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Pharmacological activity of *Trachyspermum ammi* : A Review

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ABSTRACT

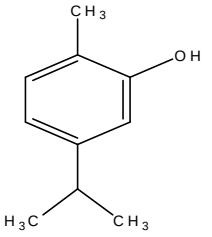
Ayurveda is an important system of medicine and drug therapy in India. Among traditional potential herbs, *Trachyspermum ammi* family Apiaceae commonly known as Ajwain is widely used for curing various diseases in both humans and animals. The active principle are extracted and purified for therapeutic utility for their selective and regulated activities. The quality control of herbal drug and their bio-constituents are of prime importance justifying their acceptability in modern system of medicine. *Trachyspermum ammi* is one of the most famous medicinal plants in the treatment of a large number of human ailments is mentioned in Ayurveda, Sushrita Samhita and Charaka Samhita. This review deals with the evidence-based information regarding the pharmacological activity of *Trachyspermum ammi.*

Keywords: Ayurveda, *Trachyspermum ammi*, Pharmacological activity

INTRODUCTION

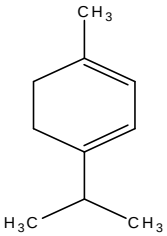
Consumers in general prefer to have food free from preservatives or added at low levels (1). Moreover, there has been a demand for food with long shelf life and without any risk of food contaminants. This warrants the use of natural preservatives as alternatives to chemical ones leading to increasing interest in testing natural compounds as antimicrobials for food preservation (2, 3). Accordingly, natural plant products with antimicrobial properties have obtained recognition for its possible applications in food in terms of preventing bacterial and fungal growth (4). Ajwain has characteristic aromatic smell and pungent test, and it's widely used as a spice in curries. It is employed either alone or in mixture with other spices and condiments. It is also used in pickles, certain types of biscuits, confectionery, beverages and pan mixtures (5). Ajwain is one of the aromatic seed spices, which is generally used for medicinal purposes as a digestive stimulant or to treat liver disorders. Thymol, the major phenolic compound present in Ajwain, has been reported to be a germicide, antispasmodic, and antifungal agent (6). The principle active constituents of the oil are the phenols, mainly thymol (35-60%) and some carvacrol. The Indian Pharmacopoeia requires Ajwain oil contain not less than 40% thymol. Thymol easily crystlizes from the oil on cooling and commonly known as *Ajwain ka phool* or Satajwain. The reminder of oil is called thymine on account of it's similarity with the corresponding portion of *Thyme vulgaris* (7).

The maximum requirement for volatile oil content is 1.2 %v/w with the phenol values not less than 0.5% expressed as thymol and calculated with reference to the anhydrous drug. The phenol in isolated oil is determined by reaction with amino pyrazolan and potassium ferricyanide in ammonical solution with subsiquent measurement of absorbance at 450 nm. A number of chemical reaction e.g. Thymol and carvacrol type are known and it is these phenol that are held largely responsible for the antiseptic, antitussive, and expectorant properties of thyme (8). Different researcher investigated the oestrogenic content of some herbs (including *T. ammi*) that are traditionally used to increase milk yield in dairy cattle (*T. ammi*.) has also been traditionally used as a galactogogue in humans (9). Thymol is a widely known anti-microbial agent. Due to its bactericidal action against oral bacteria, it is commonly incorporated in mouthwashes. Its action seems to be mainly related with harmful effects on both the cellular cytoplasmic membrane (perforation) and the generation of ATP (10, 11). It has also demonstrated a fungicide activity that could involve effects on the membrane (12). It is emphasized that, in lamiaceae plants, thymol is always accompanied by its isomer carvacrol (13). Thymol also has antiseptic activity and carvacrol possesses antifungal properties (14). It has been established that thymol and carvacrol inhibit the peroxidation of liposome phospholipids in a concentration dependent manner (15). It appeared that both isomers were equally effective in the autoxidation of lard at 35 °C at a concentration of 0.1% (16).



