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THERAPEUTIC POTENTIAL OF ARGEMONE MAXICANA L. IN THE PERSPECTIVE OF AYURVEDA AND RECENT RESEARCH ACTIVITIES

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ABSTRACT

Argemone mexicana commonly known as Maxican poppy or Prickly poppy. "*Satyanasi*, *kataila* and *Bhatkatiya*" are the local names of *Argemone maxicana* used in India. It belongs to the family Papaveraceae. It is a valuable medicinal plant which has vast therapeutic potential. It is described as *Svarnkshiri* in the some classical text of Ayurveda and used to cure several diseases. *Argemone mexicana* is extensively used as traditional medicine for the treatment of numerous diseases. Its leaves, stem, latex, roots and seeds have several pharmacological properties. It is reported to have antimicrobial activity, wound healing property, nematicidal, antimalarial, antibacterial and antifungal, anticancer, hepatoprotective, anti-HIV and neuropharmacological activity. Many of the bioactive compounds obtained from the *Argemone* seeds are especially effective in the treatment of chronic diarrhea, dysentery, peptic ulcers, as well as respiratory infections. Scientific studies have validated numerous medicinal applications of *Argemone mexicana*, which include analgesic, antispasmodic, depurative, emetic, antipyretic, emmenagogue, sedative, vulnerary, healing dermatological problems etc. *Argemone* mexicana is a plant traditionally used in Nigeria and some African countries to treat peptic ulcer disease. However, its medicinal property is not much highlighted due to a popular misconception that this plant is poisonous and causes epidemic dropsy, with symptoms including extreme swelling, particularly of the legs, but this is what after the adulteration process of edible oils. The present review deals with pharmacological profile of *Argemone mexicana*, emphasizing its medicinal property against various human ailments.

KEYWORDS: Traditional medicine, Mexican poppy, Antimicrobial, Antiulcer activity, peptic ulcer, antioxidant, chromosomal.

INTRODUCTION

Argemone mexicana is used in different parts of the world for the treatment of several ailments including tumors, warts, skin diseases, inflammations, rheumatism, jaundice, leprosy, microbial infections, and malaria. Interestingly, the plant is the source of a diverse kind of chemical constituents although alkaloids are mostly abundant. Beyond pharmaceutical efficacies,certain plant parts also show toxic effects as well.

Available literature contains several review articles revealing the medicinal property of *Argemone mexicana* and its therapeutic importance in human ailments. However, on careful examination of available research reports leaves a number of grey areas of advance research to be conducted in establishing full potential for disease management.

Pharmacological profile of *argemone maxicana*

The present review provides detailed information on the medicinal uses of *Argemone mexicana* based on the classical literature of Ayurveda and the results of various in-vitro and in- vivo experimental studies carried out in last ten years.

According to literature of Ayurveda *Svarnkshiri* has a wide range pharmacotherapeutic potential and exhibits the various pharmacotherapepeutic actions such as *rechan, bhedan* etc. and it is useful for *krimi* (microbial diseases), *kushta* (skin diseases), *visha* (stings), *aanaha* (flatulence), *kamla* (jaundis), *mutrakrichcha* (urinary disorders), *ashmari* (stones), *shofa* (inflammation), *jvara* (fever), *shvash* (asthma) and *kasa* (cough) diseases. These pharmacotherapeutic properties of *Argemone maxicana* can also identified with recent research finding.

Antioxidant activity

The antioxidants are compounds that inhibit the oxidation process which produce free radicals. So antioxidants are known as free radical scavengers which are useful to balance oxidative stress. Free radicals are reactive oxygen species (ROS) and reactive nitrogen species (RNS). These are superoxide (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical (OH), nitrous oxide (N_2O), nitrosyl cation (NO^+), nitroxyl anion (NO^-), peroxynitrite ($OONO^-$), nitrogen dioxide (NO_2) and nitrous acid (HNO_2). Free radicals are responsible in

the evolution of variousdiseases such as cardiovascular disease and cancer.

Antioxidants can effectively neutralise ROS and RNS species, resulting in a delay in disease progression.

Polyphenol compounds present in plant flavonoids, alkaloids, terpenoids, tannins, saponins are the natural antioxidants, which are healthier substitute of synthetic antioxidants like butylated hydroxyl anisole (BHA), butylatedhydroxytoluene (BHT) and gallic acid esters.

