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Pharmacological and phytochemical profile of *Trachyspermum ammi*: evidence from the traditional medicine and recent research

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Abstract

Medicinal plants always played an important role in the health development of mankind. *Trachyspermum ammi* is one of the oldest spice plants which, due to its economic importance and significant pharmaceutical industry applications, are considered as one of the world's most important medicinal plants. In order to gather the information the keywords *Trachyspermum ammi*, therapeutic, and pharmacology have been searched until August 30, 2020 from journals accessible in databases such as Science Direct, Scopus, EBSCO, Medline, PubMed, Embase, SID, and Iran Medex. The results showed that this plant has various pharmacological properties including analgesic, antioxidant, digestive, anti-cancer activity, anti-inflammatory, antifungal, Anti-bacterial and estrogenic effects which are probably due to the presence of aromatic compounds such as carvone, limonene, thymol, hygroscopic saponin, crystalline flavone and dillapiole. *Trachyspermum ammi* possesses various pharmacological properties and play an important role in human health; hence, it might be used for different drug productions.

Keywords: medicinal plants, *Trachyspermum ammi*, unani medicine, analgesic, digestive, anti-inflammatory

Introduction

Trachyspermum ammi Linn, belonging to Umbelliferae family, is a plant with important medicinal properties. *Trachyspermum ammi* is native of Egypt and grows widely around Mediterranean Sea and in Southwest Asia. It is cultivated in India, Iran, Afghanistan, Pakistan and Iraq^[1]. *Trachyspermum ammi* is an annual herb 60-90 cm tall. Stem is much branched and striated. Inflorescence is compound umbel having 16 umbels each containing up to 16 flowers. Flower is white in color, corolla 5, petals bilobed, stamen 5, and ovary inferior. Leaves pinnate, upper leaves are smaller and shortly petiolate while lower leaves have long petioles (Figure-1). Fruit (Figure-2) is grayish brown, ovoid, consisting of two mericarps with prominent ridges. Fruit is 2 mm long and 1.7 mm wide^[2]. Transverse section of *Trachyspermum ammi* fruit demonstrates two hexagonal structures attached with each other by a carpophores, single layer of tangentially elongated tabular cells are present in epicarp, mesocarp tissues consists of moderately thick-walled, rectangular tangentially elongated cells having some vittae, integument, barrel shaped of tangentially elongated cells, endosperm consists of thin walled cells filled with embryo, oil globules, small and circular, composed of polygonal thin walled cells. The microscopic characteristic of powder shows the presence of oil globules and groups of endosperm cells^[3]. A number of chemical constituents have been reported for the herb. Fiber (11.9%), carbohydrates (24.6%), tannins, glycosides, moisture (8.9%), protein (17.1%), fat (21.1%), saponins, flavones and other components (7.1%) involving calcium, phosphorous, iron, cobalt, copper, iodine, manganese, thiamine, riboflavin and nicotinic acid are of reported phytochemical constituents of Ajwain. In the alcoholic extraction process, a large amount of saponin has been derived. Flowers and fruits are bearing from January–April. The action of Jain seeds lasts for four years. Its extract is called Jawahar Kamun Mulki in Arabic, Jawahar Nankhah in Persian, Azwain in Urdu and Thymol in English. There is another type of this whose botanical name is *Trachyspermum amru* Linn.

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Fig 1: The photo of *T. ammi*.



Fig 2: *T. ammi* seeds.

Vernacular names

Hindi - Ajwain
 Bengali - Jain,
 Arabic - Kamun Mulki,
 Persian - Nankhah,
 Urdu - Azwain Desi,
 Sanskrit - Yamani,
 English - Bishop's weed.

Scientific name- *Trachyspermum ammi*

Taxonomical classification

Kingdom: Plantae, Plant
 Subkingdom: Tracheobionta, Vascular plant
 Superdivision: Spermatophyta, Seed plants
 Division: Magnoliophyta, Flowering plants
 Class: Magnoliopsida, Dicotyledons
 Order: Apiales
 Family: Apiaceae
 Genus: *Trachyspermum*
 Species: *ammi*

Distribution and Habitat: It belongs to the family 'Apiaceae' comprising 270 genera and species, mostly grown in the temperate regions of the world but species which are cultivated in tropics regions. Ajwain is grown in Iran, Egypt, Afghanistan and India (largely in Uttar Pradesh, Bihar, Madhya Pradesh, Punjab, Rajasthan, Bengal, Tamil Nadu and Andhra Pradesh). It is generally grown in October- November and harvested in May -June. Though

the plant is widely cultivated, it is indigenous to Egypt where it grows as a common weed in the fields [4].

Unani description

Mijaz: According to Ibn Sina, Jain is 3rd class hot and dry. According to another scientist, it is 2nd class hot and dry.