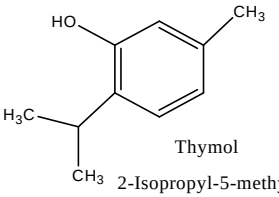
Carvacrol

5-Isopropyl-2-methyl-phenol



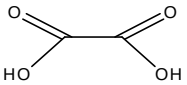
α Terpine

1-Isopropyl-4-methyl-cyclohexa-1,3-diene



Thymol

2-Isopropyl-5-methyl-phenol



Oxalic acid

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PHARMACOLOGICAL AND BIOLOGICAL ACTIVITIES

Traditional therapeutic uses of *T. ammi* fruits include: galactogogue, stomachic, carminative (18), Expectorant, Antiseptic (19), Amoebiasis, Antimicrobial (20), seeds fried in oil and used as a thin soup as a galactogogue (21), used in curing diarrhoea, Parasiticidal, and given in treatment of amenhorroea (22), Bronchitis, colic pain (23), Antipyretic, febrifugal (24). The seed of ajwain is bitter, pungent, and it acts as anthelmintic, carminative, laxative, and stomachic. It also cures abdominal tumors, abdominal pains, and piles (25). Catecholamines from the adrenal medulla would have contributed either to a stress associated release of ACTH or to a rise in intracellular cyclic AMP and catecholamine release is associated with enlargement of adrenal gland (26). Presence of terpenes, glycosides and sterols in plant has been found to exert active antiinflammatory effects (27).

Anti-lithiatic Properties

T. ammi in a list of 14 indigenous medicinal plants that were reported to have been used for abortion in some districts of Uttar Pradesh (India) in their survey conducted in 1987. Specifically, in the village of Kallipuschium, Lucknow district, 50 of the 75 pregnant women who were surveyed (of a total of 155 women in the fertile period) claimed to have used *T. ammi* seed for abortion. Investigated the oestrogenic content of some herbs (including *T. ammi*) that are traditionally used to increase milk yield in dairy cattle (*T. ammi* has also been traditionally used as a galactogogue in humans. (28).

Anti-hyperlipidaemic Activity

The cardiovascular diseases have increased several folds in most developed and underdeveloped countries of the world. These cardiac aliments are directly related to hyperlipidaemia (29). During the last two decades, both retrospective and prospective studies have shown correlation between levels of circulating lipids and mortality rates from coronary atherosclerotic heart disease several synthetic drugs have been reported having serious side effects (30). *Trachyspermum ammi* is reported to have platelet aggregation inhibitory action (31), antifungal potency (32) and blood pressure lowering action (33*).* Antihyperlipidaemic effect of *T.ammi* seed has been obtained in albino rabbits. It was assessed that *T. ammi* powder at dose rate of 2 g/kg body weight and its equivalent methanol extract were extensively effective lipid lowering action. *T. ammi* seed powder more effectively decreased 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. (34). Researcher also suggested that the beneficial effects of *T.* ammi on fat metabolism may be due to the considerable amounts of fibre' in the *T. ammi* (35).

Anti-inflammatory Effects

The study was obtaining the anti-inflammatory activity of the total alcoholic extract (TAE) and total aqueous extract (TAQ) from the seeds of *Carum copticum*. *Linn*. using rat models. These activity exerted by TAE and TAQ extracts suggest that they could have acted by affecting kinnin, prostaglandin, bradykinin and lysozyme synthesis. Its efficacy to inhibit the inflammation might be due to an increase in the number of fibroblasts and synthesis of collagen and mucopolysaccharides during granuloma tissue formation (36)**.** TAE and TAQ in 100 mg/kg doses exhibited significant ($P<0.001$) antiinflammatory activity in both the animal models. (37).