Numerous studies in connection of antioxidant properties of *Argemone maxicana* have been carried out. Studies related to antioxidant activity of defferent extracts of *Argemone maxicana* are listed below:

a. The hydrogen-peroxide scavenging activity of ethanolic extract of *Argemone mexicana* was investigated in a study and found to be 87.1% which is comparable to the standard Ascorbic acid (90.5%).[1]

b. One another study reports the antioxidant efficacy of methanolic extracts of different parts (leaves, stems, roots, flowers and fruits) of *Argemone mexicana*. In DPPH (1,1-diphenyl-2- picrylhydrazyl) scavenging assay it was observed that flower methanol extract has high potential of radical scavenging activity with IC50 = 23.75µg/ml.[2]

c. Monica et al examined the free radical scavenging activity of different parts of *Argemone* mexicana using peroxidase assay, ABTS (2, 2'-azinobis-(3- ethylbenzothioline-6-sulfonic acid) diammonium), Ferric Reducing Ability of Plasma (FRAP) and Lipid Peroxidation assay (LOP). The fruits exhibited remarkable ability to scavenge the species LPO (39.193±1.256MDA/gDW), ABTS (68.23±3.02mML-1 g -1) while flowers showed maximum peroxidase activity (0.513mM/min-1 g -1 DW) and FRAP (287±9.64).[3]

Based on these findings, it's clear that *Argemone mexicana* has the potential to treat the disorders caused by free radicals.

Anti-diabetic activity

Argemone mexicana has been used for the treatment of diabetes in traditional medicine system. Many in vitro and in vivo studies have been done to determine the anti-diabetic potential of various extracts of *Argemone mexicana*.

a. The antidiabetic effect of *Argemone mexicana* aqueous extract was evaluated in a study

involving alloxan induced diabetic rats.[4] The results confirmed the anti-diabetic property of *Argemone mexicana*, as the test extracts showed a persistent decrease in blood glucose level till the end of 10 hr., with maximal decrease noted in aqueous extract at 400 mg/kg dose, reaching 70.25% while the standard drug glibenclamide showed 66.65% decrease.

b. In continuation of above work, the researcher further investigated a mechanistic approach towards hypoglycaemic potential of *Argemone mexicana*. They concluded that the test fractions significantly increase the activity of antioxidant enzymes such as superoxide dismutase (SOD) and catalase in liver, kidney and pancreas, suggesting that the anti-hyperglycaemic activity of *Argemone mexicana* is accompanied by the phytochemicals augmenting the endogenous antioxidant mechanisms.[5]

c. The hypoglycemic activity of hydro-alcoholic extract of aerial parts of *Argemone mexicana* were evaluated in another study involving normal, glucose loaded, and streptozotocin induced hyperglycaemic rats, at dose levels of 200 and 400 mg/kg by taking Metformin (300 mg/kg) as standard drug.[6] It has been reported that at higher dose and repeated administration the efficacy of the extract is comparable with that of the standard drug. After two weeks of treatment, the blood glucose level returned to level comparable with metformin treated group with 400 mg/kg dose indicating that the plant extract possesses great anti- diabetic potential.

d. Sakshi Gupta and co-workers evaluated the aldose reductase inhibitory potential of alkaloidal fractions of Piper nigrum, Murraya koenigii, *Argemone mexicana*, and Nelumbo nucifera toexamine their anti-diabetic effect by measuring biochemical parameters.[7] Among the alkaloidal extracts, highest inhibitory activity was shown by A. mexicana (IC50 value 25.67± 1.25 µg/mL), followed by N. nucifera (IC50 value 28.82 ± 1.85 µg/mL), P. nigrum (IC50 value 30.21 ± 1.63 µg/mL), and M. koenigii (IC50 value 35.66 ± 1.64 µg/mL). Based on these, it can be concluded that *A. mexicana* possess great anti-diabetic activity and may be exploited therapeutically in diabetes-related complications. Aldose reductase is primarily involved in development of long-term diabetic complications due to increased polyol pathway activity. Aldose reductase catalyzes the reduction of glucose to sorbitol in the polyol pathway and has been associated with development of DN (Caramori et al 2003). Therefore, the pharmacological inhibition of aldose reductase has been recognized as an important strategy in the prevention and attenuation of long-term diabetic complications.

