Argemone mexicana L.
(Papaveraceae)

Abstract

The plant is a native of tropical America, West Indies, and India. It is used in Indian traditional medicines as diuretic, anti-inflammatory, antibacterial, antifungal, and for its wound-healing property. In *Unani* medicine, decoction of all its parts is used to induce diuresis, and to relieve urinary burning; seeds are more sedative and hypnotic than opium, and cause nausea. Yellow juice of the plant is used for the treatment of dropsy, jaundice, and cutaneous afflictions, and with the juice of *Aristolochia bracteata* used in syphilis, leprosy and gonorrhea. Seed oil is a drastic purgative, nauseant, expectorant, aperient, and sedative, and used in cholera, dropsy, and painful colic. In Mexico, infusion of the entire plant is used to relieve kidney pain, to help expel torn placenta, and to cleanse body after childbirth, as narcotic, sedative and analgesic, and the seeds are used as antidote to snake venom. The plant contains alkaloids, flavonoids, tannins, and sterols and/or triterpenes. Ethanol extract of aerial parts, and an alkaloid-enriched extract produced anxiolytic-like effects without affecting locomotor activity, and significantly reduced severity of pilocarpine-induced status epilepticus in rats, and reduced oxidative stress. A decoction of the plant was effective in 89% cases of uncomplicated malaria in a remote Malian village, compared to 95% success with artesunate-amodiaquine therapy. Consumption of adulterated mustard oil with Argemone oil (AO) has caused "Epidemic Dropsy" in India. Safe limit of AO in humans was calculated as 0.00001%; i.e. 100 ppb or 100 ng AO/g oil.

Keywords

Amapola montes · Bharbhand · Lao chou · Mexican poppy · Papavero messicano · Satyanasi · Stekelpapaver · Swarnaksiri · Teshimizing · Teufelsfeige

S. Akbar, *Handbook of 200 Medicinal Plants*,
https://doi.org/10.1007/978-3-030-16807-0_29

Vernaculars: Urd.: Satyanasi; **Hin.**: Bharbhand, Firangi dhotra, Kutila, Satyanasa, Shiyal-kanda, Siyal-kanta, Ujar-kanta; **San.**: Haimavathi, Hemaksiri, Himavatel brahma-danda, Kãñcanaksiri, Katuparni, Pitadugdhã, Srigalakantaka, Swarnaksiri; **Ben.**: Buro shyala-kanta, Shialkanta, Sialkanta; **Mal.**: Brahma-danti, Ponnummattum; **Mar.**: Daruri, Kanta-dhotra, Pivla dhotra; **Tam.**: Birama-dandu, Brahmmadandu, Karukkansedi, Kudiyotti, Kurukkum, Pirammathandu; **Tel.**: Brahmadandi, Brahmdandidandu, Bramha-dandi-chettu, Datturi, Pichy kusama chettu; **Ara.**: Teshimizing; **Chi.**: Lao chou; **Dut.**: Stekelpapaver; **Eng.**: Golden thistle of Peru, Mexican poppy, Mexican prickly poppy; **Fre.**: Chardon bénit, Chardon du pays, Pavot du Mexique, Pavot épineux, Tache de l'oeil; **Ger.**: Mexikanischer stachelmohn, Teufelsfeige; **Ita.**: Papavero messicano, Papavero mexicano, Papavero spinosa; **Per.**: Khashkhash khardar; **Por.**: Papoula-do-méxico (Br.); **Spa.**: Amapola montes, Cardo santo; **Tag.**: Kachumba.

