

Phytochemical and Pharmacological Profile of *Ammi visnaga* Plant: A Potent Ethnomedicinal Plant

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Abstract

Ammi visnaga L. (Family: Apiaceae or umbelliferae) is an herbaceous plant with a long history of traditional medicinal uses in many countries in the world. The plant has been known since ancient times for its curative properties and has been utilized for treatment of circulatory problems, kidney stones, asthma, bronchitis, skin problems and whooping cough. A wide range of chemical compounds including coumarins (glycosides), flavonoids, and volatile principles have been isolated from this species. Extracts from this plant have been found to possess various pharmacological activities. This contribution provides a comprehensive review of its ethnomedical uses, chemical constituents and the pharmacological profile as a medicinal plant. In this review particular attention has been given to anti-anginal, hypoglycemic and diuretic effects of the plant and thus the potential use of this plant in pharmaceuticals can be evaluated.

Keywords: Coumarins; Curative properties; Flavonoids; Ethnomedical uses; Pharmacological profile; Volatile principles.

INTRODUCTION

Herbal medicines are being used by nearly about 80% of the world population, primarily in developing countries for primary health care. Assessing the current status of health care system in adequacies of synthetic drugs is likely to be more glaring in the coming years. It has been reported that there has been an alarming increase in number of diseases and disorders caused by synthetic drugs prompting a switch over to traditional herbal

medicine (Ghule and Patil, 2001).¹ India has over 1, 08,276 species of bacteria, fungi, animals and plants already identified and described. Out of these about 84% species constitutes fungi (21.2%), flowering plants (13.9%) and insects (49.3%)² (Khosoo, 2001).

Ayurveda is a traditional Indian Medicinal System (IMS) being practiced for thousands of years. Considerable research on pharmacognosy, chemistry, pharmacology and clinical therapeutics has been carried out on ayurvedic medicinal plants. Natural products, including plants, animals and minerals have been the basis of treatment of human diseases. The current accepted modern medicine or allopathy has gradually developed over the years by scientific and observational efforts of scientists. However, the basis of its development remains rooted in traditional medicine and therapies (Vishnukanta and Rana, 2005).³

Although modern medicine has revolutionized health care, the healing process has always been too

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complex to be explained by the use of medicine and technological advances alone. There has always been the gestalt of therapy that involves medicines and other components. Those components have reflected in recent years a trend of increasing use of alternative medicines. Alternative interventions are a major component of health care globally and many healthcare providers and healthcare organizations are being forced to consider integrating them into their practice and treatment guideline. In the US alone, in 1996, 1800 herbal products were available with sales in excess of \$ 1.5 billion and increasing about 25% per year while the global market was estimated in excess of \$ 15 billion⁴ (Muller and Clauson, 1997).

Selection of scientific and systematic approach for the biological evaluation of plant products based on their use in the traditional systems of medicine forms the basis for an ideal approach in the development of new drugs from plants. One such plant Ammi visnaga, a species of flowering plant, also known as 'toothpick weed' and 'khella'. It is native to Europe, Asia, and North Africa. Since from antiquity *Ammi visnaga* is used to treat asthma, kidney stones, and circulatory problems.

Plant Profile

Ammi visnaga Lam. Fl. Franc. (Fig. 1) is also known as *Daucus visnaga* and commonly called as 'toothpick weed' or 'Bishop's weed' (English); 'bisnaga' (Hindi); and 'khella' (Sanskrit).



Fig. 1: Plant of Ammi visnaga (Source: <https://higgledygarden.com/2011/09/01/ammi-visnaga/ammi-visnaga-2/>)

Geographical Distribution⁵ (Hammouda *et al.*, 2010)

Local: Growing mainly in the Nile region, rare in the Eastern Mediterranean region.

Regional: North Africa

Global: North America, Argentina, Chile, Mexico, Europe, Temperate, Southwestern Asia, Atlantic Islands, Ethiopia.

Taxonomic Classification⁵ (Hammouda *et al.*, 2010)

Fam.: Apiaceae (Umbelliferae)

Kingdom: Plantae

Division: Angiosperms

Class: Eudicots

Subclass: Asterids

Order: Apiales

Family: Umbelliferae, Apiaceae

Genus: Ammi

Parts Used⁵ (Hammouda *et al.*, 2010)

Fruits, rays of umbel

Traditional Medicine and Indigenous Knowledge History⁶ (Boulos, 2000)