Anti-urolithiatic activity

Argemone mexicana is also reported to possess diuretic and anti-urolithiasis activity. Urolithiasis is the calcifications that form in the urinary system, initially in the ureter (ureterolithiasis) or kidney (nephrolithiasis) and may also form in or migrate into the lower urinary system like bladder or urethra. Common signs of urolithiasis include reduced urinary volume caused by obstruction of the bladder or urethra by a stone and often described as one of the strongest pain sensations. Chilivery et al reported the anti-urolithiasis activity by in-vitro experiments (nucleation, aggregation and microscopic assay's) using petroleum ether, chloroform, methanol, and aqueous extract of *Argemone mexicana* leaves. The extracts were tested for the inhibition percentage against calcium oxalate crystal. It has been reported that methanol extract of *Argemone mexicana* leaves showed significant inhibition (77.24%) compared to standard cystone drug (69.33%) at 100 mg/ml concentration.[8]

Antiulcer, Wound healing, Anti-inflammatory and Analgesic properties of *argemone maxicana*

Argemone mexicana is traditionally used to treat ulcers, wounds and associate problems such as pain and inflammation. To evaluate these properties of *Argemone mexicana*, various scientific studies have been done, some are listed below:

a. Das et al investigated the effect of oral administration of methanolic and aqueous extract of *Argemone mexicana* against cysteamine hydrochloride-induced duodenal ulceration in rats.[9] The study revealed that both the extracts of the plant produced a significant activity to prevent the development of experimentally induced duodenal ulceration in rats. The aqueous extract at the dose-dependent manner showed the potent activity than methanolic extract.

b. Another study has been done by Raveendra Singh et al when they induced gastric ulcer in albino wistar rats by administering 90% ethanol (5ml/kg) in one model for seven days and indomethacin (IND; 5mg/kg) in another model for five days, then investigated the protective effect of the ethanolic extract of aerial part of *Argemone mexicana* at the dose of 300mg/kg and 600 mg/kg rat body weight.[10] In both models the ulcer index (UI) was common and results of this study showed significant dose dependent reduction in the animal pretreated with ethanolic extract of *Argemone mexicana*. The UI was found to be 4.38 ± 0.66 at dose of 300 mg/kg and 4.12 ± 0.69 at dose of 600 mg/kg which corresponds to 68.51% and 70.38% gastro protection respectively as compared with

reference drug (ranitidine and misoprostol).

c. Fatima et al investigated anti-ulcer activity of 70% Hydro-Ethanolic leaf extract of *Argemone*mexicana L. at a dose of (100, 200 & 400 mg/kg b.w p.o) in Pylorus ligation, Aspirin induced mucosal damage and water immersion stress induced gastric ulcer models in Albino wistar rats.[11] The maximum ulcer protection in all the three models was found to be 39.9%, 43.6% and 54.7% respectively at highest studied extract dose of 400mg/kg b.w.p.o. The antiulcer activity is probably due to the presence of bioactive compounds like phenolics compounds, glycoside, alkaloids, flavonoids, saponins and tannins. The presence of flavonoids in the extract which have astringent property could be responsible for the anti- ulcer activity.[12] Owing to above results it can say that *Argemone maxicana* has ulcer protective effects.

d. Das & Murthy investigated wound healing activity using excision; incision anddead space wound models in Wistar albino rats with different extracts of *Argemone mexicana* leaves.[13] The petroleum ether, chloroform, and aqueous extracts of the leaves of *Argemone mexicana* have shown significant wound healing activity.