Parts use: Jain trees, roots and seeds are used.

Color: Jain seeds are brown in color.

Taste: Jain has a bitter and pungent taste.

Smell: Jain intense scent.

Dosage: 3 to 5 grams of Jain seeds and 1 to 3 drops of oil can be consumed.

Reaction: Excessive consumption of Jain is harmful for person with hot in nature and causes headaches.

Corrective: It is corrective by the coriander, watermelon and sour materials.

Representatives: *Nigella sativa* can be used in the absence of Jain.

Therapeutic use: Jain is especially effective in relieving pain and swelling of the whole body and increasing the strength of digestive organs.

Important formulations: Important Unani formulations containing *Trachyspermum ammi* are as follows:

- Syrup/ Tablet Carmina: Indication- Hyperacidity, flatulence, abdominal pain due to gases, indigestion, loss of appetite, constipation, weakness of stomach and liver, nausea and vomiting, belching & heart burn. Produced by Hamdard Laroratories (waqf) Bangladesh.
- Tablet Dysni (pachis): Indication- Amoebic dysentery, bacillary dysentery, diarrhoea, abdominal pain & cramps. Produced by Hamdard Laroratories (waqf) Bangladesh.
- Jowarish Zarooni: Indication- Renal colic, urolithiasis, oliguria & back pain. Produced by Hamdard Laroratories (waqf) Bangladesh.
- Jowarish Kamuni: Indication- Hyperacidity, indigestion, hiccup, flatulence & constipation. Produced by Hamdard Laroratories (waqf) Bangladesh.
- Arq. Ajwain: Indication- Flatulence, indigestion & anaemia due to liver disorders. Produced by Hamdard Laroratories (waqf) Bangladesh.

Chemical composition: *Trachyspermum ammi* seed analysis has revealed it to contain fibre (11.9%), carbohydrates (38.6%), tannins, glycosides, moisture (8.9%), protein (15.4%), fat (18.1%), saponins, flavone and mineral matter (7.1%) containing calcium, phosphorous, iron and nicotinic acid [5]. The *Trachyspermum ammi* fruits yields 2% to 4% brownish essential oil, with thymol as the major constituent (35% to 60%) [6]. The nonthymol fraction (thymene) contains para-cymene, γ -terpinene, α - and β -pinenes, dipentene, α -terpinene, and carvacrol. Minute amounts of caphene, myrcene, and α -3-carene also have been found in the plant. Alcoholic extracts contain a highly hygroscopic saponin. From the fruits, a yellow, crystalline flavone and a steroid-like substance have been isolated and also contain 6-O- β -glucopyranosyloxythymol, a glucoside and a yield of 25% oleoresin containing 12% volatile oil (thymol, γ -terpinene, paracymene, and α - and β -pinene). The principal oil constituents of *Trachyspermum ammi* are carvone (46%), limonene (38%) and dillapiole (9%) [7].

Traditional use: Oral application of seed was reported to be

useful for paralysis and palsy as well as other neural disorders in the field of neurology. Persian practitioners also applied the eye and ear drop formulated from seeds of Ajwain in order to control the infected conditions and correct the auditory weakness. In the field of respiratory, Ajwain was said to be effective on cough, pleurisy and dysphonia. Fruits were widely administered for liver spleen as well as gastrointestinal disorders such as nausea, vomiting, reflux, abdominal cramps and loss of appetite. They were also said to be beneficial in stomach troubles and possess stimulant and carminative properties. Ajwain was reported as an anthelmintic medicine and also antidote for various natural toxic agents. It was also believed to be beneficial for dissolving the calculi and stones if taken with wine. Persian practitioners also considered the seeds as an aphrodisiac, galactagogue and diuretic agent as a cosmetic agent, local administration of Ajwain as a paint results in yellowish complexion on the skin. It was also incorporated in medicine prepared for pityriasis and leukoderma and plastered with honey in cases of all types of ecchymosis. Persian practitioners also used the seeds in the form of fumigation for the female genital disorders. In the field of toxicology, it was reported that bathing the affected part with the decoction of Ajwain seeds alleviates the pain caused by scorpion's bite. Also it was used for the reduction of undesired effects related to the opioid withdrawal. Ajwain was also introduced as a potent analgesic and anti-inflammatory agent. Therefore it was applied on the affected area solely or in combination with egg white or honey. Persian practitioners used Ajwain in chronic fevers and gripes Hydrosol and oil extracted from the seeds of Ajwain was also used for medical purposes. Of those, management of paralysis, palsy, tremor and neurological disorders such as neuropathic pain as well as chronic pains are cited in Persian medical and pharmaceutical manuscripts. The Ajwain hydrosol combining with Borage and Cinnamon was highly recommended as a great enlivening medicine.