The Arabs discovered centuries ago that the small, greyish, egg shaped, visnaga could ease a multitude of ailments, including the stabbing pain caused by a reduction in the flow of blood to the heart. Khellin, the substance in the fruits that accomplishes this feat, is described by scientists today as a selective coronary vasodilator. However, khellin is not without side effects. Researchers have found that it has a cumulative toxicity. Its active principles build-up in the body when the drug is taken over a period of time, and can cause nausea and vomiting. For this reason, the drug is no longer used in the United States. However, it is still employed by doctors in the regions around the Mediterranean Sea where it is originated and where it grows profusely. It has been used for the treatment of psoriasis. The ancient Egyptians rubbed red, scaly skin patches, presumably psoriasis, with the *Ammi visnaga* plant, and then the patients sat in the sun. *Ammi visnaga* fruits have long been used in Egypt, as a diuretic for renal colic and ureteric stones, angina pectoris, the coronary vessels, cardiovascular disorders and asthma. A new therapeutic product has been produced as a result of an Egyptian discovery (Professors of the Pharmaceutical Science Department, National Research Center, Egypt) for the treatment of vitiligo and psoriasis.

BOTANICAL DESCRIPTION

Morphological Description⁷ (Anonymous, 2001)

Annual herb, 30-150 cm high, slightly aromatic

stems erect, robust, much branching, cylindrical, furrowed, densely leafy. Leaves alternate, with special odor, with broad leaf sheath, lower leaves pinnate, with narrowly linear lobes; middle and upper leaves 2-3 pinnate, with filiform lobes. Inflorescence dense umbel with numerous rays (to 120 or more) slender in flower, thickened and stiff in fruit, hence used as toothpick. Bracts pinnatisect, as long as or longer than the rays; bracteoles small, flowers white, pedicels erect, rigid in fruit, fruit cremocarp about 2 mm long, glabrous with thick ribs, separated into two mericarps.

Microscopical Description⁷ (Anonymous, 2001)

A transverse section of the mericarp is an almost regular pentagon with one of its sides slightly longer which is the commissural surface at which the two mericarps are attached. The epicarp is composed of a layer of indistinct colourless, polygonal, papillose, thin walled parenchyma covered with faintly striated cuticle. The mesocarp encloses vascular strands on the outer side of which is found a large space (lacuna) just below the epidermis of each primary ridge. Below the epidermal part of the secondary ridges, a group of radiating club-shaped parenchyma cells that are associated with the secretory canals known as vittae which are filled with dense brown contents. The endocarp is composed of elongated thin walled cells which are surrounding the seed testa. The testa is composed of one or two layers of thin walled cells that contain brown pigments. The endosperm of the seed consists of almost rounded parenchyma cells having intercellular spaces. The cells contain aleurone grains and microrosette crystals of calcium oxalate.

Physico-Chemical Evaluation

Evaluation of physical and chemical parameters is also a very promising tool for standardization purpose of a drug. Various standardized

Table 1: Standardized physico-chemical parameters of *Ammi visnaga*⁷ (Anonymous, 2001)

Parameters	Specifications
Loss in weight on drying at 105°C	4.60%
Solubilities	
-Alcohol solubility	16.8-18.40%
-Water solubility	34.4-35.04%
-10% ethanolic extractive	32 - 34%
Ash values	
-Total ash	9.4%
-Acid insoluble ash	0.6%
-Water soluble ash	2.9%

Successive extractives	
-Petroleum ether	3.40%
-Chloroform (60-80°C)	6.10%
-10% ethanolic water extract	19.50%
pH values	
pH value of 1% solution	5.92
pH value of 10% solution	5.64

physicochemical parameters are as follows, as per WHO guidelines (Table 1).

PHYTOCHEMISTRY

Mainly *Ammi visnaga* contains flavones, coumarins

Table 2: Chemical composition of *Ammi visnaga*⁷ (Anonymous, 2001)

Type of chemicals	Amount of chemicals (%)	Active principles
Furanochromones (-py-ones)	2-4%	Khellin (0.3-1.2%), visnagin (0.05-0.3), khellol and its glucoside, khellenin, khellinol, ammiol and its glucoside, visammiol, khellinone, visnaginone.
Coumarins	0.2-0.5%	Visnadin, samidin and dihydrosamidin (pyranocoumarines) xanthotoxin and ammoidin (furanocomarines)
Flavonoids	0.02-0.03%	Quercetin and isorhamnetin kaempferol.
Volatiles	Trace in amount	Camphor, carvone, (-terpineol, terpinen-4-ol, linalool, cis and trans linalool oxides).
Fixed oil	12-18%	-----

and volatile principles, as major group of phytoconstituents; those are responsible for various pharmacological activities (Table 2).

