International Journal of Botany Studies
ISSN: 2455-541X; Impact Factor: RJIF 5.12
Received: 03-04-2021, Accepted: 01-05-2021, Published: 18-05-2021
www.botanyjournals.com
Volume 6, Issue 3, 2021, Page No. 188-191

Ammi majus: A plant with multifunctional medicinal properties

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Abstract
Ammi majus L. belongs to family Apiaceae is one of the unique source of various types of chemical compounds, which are responsible for a variety of activities. It has various medicinal properties and is useful in the treatment of leucoderma, vitiligo, as a diuretic, emmenogogue, abortifacient and blood purifier. *A. majus* extracts showed significant biological activity such as antiviral, antimicrobial, antioxidant, relaxant effect, cardiovascular effect, hypotensive etc. More than fifty bioactive phytochemicals were isolated from the particular plant species but the main groups of phytochemicals that are potential against different biological activities are flavonoids and coumarins. The purpose of this review was to provide a brief summary of the knowledge of biopharmaceutical effects of secondary metabolities of *Ammi majus* L. and the mechanism of their action. As the worldwide scenario is now changing towards the use of non-toxic plant products having traditional medicinal use, development of modern drugs from *Ammi majus* L. should be emphasized for the control of various diseases.

Keywords: *Ammi majus* L., leucoderma, vitilago, xanthotoxin and psoralen

Introduction
Ammi majus L., a member of family Apiaceae, is an important medicinal plant. The botanical name *Ammi majus* L. is derived from two Greek words - *Ammi* (Dioscorides), from the Greek term 'ammos' meaning sand and refers to the plant's habitat and 'majus' meaning bigger or larger. The standard author abbreviation L. is used to indicate Carl Linnaeus (1707 – 1778). Its common names are Aatrilal, Bishop's weed, Greater *Ammi*, False Queen Anne's lace, Bullwort, Lace flower and Honey flower.

Ammi majus L. is a native of Nile Delta of Egypt and widely grown throughout the Mediterranean region, Abyssinia, Africa and some parts of Egypt. In India, it was first introduced in the Forest Research Institute, Dehradun, in 1955 through the efforts of UNESCO. Since then its experimental cultivation has been tried in several parts of the country including Jammu, Dehradun, Mumbai, Chennai, Delhi and Punjab.

It is stout, erect, coarse and glabrous. The stem is round and solid with tap root system. Its large leaves are 5-8 cm long, alternate, and light green, decompound, pinnately divided and lanceolate in shape. The inflorescence is umbel, axillary and terminal in position with flowers white in colour. Calyx tube is adnate to bracts, 5 in number and teethed. Petals -5, epigynous, distinct and bifid. Stamens - 5, epigynous, alternate with petals. Ovary is inferior, 2 celled, disk epigynous, 2 lobed, ovule solitary in each cell. Style - 2, stigma is minute and capitulate. The flowering is seen after 3-4 months of seed sowing. Fruit is pod, ribbed, ellipsoid, greenish brown in colour, turning reddish brown on maturity and is ready within 30-35 days from blossoming of flower. The seeds are flat bearing thin wings, having a characteristic terebinthinate odour becoming strong on crushing with extremely pungent and slightly bitter taste.

Medicinal Uses
Most of the plant species detected as medicinal plants have been used to treat human diseases for centuries as medications or prevention of ailments because the plant species contain significant active phytochemicals such as flavonoids, coumarins, alkaloids, terpenoids, amino acid, essential oil with therapeutic value (Marimuthu P., 2008; Nostro, 2000; Milic, 2000) [38, 41, 39]. *Ammi majus* L. is widely used for the treatment of skin disorders such as psoriasis and vitiligo (acquired leukoderma) (Egyptian Pharmacopoeia, 1972; Hakim, 1969; El-Mofty, 1948; Fahmy and Abu-Shady, 1948; El-Mofty 1952) [14, 24, 18, 19, 16]. It is used as an emmenagogue to regulate menstruation, as a diuretic, and for the treatment of leprosy, kidney stones, and urinary tract infections (Farnsworth, 2001) [20]. *A. majus* fruit and *Trigonela foenum-graecum* seeds are commonly used for a variety of kidney disorders and as diuretics (Al-Antaki, 1923; Karim, 1885; Ageel *et al.*, 1987; Ahsan *et al.*, 1989) [5, 2, 3].

The seed is contraceptive, diuretic and tonic (Bown, 1995) [8]. An infusion is used to calm the digestive system, whilst it is also used in the treatment of asthma and angina (Chevallier, 1996). A decoction of the ground-up seed, eaten after intercourse, appears able to prevent implantation of the fertilized ovum in the uterus (Bown, 1995) [8]. This decoction is also used as a gargle in the treatment of toothache (Bown, 1995) [8].

