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General Article

AJWAIN (*TRACHYSPERMUM AMMI*): BRIDGING TRADITIONAL KNOWLEDGE AND MODERN PHARMACOLOGY

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ABSTRACT

Trachyspermumammi (L.) Sprague ex Turrill (Apiaceae) with common name Ajwain is an important medicinal plant, extensively used in Indian Ayurvedaas well as Chinese and Persian medicines. The ethnobotanical significance of the plant is evident from the numerous traditional uses attributed to this plant. It has been widely used in traditional ayurvedic medicine to treat abdominal pains, coughs, headaches, heartburn, asthma, diarrhea, cholera, atonic dyspepsia, bronchial problems, spleen disorders, worm infestation, flatulence, lack of appetite, piles and used to facilitate as a galactagogue and post-partum recovery in women. The present review provides deeper insights into the ethnobotany, geographical distribution, phytochemistry, pharmacological activity and, toxicity of *Trachyspermumammi (TA)*. Phytochemical analyses have identified bioactive compounds within the root bark, stem branches, leaves, and fruits of TA. The comprehensive review of the TAhas provided insights into its ethnopharmacological and therapeutic applications. The main bioactive principles identified are terpenoids, flavonoids, sugars, glycosides, phenylpropanoids, alkaloids, phenols and phenolic glycosides. The plant possesses varied pharmacological effects particularly, antioxidant, anti-inflammatory, anti-proliferative and anti-microbial, antihypertensive, bronchodilator, and anti-hyperlipidemic agent due to its potent bioactive compounds like thymol, p-cymene, phyllandrene. Traditionally, the plant is used to treat and relieve ailments like abdominal pains, abdominal tumors, amenorrhea, asthma, atonic dyspepsia, bronchial problems, flatulence, piles, etc.Extensive literature survey reveals that multiple demographics have leveraged *Trachyspermumammi* globally and the plant possess varied pharmacological activities. Very few studies have been reported on the scientific evidence of the traditional uses of the plant. Delving deeper into its pharmacological effects andfilling existing research gaps regarding its traditional uses are important. Moreover, broader research on safety is needed to support clinical application.

Keywords: *Trachyspermumammi*, phytochemical constituents, Therapeutic potential, Toxicity, pharmacological activities.

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Introduction

Trachyspermumammi (L). family (Apiaceae) is an important medicinal herb, extensively used in Indian Ayurvedic, Chinese, and Persian medicine emphasizing the importance of the plant's versatility in traditional healing practices across different cultural contexts (Vitali et al., 2016). The Ayurvedic text Charak Samhita mentions the Ajwain extract as Admoda Arka, underscoring its efficacy in alleviating colic and pain, enhancing digestive fire, and relieving anorexia (Saraswat et al., 2020). The plant, originally indigenous to Egypt, is extensively grown in Asian countries like India, China, Pakistan, Afghanistan, and Iran, as well as in European countries such as Sweden, and Northern Africa (Modareskia et al., 2022). The plant is known by various vernacular names.In Sanskrit, it is referred to as "Yamani," while in English, it is called Ajwain, Ajowan, and Lovage. In different languages, it goes by names such as Ajmud, Ajmoda, Ajamodhavoma, Bishop's weed, Carom, Ethiopian cumin, Xi Ye Cao Guo Qin, Adiowa, and Agyptischer (Lim, 2012). The Plant List, an online resource developed by the Global Strategy for Plant Conservation and the World Flora Online, documents approximately 29 Latin synonyms for *T. ammi*. Some of these synonyms include *Carom copticum* (L.) Benth & Hook.f. ex Hieren, *Apium ammi* Urb., *Ammi copticum* L., and *Trachyspermumcopticum* Traditionally, the plant has been utilized as a multifunctional ethnomedicine, offering various remedies for a wide range of ailments. These include abdominal pains, coughs, headaches, heartburn, asthma, diarrhea, cholera, atonic dyspepsia, bronchial problems, spleen disorders, worm infestation, flatulence, galactagogue, lack of appetite, piles, etc. The initial utilization of the plant worldwide stemmed from its recognized abilities as purgative and in facilitating the evacuation of kidney stones (Goyal et al., 2022). The seeds of the plant are shown to have carbohydrates, fiber, glycosides, tannins, saponins (Asif et al., 2014). The oil extracted from *T. ammi* leaves and flowers are characterized by significant constituents such as iso-thymol (51.1%), p-cymene (14.1%), thymol (13.0%), limonene (11.8%), and γ-terpinene (6.8%) (Kambouche& El-Abed, 2003a) The aromatic spice is utilized as an important culinary spice because of its high nutritional and medicinal value. Pharmacological studies have reported antioxidant, antibacterial, anti-fungal, anti-cancer, immunomodulatory, antispasmodic, anti-flatulent, anti-diabetic, anti-filarial, antirheumatic, hepatoprotective, and neuroprotective properties (Timalsina et al., 2023). Thymol has been identified as the key monoterpene responsible for the activities (Anusha et al., 2024). Recent research confirmed the utilization of *T. ammi* plant parts in the synthesis of gold and silver nanoparticles for enhanced biological activity. While *T. ammi*is employed in traditional medicine for numerous ailments, its effectiveness must be rigorously assessed. The paper explores the ethnobotanical uses, nutritional properties, isolation and characterization of active phytoconstituents, and pharmacological attributes. There is a pressing need to collect comprehensive information and compile the review which can lead to drug discovery and therapeutics for various diseases.