e. The effect of *Argemone mexicana* roots and its stem is verified in a study on experimentally induced excision wound in Swiss albino rats. The ethanolic extracts of stem, root and other parts of the plant *Argemone mexicana* were examined for wound healing activity and compared with gentamycin (0.3% w/w), a standard wound healing agent. The results of this study revealed that the ethanolic extract ointment of root of *Argemone mexicana* possesses better wound healing potency, which was evidenced by the increased rate of wound contraction, reduction in the period of epithelisation justify its use as potential wound healingherbal medicine as claimed in folk literature.[14]

f. The study on anti-inflammatory activity of *Argemone mexicana* is reported by using carrageenan-induced paw edema method, whereas hot plate test method and acetic acid writhing method has been used for its analgesic property. The lyophilized leaves extract was used and found very effective in acute inflammatory disorders. The plant extract was lyophilized and tested to exhibit significant analgesic activity. The experiment for both the activity was performed in-vivo on young male and female mice. The observed anti-inflammatory activity can be explained due to presence of phytochemicals tannins, flavonoids etc. and the analgesic activity exhibited by the lyophilized extract of plant can

be attributed to phytochemical such as tannins, flavonoids, isoquinoline and alkaloids, etc.[15]

g. In an interdisciplinary study concerned with antimicrobial, anti-inflammatory and wound healing activity of polyherbal formulation of *Plumbago zeylanica Linn, Datura stramonium Linn* and *Argemone mexicana Linn* revealed the synergistic effect on wound healing process. The anti-inflammatory and antimicrobial activities of polyherbal composition might be the contributing factors that accelerated the wound healing activity. These works have provided clear justification for the traditional medical use of *Argemone mexicana* particularlyas anti-inflammatory agents and also supporting analgesic activity. It has been reported wound healing activity in rats was much faster when treated with methanol extract of *Argemone* mexicana leaves.[16]

Antimicrobial activity

Argemone maxicana has a potential to inhibit the growth of numerous microbes such as bacteria, viruses and pathogenic fungi. A large number of research papers have published which describe the antimicrobial properties of *Argemone Mexicana.* Some of them are denoted below.

Antibacterial

a. Rahman et al studied various extracts (hexane, chloroform, ethyl acetate and ethanol) of *Argemone* mexicana stems in vitro and determined the antibacterial activity, using agar diffusion and minimum inhibitory concentration (MIC) determination method against ten (five Gram positive and five Gram negative) food-borne pathogenic bacteria.[17] The chloroform, ethyl acetate and ethanol extracts exhibited strong antibacterial effects against all five Gram positive bacteria (Bacillus subtilis, Staphylococcus aureus, Listeria monocytogenes, Clostridium botulinum and Clostridium perfringens) and three Gram negative bacteria (Escherichia coli, Pseudomonas aeruginosa and Salmonella typhimurium) with their MIC values ranging from 62.5 to 500 µg/ml. However, no antibacterial activity was observed against two Gram negative bacteria: Campylobacter jejuni and Vibrio cholerae at the studied concentration of 300 µg/disc of plant extracts.

b. Sahu and co-workers studied antipseudomonad activity of *Argemone mexicana* on 27 clinically isolated strains of multidrug resistant (MDR) Psudomonas aeruginosa bacteria along with a standard strain, which was sensitive to all antibiotics.[18] The MIC values of

leafextracts of *Argemone mexicana* using acetone, methanol and ethanol as solvent were found tobe 10, 8 and 8 mg/ml respectively. The study concluded that the methanol extract of leaf had the highest level of antipsudomonad activity both with cold and hot extracts. Many other researchers have also confirmed great antimicrobial activity of *Argemone mexicana* seeds and leaves against grampositive as well as gram-negative bacteria, fungi and other pathogenic micro-organisms which are listed in the table.

c. Silver nanoparticles of *Argemone mexicana* (AgNPs) were tested for antimicrobial activity. Significant antimictobial potential was found against the gram positive bacteria and mild potential was observed against gram negative bacterium *P. aeroginosa*.

d. Antiamoebic Activity of methanolic extract of leaves was observed against trophozoites of the *E. histolytica* strain in a In vitro study performed by Joel HEL et al.[19]

Antifungal activities

a. In one of the study, the protein and alkaloids was extracted from *Argemone mexicana* leaves and tested against four different fungal strains viz. *Aspergillus niger, Aspergillus terreus, Aspergillus flavus* and *Rhizopus stolonifera*.[20] A good antifungal activity was observed at temperature 20°C-25°C. Among the various extracts, methanol extracts have been reported toshow maximum potency.