Antibacterial Activity

The present invention relates to a novel synergistic composition useful in the treatment of drug resistant bacterial infections. The composition comprises an effective amount of thymol, a mixture of the essential oils of *Mentha arvensis* and *Mentha spicata* or their monoterpene components in appropriate ratio and conventional additives. The composition is useful in the treatment of drug resistant enteric and systemic infections. The formulation with enhanced activity of thymol action comprises thymol in combination with the oil which is a combination containing the rare mixture of carvone, limonene and menthol. The invention also provides methods of producing the composition and a method of using thymol obtained from the seeds of the plant *Trachyspermum ammi* (Ajwain) as a fourth generation antibiotic formulation for control of drug resistant bacteria. More particularly, the invention relates to the use of a compound 'Thymol' isolated from the oil distilled from the seeds of the plant *Trachyspermum ammi* (Ajwain) to kill the bacteria resistant to even prevalent third generation antibiotics and multi-drug resistant (mdr) microbial pathogens and thus useful as a plant based fourth generation herbal antibiotic formulation (38).

Most of the gram-positive bacteria, such as *B. cereus, B. subtilis, S. aureus, and L. monocytogenes*, showed good inhibition action when compared to gram-negative bacteria (e.g. *E. coli and P. aeruginosa*). Generally, gram-negative bacteria have been reported to be more resistant than gram-positive samples to the antimicrobial effect of essential oils given the differences in the lipopolysaccharide constitution of their cell walls (39). A number of hypotheses have been put forward which involve hydrophobic and hydrogen bonding of phenolic compounds to membrane proteins, followed by partition into the lipid bilayer, perturbation of membrane permeability, membrane disruption, destruction of electron transport systems, and cell wall perturbation (40 -41).The high activity of the phenolic component may be further explained in terms of the alkyl substitution into phenol nucleus, which is known to enhance the antimicrobial activity of phenols. Phenolic compounds, such as thymol and carvacol, are known to be either bactericidal or bacteriostatic agents depending on the concentration used (42).

Antifungal Activity

The Ajwain Ethanol Extract (AEE), which was prepared from Ajwain seeds, was assessed for antibacterial and antifungal activity against selected pathogenic bacteria and fungi by agar well diffusion assay. The antifungal activity of the AEE was tested at different growth periods. The spore suspension from *A. ochraceus* CFR 221 was in-

oculated on PDA by spread plate technique. AEE (12.5 mg) was added into the fungus-seeded plate in agar wells on days 1, 2, 3, 4 and 5, and the treated plates were incubated at room temperature (28 ± 2 °C) for 7 days, and observed for zone of inhibition. Fungal toxicity was measured in terms of percentage of mycelia inhibition calculated. According to the following formula the Inhibitory effects of Ajwain ethanolic extract on *A. ochraceus* growth and ochratoxin production.

Percentage of mycelial inhibition = [(dc - dt) / dc] × 100

dc and dt are the average diameter of mycelial colony of control and tested sets, respectively(43) .The antifungal activity of the AEE was studied by agar well assay against various fungi (*A.flavus, A. ochraceus, A. niger, A. orzyae, Fusarium moniliforme, Penicillium* sp.) (44).

Nematicidal Activity

Pine wilt disease, caused by the pinewood nematode (PWN), *Bursaphelenchus xylophilus*, is the most serious problem in Korean forests. In the nematicidal constituents of oils were identified by GC-MS analysis. Among identified components of Ajwain oil, nematicidal activity of pinene, camphene, pinene, myrcene, limonene, terpinene, terpinen- 4-ol, thymol and carvacrol against PWN have been reported in a previous study (45). Reported that PWN bodies treated with the muscle activity blockers levamisole hydrochloride and morantal tatrate usually exhibited semicircular and coiling shapes, respectively (46). Amino and hydroxyl groups have been hypothesized as target sites of methyl isothiocyanate in nematodes (47). Some essential oils have been reported to interfere with the neuromodulator octopamine (48) or GABA-gated chloride channels of insect pests (49).Thymol and carvacrol were very effective against PWN. These studies confirm that the nematicidal activity of Ajwain oil was mainly attributed to the activity of thymol and carvacrol (50).