The seed contains furanocoumarins (including bergapten), which stimulate pigment production in skin that is exposed to bright sunlight (Bown, 1995; Chevallier, 1996) [8, 9]. The plant is widely cultivated in India for these furanocoumarins which are used in the treatment of vitiligo (piebald skin) and psoriasis (Bown, 1995; Chevallier, 1996) [8, 9]. Preparations containing psoralen or other furocoumarins, plus sunlight, have been used for thousands of years for vitiligo (Ivie, 1987) [27].

The root is chewed to give protection from strong sunlight. It contains 8-methoxypsoralen which stimulates production of pigment in skin exposed to U.V. light. Caution is advised; however, since it can cause side-effects (Natural Food Institute, Wonder Crops, 1987) [40]. Other reports suggest

that it is the seeds that are used (Bown, 1995; Chevallier, 1996) [8, 9].

The fruits are valued in indigenous medicine and have been employed for long time in folklore therapy for the treatment of leucoderma, vitiligo and diuretic, emmenogogue, as abortifacient and blood purifier (Khan *et al.,* 1991) [33]. It has been recommended as a diuretic, expectorant and useful in jaundice (Khan & Rahman, 1985 and Lal, 1977) [32, 37].

Some psoralens are also synthesized for medicinal use in treating leukoderma and more recently, psoriasis (Scott et. al., 1976; Iive, 1978) [46]. The plant is used for the treatment of leucoderma and psoriasis (Anup Kumar, 1988 and Hansen, 1979) [35, 25]. It also used in treatment of wheezing or coughs (Ekiert and Gomółka, 2000; Pande *et al*., 2002) [15, 43]. *A. majus*, as it is showing promise in cancer and AIDS therapy (El Gamal *et al.*, 1993; Gala, 2012) [17, 22]. These medicinal properties of *Ammi majus* L. caused it to be considered as a plant with multifunctional medicinal properties.

Biological Activity

Allelopathy

Allelopathic activity of *A. majus* L. fruit waxes was investigated by (Garcia *et al*., 2002). *A. majus* seeds are known to have a strong allelopathic effect due to the presence of coumarins which are shown to be present in the seed epicuticular waxes which are inhibitors of seed germination and seedling growth.

The Aqueous eludate from fruits of *A. majus* remarkably inhibited germination of adjacent seeds of *Anastatica werochuntica*, lettuce or tomato but had no effect or autoinhibition on intact fruits of *Ammi majus* (Friedman *et al.*, 1982) [21].

Cytological Effects

The cytotoxic activity of the selected plant extracts was assessed by well-established *in vitro* and *in vivo* methods (Lai *et al*., 2004) [36]. Among the extracts, the cytotoxic activity results displayed that the aqueous ethanol extract gives maximum activity on the breast cancer cell line (Vanachayangkul et. al., 2010) [48].

Influence of water extract of *Ammi majus* on meiosis of *Vicia faba*, was investigated. High percentage of chromosomal abnormalities was reported which included bridges, Spindle disturbance, lagging chromosome, breaks, fragments and multinucleate cells. It also caused increase in pollen abortiveness and decrease in pollen length.

Mutational Effects

Mutagenicity of coumarin psoralen epiorcides was tested to investigate side effects of *Ammi majus*. It has been found that naturally occurring psoralen epioxides have low mutagenic potential and thus unlikely to have significant toxicological significance, while syhthetic psorlen epioxide (PSGE) is highly mutagenic.

Induction of mutation in *A. majus* L by ionizing radiation on seed germination morphology, pollen fertility and yield was explored by Khalil *et al.,* (1996) [30] by using different doses of gamma rays. Decreased and delayed germination, variations in cotyledonary and vegetative leaves, reduced plant growth, decreased pollen fertility and yield have been observed in higher doses.

Photosensitization

The experimental evidence supporting photosensitization as a cause of cataracts has been reviewed. Methoxsalen caused UVA alteration of lens DNA or protein could lead to delayed onset of cataracts and because of the serious nature and potential preventability of phototoxic lens opacification, appropriate protective eye wear is recommended for all patients receiving oral Psoralen from *Ammi majus*.

Dermatological and ocular examination in rabbits chronically photosensitized with methoxsalen and photosensitization in cattle and sheep caused by feeding *Ammi majus* have been investigated (Parrish *et al.*, 1979; Dollahite *et al.,* (1978) [44, 49].