Antiviral activities

a. The active principles of *Argemone mexicana* effectively inhibited viral multiplication and stimulating immune system in Pacific white leg shrimp Litopenaeus vannamei against white spot syndrome virus,[21] Ridge gourd mosaic virus (RGMV).[22] demonstrated a promising anti-HIV potential in human through CD4+ T-cell line, CEM-GFP cells infected with HIV-1NL4.3[23]

b. The aqueous extract of leaves had the antiviral effects against Newcastle disease virus (NDV) and Infectious bursal disease Virus (IBDV) through chicken embryo fibroblast (CEF) cell culture.[24] These studies clearly indicate that various extract of *Argemone mexicana* suppressed the propagation of micro-organism and also boosted the hematological and immunological parameters against virus challenge.

Argemone mexicana is a precious medicinal plant with good healing potential. It has multidimentional pharmacotherapeutic potential. It has been used to treat many other

diseases. Numberous other medicinal properties of this plant have been proven with vast scientific research studies. Such as anticancer, antivenum, neuropharmacological and anti-hiv potential, effectiness in dropsy and jaundice and hepato-protective property etc. These are listed below in the table.

Digestive system relative properties

The oil of *Argemone maxicana* is useful in constipation, flatulence, colic.[25]

Hepatoprotective activity

The antihepatotoxic action of aqueous extract of *Argemone mexicana* stem was reportedin CCl4 induced hepatotoxic male Albino wistar rats. Oral administration of 150 and 250 mg/kg body weight of the extract decreased serum asparate transaminase, alanine aminotransferase andalkaline phosphatase levels. Increase in the body weight of treated rats was also reported.[25]

Sedative /Anti venom activity

A study evaluating the anxiolytic and sedative effects of *Argemone mexicana* shed light on significant central and peripheral nociceptive activity on Swiss albino mice. Methanolic and ethyl acetate extract have also showed significant decrease in motor activity and fall off time of animals on rotating rod. This study demonstrated that phytochemicals such as flavonoids, steroids, alkaloids and tannins present in plant extracts may be responsible for the CNS depressant activity.[26]

Anti-HIV drug

Argemone mexicana contains many isoquinoline alkaloids of the protoberberine type and related types, including sanguinarine. The alkaloid 6- acetonyldihydrochelerythrine has recently been isolated from whole plant extracts and was found to have significant anti-HIV activity (Chang et al., 2003).[27]

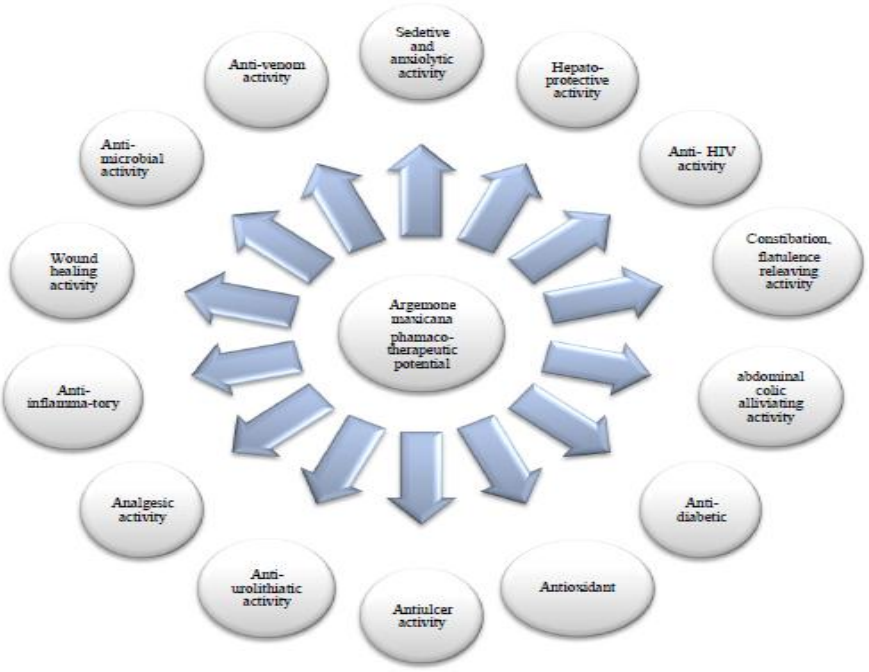

Figure: Pharmacotherapeutic uses of agemone maxicana.

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