Anthelmintic Activity

Thymol might exert its anthelmintic activity by interference with the energy metabolism of parasites through potentiation of AT-Pase activity and thus loss of energy reserves (51). A dose-dependent response was observed with the crude powder of *T. ammi* which exhibited maximum (78.1%) reduction in egg count at 3 g/kg on day 5 post treatment, followed by a smaller (53.3%;) reduction with the crude aqueous extract (CAE) treated group at 3 g/kg on day 10 post treatment. An increase in the dose of both crude powder (CP) and CAE resulted in an increase in and earlier onset of the anthelmintic activity. The anthelmintic activity of CAE of *T. ammi* was, however, more persistent compared with that of CP. The standard anthelmintic agent levamisole exhibited much higher reduction (99.2%) in egg count at 7.5 mg/kg. The first scientific evidence of anthelmintic activity of *T. ammi* in mixed natural helminth infestations in animals, although preliminary studies of its effect against specific helminths, e.g. *Ascaris lumbricoides* in humans and *Haemonchus contortus* in sheep, have been reported (52, 53). The plant has also been reported to possess cholinergic activity, which might also be a contributory factor to its anthelmintic activity, with added effect from the known facilitatory effect of cholinergic agents on the peristaltic movements of the gut, thus helping in expulsion of intestinal parasites (54, 55).

Digestive stimulant actions

The addition of *T. ammi* to the diet reduced food transit time from 780 minutes (control) to 554 mins, a 29% reduction ($p<0.05$). The dietary spices that markedly reduced the food transit time also enhanced the activity of digestive enzymes and/or caused a higher secretion of bile acids. They suggested that the reduction in food transit time could probably be attributed to an acceleration of the overall digestive process as a result of increased availability and potency of digestive secretions (56).

Abortifacient activity

T. ammi that were identified as being commonly used as abortive plants from a survey in and around the villages of Uttar Pradesh.The *T. ammi* seed aqueous extract dosed at 175 mg/kg in rats (n=5) was 62.5% effective as an abortifacient. In cases where pregnancy was continued in spite of herbal drug administration, foetuses showed various skeletal defects and several other visceral defects; they expressed concern at the remarkable potential of the putative abortifacient herbal drugs to affect foetuses adversely, and the large number of people in rural areas of India who continue to be exposed to these plants without being fully aware of the potential side effects (57).

Hypotensive activity

T. ammi seed was ground into a coarse powder and extracted at room temperature for three Days in 70% aqueous methanol; (yield about 13% based on dry seed). The test substances injected included *T. ammi* at doses of 3.0, 10.0, 30.0 and 100.0 mg/kg, and acetylcholine. The *T. ammi* extract administered Intra veinas was found to cause a dose-dependent hypotensive effect ranging from about 6% reduction in mean arterial blood pressure (BP) at a dose of 3.0 mg/kg to about 42% reduction in mean arterial BP at a dose of 100.0 mg/kg. Acetylcholine also caused a hypotensive effect at 1 µg/kg comparable in magnitude to the effect *of T. ammi* extract at 30.0 mg/kg (58).

Detoxification of aflatoxins by *Trachyspermum ammi*

Aqueous extracts obtained from leaves/seeds of various medicinal plants were evaluated for their ability to detoxify aflatoxin G1 (AFG1) by thin-layer chromatography and enzyme-linked immunosorbent assay (ELISA), the seed extract of Ajowan (*Trachyspermum ammi* (L.) showed the maximum degradation of AFG1 up to 65%. The aflatoxin detoxifying activity of the *T. ammi* extract was significantly reduced upon boiling at 100 ^{0}C for 10 min. Significant levels of degradation of other aflatoxins viz., AFB1 (61%), AFB2 (54%) and AFG2 (46%) by the dialyzed *T. ammi* extract was also observed. Time course study of AFG1 detoxification by dialyzed *T. ammi*

extract showed that more than 78% degradation occurred within 6 h and 91% degradation occurred 24 h after incubation (59).

CONCLUSION

Major thrust by whole of the pharmaceutical industry is focused towards design and development of new innovative/indigenous plant based drugs through investigation of leads from traditional system of medicine. Recent years, ethno-botanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. It is best classical approach in the search of new molecules for management of various diseases. Thorough screening of literature available on *Trachyspermum ammi* depicted the fact that it is a popular remedy among the various ethnic groups, Ayurvedic and traditional practitioners for treatment of ailments. Researchers are exploring the therapeutic potential of this plant as it has more therapeutic properties which are not known.

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