Methods of use

1. In case of hemorrhoids: Those who have been bleeding for a long time, mix 100 grams of fried *Trachyspermum ammi* and 100 grams of fried *Nigella sativa* together, grind them and store them in an airtight container. In the morning and afternoon, if you take 1-2 grams of powder, in most cases, the bleeding of the hemorrhoids will stop and the hemorrhoids will be reduced. Should be taken for 2-3 months.
2. Urinary obstruction: In some cases, urinary obstruction occurs when the prostate gland is enlarged or if it is pressed for a long time. In this case, taking 1-2 grams of *Trachyspermum ammi* powder is especially beneficial.
3. In case of indigestion and flatulence: Grind 100 gm of *Trachyspermum ammi*, 50 gm of dry ginger and 50 gm of black salt and store it in an airtight container. Taken 3-5 grams of powder twice a day after meals for a few days, it has unexpected benefits in indigestion and flatulence.
4. Menstruation problem: In case of austerity and some women have menstrual cramps in small amounts or it does not occur clearly or after stopping it may occur again in a few days. In this case, taking 2-3 grams of *Trachyspermum ammi* powder is especially beneficial.
5. In case of wound healing and any wound or

decomposition of the body, it is especially beneficial to apply *Trachyspermum ammi* paste on the affected area for a few days.

6. If there is bleeding from the gums of the teeth then in most cases the bleeding stops if the *Trachyspermum ammi* is crushed and paste to the gums.
7. An unexpected benefit of headache is obtained by taking 2-3 grams of *Trachyspermum ammi* powder twice a day.
8. Arthritis Pain: Massage of *Trachyspermum ammi* oil on the affected area is especially beneficial for arthritis pain.

Pharmacological screening

Analgesic and antinociceptive effects

In order to evaluate the analgesic and antinociceptive activity of Ajwain, an *In vivo* investigation was carried out using a Tail-flick Analgesiometer Device [8]. The study revealed that the ethanolic extract significantly increase in Tail-Flick Latency (TFL) within 2 hours post-drug administration. An experimental trial study has also been carried out to compare the antinociceptive effect of the hydroalcoholic extract of Ajwain with morphine sulphate using formalin test. Findings revealed that Ajwain extract exhibited antinociceptive effect on both early and late phases [9]. Similar study has been done on the Ajwain total essential oil which was significantly effective on the late phase of formalin test [10] and it may be due to the presence of thymol in essential oil. In addition, under a randomized controlled placebo control clinical trial, the herb essential oil was assayed for the analgesic effect in neuropathic feet burn. Results revealed that Ajwain essential oil significantly reduced the feet burn compared to placebo [11].

Antibacterial activity: Acetone and aqueous extracts of *Trachyspermum ammi* were tested against *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Salmonella typhimurium* and *Shigella flexneri* by using agar diffusion assay [12]. Methanolic extract of seed of *Trachyspermum ammi* tested against 11 bacterial species *Pseudomonas aeruginosa* and *Bacillus pumilus*; *Staphylococcus aureus* and *Staphylococcus epidermidis*; *Escherichia coli*, *Klebsiella pneumonia* and *Bordetella bronchiseptica* respectively and showed significant antibacterial activity [13].

Antifilarial activity: A methanolic extract of fruits of *Trachyspermum ammi* was exhibited activity against adult bovine filarial *Setaria digitata* worms. It's showed antifilarial activity against the human filarial worm *B. malayi* in *Mastomys coucha*, showing macro filaricidal activity. The research thus provided a new way for development of a macrofilaricidal drug from natural products [14].

Anthelmintic Activity: *Trachyspermum ammi* exhibited its effect against specific helminths, e.g. *Haemonchus contortus* in sheep and *Ascaris lumbricoides* in humans. Its anthelmintic activity is due to loss of energy reserves by interference with the energy metabolism of parasites through potentiation of ATPase activity. A contributory factor to its anthelmintic activity is due to possess cholinergic activity that interfere peristaltic movements of

the gut [15].

Insecticidal activity: It is reported that the essential oil extracted from the seeds of Ajwain can exhibit insecticidal activity in the oviposition step as well as egg hatching and developmental inhibitory activities against *Callosobruchus chinensis* [16].

Antiplatelet activity: *T. ammi* ethereal extract was found to inhibit platelet aggregation induced by arachidonic acid (AA), epinephrine and collagen. Inhibition of aggregation by ajwain could be explained by its effect on platelet thromboxane production (i.e. reduced Tx_{B2} formation in intact platelet preparations from added arachidonate and it also reduced the formation of Tx_{B2} from AA-labelled platelets after stimulation with Ca²⁺-ionophore A23187 by a direct action on cyclooxygenase) [17].