Description: The plant is a native of tropical America, West Indies, and India. It is an erect, stout, branched, annual herb, up to one meter high. Leaves are 5–11 cm long, more or less blotched with green and white, galucous, broad at the base, half clasping the stem, prominently sinuate-lobed and spiny. Flowers are terminal, yellow, scentless, and 4–5 cm in diameter; the seeds are spherical, shining black and pitted (Fig. 1).[CXVII]

Actions and Uses: In Indian traditional medicines, the plant is used as diuretic, anti-inflammatory, antibacterial, antifungal, and for its wound-healing property [16]. In *Unani* medicine, decoction of all its parts is used to induce diuresis, and to relieve urinary burning; seeds are more sedative and hypnotic than opium, and cause nausea.[L] Yellow juice of the plant is diuretic, alterative, anodyne, and hypnotic,[CV] is used for the treatment of dropsy, jaundice, and cutaneous afflictions,[XXI, LXXXIV,CXXII] and with the juice of *Aristolochia bracteata* used in syphilis, leprosy and gonorrhea.[CV] Seeds are laxative, nauseant, emetic, expectorant, demulcent and

Fig. 1 *Argemone mexicana*, Leaves and Flower, B. Navez, WikimediaCommons; ShareAlike 3.0 Unported CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:Argemone_mexicana_flower_2.jpg; https://creativecommons.org/licenses/by-sa/3.0/

narcotic, and are useful for the treatment of coughs and catarrhal afflictions of throat, pulmonary mucous membrane, and in whooping cough and asthma. Seed oil is a drastic purgative, nauseant, expectorant, aperient, and sedative,[LXXXIV,CV] and used in cholera, dropsy, and painful colic.[LXXXI] In *Ayurveda*, it is used in *kustha*, *kandū*, *krmi*, and *ãnãha*.[LIX] In Mexico, infusion of the entire plant, both fresh and dried, is used to relieve kidney pain, to help expel torn placenta, and to cleanse body after childbirth,[XLIV] as narcotic, sedative and analgesic [10],[XCVII,XCIX,CXIX] and the seeds are used as antidote to snake venom [10]. Latex is used externally for indolent ulcers, and on eyelids in case of conjunctivitis [10].[CIX]

Phytoconstituents: The plant contains alkaloids, flavonoids, tannins, and sterols and/or triterpenes, and numerous studies on alkaloids have been reported [8, 9, 13, 19, 22, 24, 26, 31, 46]. Total alkaloid content (0.125%), consisting of protopine and berberine, tannins (1.1%), resin (1.75%) and a toxic principle in argemone oil [8]; flavonoids from flowers [23, 29, 30], and seeds [21], and two phenolic compounds from the seeds [6], are reported. Seed oil yield, by various methods, varies between 26.7 and 39.5%. Benzophenanthridine-type alkaloids, N-demethyloxysanguinarine and pancorine; benzylisoquinoline-type alkaloids, (+)-1,2,3,4-tetrahydro-1-(2-hydroxymethyl-3,4-dimethoxyphenyl-methyl)-6,7-methylenedioxyisoquinoline, (+)-higenamine and (+)-reticuline [12]; and protopine-type alkaloids, argemexicaine A and B from aerial parts have been reported [11]. A benzylisoquinoline alkaloid, argemexirine, and two protoberberine alkaloids, dl-tetrahydrocoptisine and dihydrocoptisine [36], and four quaternary isoquinoline alkaloids, dehydrocorydalmine, jatrorrhizine, columbamine, and oxyberberine [37], were isolated from whole plant. A new protopine alkaloid, protomexicine and a new isoflavonoid, mexitin, and 8-methoxydihydrosanguinarine, 13-oxoprotopine, quercetrin and rutin have been isolated from aerial parts [35].

