower limbs, fever, and darkening of the skin were the most consistent features, found in all cases. Other prominent features such as local erythema (82 per cent) and tenderness (88 per cent) of the lower limbs were present in most cases. Two striking features not previously noted were perianal itching (100 per cent) and severe carditis (35 per cent) with congestive cardiac failure (29 per cent). Other unique features noted were 'sarcoid' skin changes (18 per cent), bilateral pleural effusion, and Roth's spots and subhyoid haemorrhages in the fundus in one patient. Other important findings were anaemia (88 per cent), hepatomegaly (41 per cent), pneumonia (35 per cent) and ascites (12 per cent). There were no deaths due to epidemic dropsy. In the majority of cases, oedema, cutaneous changes, and carditis showed a marked improvement in 2-3 weeks and patients were well after 6-8 weeks of follow-up [Singh et al, 1999].
In third case study, during an outbreak of epidemic dropsy in Delhi, 233 patients were studied. Retinal changes including venous dilatation and tortuosity, haemorrhages and disc oedema were observed. A clinical picture compatible with type I optic disc vasculitis was seen in 13 eyes and that of type II in 3 eyes. Fluorescein angiography was carried out in 23 randomly selected cases. Relevant angiographic findings included dilated and tortuous retinal veins, prominent vascular staining, blocked fluorescence, microaneurysms, disc oedema and peripapillary dye spillage. Presence of positive angiographic findings correlated well with the severity of the systemic disease, glaucoma, however, revealed no correlation. Papillophlebitis, a new ocular manifestation of *Argemone mexicana* oil toxicity, as also the fluorescein angiographic picture in epidemic dropsy is being reported for the first time in the literature [Sachdeva et al, 1987].