Antioxidant activity: The antioxidant and ameliorative property of Ajwain extract has been evaluated on hexachlorocyclohexane induced oxidative stress and toxicity in an *in vivo* investigation. Accordingly, results revealed that the dietary Ajwain extract would reduce the toxicity resulted from hepatic free radical stress [18].

Antihistaminic effect: Macerated, aqueous and ethanolic extracts and essential of *T. ammi* were studied on guinea pig tracheal chains. The results showed clear rightward shifts in histamine response curves which indicated a competitive antagonism effect of *T. ammi* at histamine H₁ receptors [19].

Gastro protective activity: Its digestive stimulant action exerted by produced a significant shortening of the food transit time. *Helicobacter pylori* cause pathogenesis of peptic ulcer and gastric cancer. Ethanolic extract of *Trachyspermum ammi* exhibited anti-bacterial effect against various strains of *Helicobacter pylori* hence produced gastro protective activity [20].

Antitussive activity: Antitussive activity of areoles of two different concentrations of aqueous and macerated extracts and carvacrol, codeine, and saline were tested by counting the number of coughs produced. Significant reduction of cough number obtained in the presence of both concentrations of aqueous and macerated extracts [21].

Abortifacient and galactogogic actions: There was a high risk of potential human foetus toxicity of *T. ammi*, based on teratogenicity observed in rat foetuses. *T. ammi* has also been traditionally used as a galactogogue in humans. The total phytoestrogen content of dry *T. ammi* seed was 473 ppm, which was the second highest in the list of eight herbs tested (total phytoestrogen contents 131-593 ppm) [22].

Anti-hyperlipidemic activity: The cardiovascular ailments have increased in most developed and underdeveloped countries of the world. These cardiac problems are directly associated with hyperlipidemia. During the last two decades, both retrospective and prospective studies have revealed link between levels of circulating lipids and mortality rates from coronary atherosclerotic heart disease. Numerous synthetic drugs have been reported having severe side effects. Anti-hyperlipidemic activity of methanol extract of *T. ammi* was evaluated and found that methanol extract of *T.*

ammi possesses lipid lowering action by decreased total cholesterol, LDL-cholesterol, triglycerides, total lipids. *T. ammi* seed powder more efficiently reduced total cholesterol by 71% and then, in the descending order, LDL-cholesterol by 63%, triglycerides by 53% and total lipids by 49% on post treatment Day 135. Researcher also recommended that the valuable effects of *T. ammi* on fat metabolism may be due to the considerable amounts of fibers in the *T. ammi* [23].

Antihypertensive, antispasmodic and broncho-dilating activity: The antihypertensive effect of *T. ammi* administered intravenously *in vivo*, and the antispasmodic and broncho-dilating actions *in vitro* have been evaluated. The studied of calcium channel blockade that has been found to mediate the spasmolytic effects and this property proved that this mechanism contributed to their hyperactive disease states of the gut such as colic and diarrhoea as well as in hypertension [24].

Anti-inflammatory potential: Anti-inflammatory principles of the total alcoholic extract (TAE) and total aqueous extract (TAQ) of the Ajwain seeds. TAE and TAQ exhibited significant ($P < 0.001$) anti-inflammatory activity in both the animal models. The weights of the adrenal glands were found to be significantly increased in TAE and TAQ treated animals. The TAE and TAQ extracts from the ajwain seeds exhibit significant anti-inflammatory potential [25].

Drug interaction: *T. ammi* seeds when taken with drugs such as abciximab, (ReoPro) antithrombin III, (thrombate III) argatroban, (argatroban) aspirin, (bufferin, ecotrin) aspirin and dipyridamole, (aggrenox) bivalirudin, (angiomax), clopidogrel, (plavix) dalteparin, (fragmin) danaparoid, (orgaran) dipyridamole, (novo-dipiradol, persantine) enoxaparin, (lovenox) eptifibatide, (integgrillin) fondaparinux, (arixtra) heparin, (hepalean, hep-lock) indobufen (ibustrin) may increase the risk of bleeding and bruising [26].

Toxicity and Teratogenicity: It was reported that Ajwain showed teratogenicity in rat fetuses. Therefore it may be harmful to be intake during pregnancy [27].

Conclusion

Whole of the pharmaceutical industry is now paying consideration towards design and development of new indigenous plant based drugs through searching of leads from traditional system of medicine. With reference to the mentioned pharmacological activities, Ajwain seeds can be used for clinical applications. However, in spite of various experimental and animal studies, lack of comprehensive clinical trials aimed on regarded effects still remains to reconfirm the traditional knowledge.

Conflicts of Interest

The author declares no conflict of interests.

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