ETHNOPHARMACOLOGY

Pharmacological Actions

The drug is spasmolytic (smooth muscles), especially on the musculature of the bronchi, gastrointestinal tract, biliary tract, urinogenital system, the coronary vessels (coronary dilator), and also as a diuretic (volumetric and urinary antispasmodic). Khellin, which is now commercially available in tablets and

injection, is a potent selective coronary vasodilator and bronchodilator. It is used in the treatment of coronary insufficiency, angina pectoris, bronchial asthma, vitiligo and psoriasis, and for the removal of small bladder and kidney stones⁸ (Kenner and Requena, 2001).

Traditional Medicinal Uses⁸ (Kenner and Requena, 2001)

- Kidney stones
- Asthma
- Bronchitis
- Lithontripic
- Diuretic
- Whooping cough
- Circulatory problems
- Vasodilator

PHARMACOLOGICAL STUDIES

Cardiovascular disorders

Best and Coe, 1950 investigated the clinical effectiveness of khellin in 9 patients with angina pectoris. Evaluation was carried out electrocardiographically by means of the exercise tolerance, anoxemia and ergonovine tests. Normalization occurred in the majority of the previously abnormal tests following khellin therapy. A beneficial effect was noted on symptoms accompanied by a reduction in nitroglycerin requirement⁹ (Best and Coe, 1950).

Khellin was found to increase HDL-cholesterol in normolipaemic subjects¹⁰ (Harvengt and Desager, 1983).

Moreover Rauwald *et al.*, 1994 investigated possible calcium antagonistic mode of action of *Ammi* fruits for their effectiveness in angina. He tested most active lipophilic extract of the fruits and fractionated by carbon tetrachloride. The extract was investigated pharmacologically at K⁺ depolarized guinea pig aortic strips. Visnadin, khellin, and visnagin were isolated and determined as the effective principles in this testing model with the dihydropyranocoumarin visnadin being the most active. Further selectivity tests against norepinephrine (100 microM) induced contractions evaluated a possible pharmacological differentiation between these compounds as the furanochromones khellin and visnagin inhibited both spasms to a similar extent while visnadin's activity was significantly higher against K⁺-spasms, suggesting an involvement of a calcium channel blocking mode of action for visnadin and its effectiveness in angina pectoris¹¹ (Rauwald *et al.*, 1994).

Visnagin, an active principle extracted from the fruits of *Ammi visnaga*, exhibits peripheral and coronary vasodilator activities and has been used for the treatment of angina pectoris¹² (Duarte *et al.*, 1995).

Hypoglycemic Effect

Jouad *et al.*, 2002 investigated the aqueous extract of *Ammi visnaga* (Apiaceae) on blood glucose levels in fasting normal and streptozotocin induced diabetic rats after single and repeated oral administration. The aqueous extract at a dose of 20 mg/kg significantly reduced blood glucose in normal rats six hours after a single oral administration ($P < 0.005$) and nine days after repeated oral administration ($P < 0.05$). This hypoglycemic effect is more pronounced in streptozotocin (STZ) diabetic rats ($P < 0.001$). Acute toxicity (LD50) and general behavioural effects of an aqueous extract fruits was studied in mice. The LD50 of intraperitoneal (i.p.) and oral administration was 3.6 and 10.1 g/kg, respectively.¹³

Diuretic activity

Ammi visnaga extract was reported to be good for expulsion of urinary crystals¹⁴ (Westendorf and Vahlensieck, 1981).

Ammi visnaga seeds extract shows highly potent diuretic activity. In 2001, Khan *et al.*, investigated the effect of *Ammi* seeds on experimentally induced kidney stones in male Wistar albino rats. In study nephrolithiasis (calcium oxalate deposition in the kidneys) was induced by 3% glycolic acid (added in their diet) given for the period of four weeks. A highly significant amount of Calcium oxalate deposits were found in the kidneys. Daily oral treatment with *Ammi* seeds (500 mg/kg) highly reduced the incidence of nephrolithiasis.¹⁵

Some pharmaceutical products of *A. visnaga* in the markets⁵ (Hammouda *et al.*, 2010)

Psorvitol (Khellin), (Memphis)

Kellagon (Mepaco)

Glucolynamine (Memphis)

Khellalgin (Misr)

DISCUSSION AND CONCLUSIONS

Ammi visnaga is a well known plant used in the traditional system of medicine, besides which folklore medicine also claims its uses especially in cardiac and urinary diseases, asthma, etc. Recently *A. visnaga* fruit is widely cultivated in so many countries for its edible and medicinal uses. It is also a very important plant in a number of diseases and for that we have enough scientific reports and data. Chemically *A. visnaga* contains various biologically active phytoconstituents

like coumarins, flavonoids, and volatile principles. Thus *A. visnaga* is considered as a very important gift of *Ayurveda* to mankind.

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