Photosensitization in sheep, geese and duck fed on *Ammi majus* seeds has been reported (Witzel *et al.*, 1978, Barishak *et al.*, 1975, Egyed *et al.*, 1975) [49, 6, 13] an acute and chronic manifestations of *Ammi majus* induced photosensitization in ducks.

A study compared the ability of two closely related plants *Ammi majus* (L) and *Ammi visnaga* (L) Lam. to induce photosensitization with goslings as the experimental models. The same weight of seeds of the two plants was fed to goslings. It caused photosensitization solely in the case of geese fed by *A. majus* seeds that were exposed to sunlight. (Shlosberg *et al.*, 1974) [47]

The preliminary phytochemical investigation of *A. majus* showed presence of certain biochemical constituents namely coumarins, furocoumarins, flavonoids that are responsible for various pharmacological activities including leucoderma and vitiligo (Akhtar *et al.*, 2010) [4].

Hepatotoxic Activity

Observations on the experimental poisoning of young geese with *Ammi majus* led to severe liver damage in the birds fed on *Ammi majus* and exposed to sunlight (Egyed *et al.*, 1994). Chronic lesions of the beak, foot web and eye of geese photosensitized by consumption of *Ammi majus* has been reported (Egyed *et al.*, 1994).

The effect of imperatorin, a toxic principle from *Ammi majus*, on energy-transfer in mitochondria was examined. It was found to cause cirrhotic changes in liver, loss of oxidized pyridine nucleotides from liver and also inhibited succinate linked respiration and phosphorylation in isolated liver mitochondria (Krama and Kaiser, 1968) [34]. Effect of 8-methoxypsoralen on rat lens cations, membrane potential and protein levels were reported by (Boutros *et al.*, 1972) [7].

Antioxidant properties

Many studies showed that *Ammi majus* extract has strong antioxidant properties, produced by its many active constituents such as imperatorin (Adebajo *et al.,* 2009; Xiang *et al.,* 2004) [1, 50]. The previous antioxidant activity results related to the particular plant species showed that all prepared extracts exhibited significant antioxidant activity against various conventional models. Majority results declared that high antioxidant activity was found from the most polar extract e.g., methanol extract (Hossain, 2020) [26].

Some results on the same species done which displayed that the high activity was found in the nonpolar extracts e.g., hexane as well as chloroform extracts (Khaloud *et al*., 2016) [31].

Allergy

Incidence of occupational allergic rhinitis and contact urticaria caused by *Ammi majus* has been reported by Dollahite *et al.*, (1978) [46].

Bio pesticidal use

Like most medicinal compounds, furocoumarins might have potential as natural (or synthetic) pesticides. As plant defensive weapons, coumarins have been shown to protect the plant against mammalian herbivores, as well as insects, fungus and bacteria (García, 2002) [23].

Activated by ultraviolet, furocoumarins have bactericidal and viricidal, fungicidal, insecticidal, larvicidal, moluscicidal, nematicidal, ovicidal, viricidal and herbicidal activities (Duke 1988, Panda, 2004) [11, 42].

Physiological and egg-laying effects of *Ammi majus* were screened against *Biomphalaria alexandrina* and *Bulinus truncatus*. *A. majus* showed a definite lethal effect on egg laying and longevity of both snails.

Comparative study of the molluscicidal activity of *A. majus* on snail vector of *Schistosoma monsoni* and *Biomphalaria alexandria* revealed that aqueous suspension of *A. majus* flowers and leaves extract as well as $CuSO_4$ were found to cause the most potent cumulative mortality (Rawi *et al.*, 2011) [45].

Herbicidal Effect

Herbicidal comparison between naturally growing and in vitro regenerated *Ammi majus* proved that both natural and in vitro regenerated plants show equally potent herbicidal activity and that the regeneration of *Ammi majus* through somatic embryogensis provides an efficient method for its micropropagation.

Conclusion

Ammi majus L. can be considered a great potential therapeutic agent and have been employed for long time in folklore therapy for the treatment of leucoderma, vitiligo, as a diuretic, emmenogogue, and abortifacient and blood purifier. More than fifty bioactive phytochemicals were isolated from the particular plant species but the main groups of phytochemicals that are potential against different biological activities are flavonoids and coumarins. Although, a lot of experiments have been done on *Ammi majus* L., which showed significant biological activity such as antiviral, antimicrobial, antioxidant, relaxant effect, cardiovascular effect, hypotensive etc. However, more investigations are needed to exploit other therapeutic utility to combat diseases. As the worldwide scenario is now changing towards the use of non-toxic plant products having traditional medicinal use, development of modern drugs from *Ammi majus* L. should be emphasized for the control of various diseases.

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