Pharmacology: Ethanol extract of aerial parts, and an alkaloid-enriched extract produced anxiolytic-like effects without affecting locomotor activity in rats [2], and the ethanol extract pretreatment also significantly reduced severity of pilocarpine-induced status epilepticus in rats, and reduced oxidative stress [3]. Aqueous and methanol extracts of the plant increased healing of gastric ulceration and prevented development of cysteamine-induced duodenal ulceration in rats; aqueous extract showing better activity than the methanol extract [16]. Methanol, cold water and hot water extracts of leaves and seeds exhibited antibacterial activity against pathogenic MDR Gram-positive (*S. aureus* and *B. subtilis*) and Gram-negative (*E. coli* and *P. aeruginosa*) bacteria; methanol extract showed maximum inhibition, followed by hot water extract and cold water extract [7]. Cold aqueous and methanol extracts of stem and leaves inhibited growth of *M. indicus*, *A. flavus*, *A. niger* and *P. notatum*, comparable to Amphotericin-B [25]. Acetone fraction of petroleum ether seed extract also exhibits larvicidal and growth inhibiting activity against larvae of *Aedes aegypti* [33]. Different parts exhibited antioxidant activity which was correlated with levels of total phenolic and flavonoid contents [39].

Clinical Studies: In a quasi-clinical trial, *A. mexicana* decoction produced adequate clinical response in children aged less than one year and 5 years or older, suffering from malaria, with very few adverse effects. However, the response was better in older children, but very few patients had complete parasite clearance [45]. The decoction was effective in 89% cases of uncomplicated malaria in a remote Malian village, compared to 95% success with artesunate-amodiaquine therapy [18].

Mechanism of Action: Berberine and sanguinarine, at very low concentrations, significantly inhibit diamine oxidase or histaminase that leads to decreased catabolism of histamine, causing some of the clinical features of epidemic dropsy [43].

Human A/Es, Allergy and Toxicity: Consumption of adulterated mustard oil with argemone oil (AO) has caused "Epidemic Dropsy" in India and continue to do so [15, 17, 20, 28, 32, 34, 40, 44]. Body massage with contaminated mustard oil has produced manifestations of epidemic dropsy due to transcutaneous absorption [38]. Edema of leg is the most common presenting clinical symptom; pigmentation was found in one-third of patients, hair loss in three-fourth, and nontender hepatomegaly in a quarter of patients, and presence of sanguinarine, the toxic principle, in urine samples was reported [38, 40]. Total cholesterol, TGs, LDL-C and VLDL-C were significantly increased, with a significant decrease in HDL-C, and antioxidant enzymes in dropsy patients [15]. Bilateral wasting of deltoids, supraspinatus and infraspinatus muscles, sluggish upper limbs biceps reflex, and bilateral pansensory loss on skin over deltoids were reported in two cases of argemone oil poisoning [28]. Visual field defects, independent of rise in intraocular pressure, occur in epidemic dropsy patients [34]. Retinal changes including venous dilatation, tortuosity, hemorrhages, and optic disc edema have also been observed in affected patients [32]. Safe limit of AO in humans was calculated as 0.00001%; i.e. 100 ppb or 100 ng AO/g oil containing only 0.55% of sanguinarine equivalent to 0.6 ng sanguinarine per gram oil [4].

Animal Toxicity: Feeding of seeds to rats produced sedation, passiveness, sluggishness, feeble or no muscular jerks, abdominal contractions, increased defecation, weight loss, corneal opacity, piloerection, and edema of the hind legs, followed by death [27]. Sixty-days dietary intake of AO produced significant stimulation of LPO, liver fibrosis, hyperplasia of bile ducts, glomerular congestion, and degenerative changes in cardiac muscle fibers of rats [42]. The alkaloid, sanguinarine contained in AO is genotoxic and possesses skin tumor initiating activity [1, 5]. Sanguinarine, in a dose of 10 mg/kg, caused progressive hepatocellular degeneration in rats, substantially increasing activities of SGPT and SGOT, and significant loss of microsomal CYP450 [14].

CYP450 and Potential for Drug-Herb Interaction: A single dose of AO caused inhibition of CYP450, and its dependent mixed-function oxidases; and depletion of endogenous hepatic GSH content, with substantial increase in LPO, and decrease in GST activity [41].

Commentary: There are no clinical studies reported in the publications listed on PubMed.

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