Botanical Profile of *Trachyspermumammi L.*

T. ammi, an annual herb and mesophyte, grows to a height ranging from 25 to 65 cm. The stems are grooved, glabrous, slender, and striate; the leaves are rather distant, feather-like, and pinnately divided. It features tiny white or pinkish petal flowers in umbels that are borne in terminal or seemingly lateral stalks that develop into small, oval-shaped fruits

housing ridged seeds. (The World Flora Online database). The fruits are ovoid, aromatic, greyish brown, 2mm long, and 1.7mm(Bairwa et al., 2012). The fruit's mericarps are compressed, marked by pronounced ridges and a tubercular texture, and they have a distinctly sharp and bitter taste.(Bekhechi et al., 2010). Endospermis made of polygonal cells with oil globules (Bhutya RK, 2011). The striking similarity in aroma between the seeds of *T. ammi* and the leaves of *Plectranthusambonicus* commonly known as Indian Borage, the plant is mistaken in scientific literature as the Coleus ambonicus belonging to the family Lamiaceae. Figure 1 depicts the *Trachyspemumammi* leaves, inflorescence, and seeds.

Origin

Ajwain distributed across the arid and semiarid regions including the Mediterranean Sea and in Southwest Asian countries such as India, China Iran, Afghanistan, Pakistan, and Iraq, Sweden and Northern Africa (Naquvi et al., 2022). Though the plant is indigenous to Egypt, it was spread to other parts of the world during the Greek conquest of central Asia. In India, the plant is widely grown in Madhya Pradesh, Andhra Pradesh, Gujarat, Rajasthan, Uttar Pradesh (Asangi et al., 2023).

Habitat

The growth of the ajwain plant is favored by moist soil conditions and it displays versatility in adapting to different soil types such as loamy, black, and sandy soils, even those with high salt content. Depending on the geographic region, it can be cultivated as a summer crop or a cold-season crop in hilly areas. In India, the cultivation of ajwain is influenced by both natural rainfall and irrigation methods, ensuring its successful growth (Rajeshwari et al., 2011). Native to the Indian subcontinent and the Near East, ajwain is a herbaceous plant with the scientific name *Trachyspermumammi*.

Propagation

Trachyspermumammi is cross pollinated crop, exhibiting a somatic chromosome number of 2n = 18. The plant relies on insects for cross-pollination, as the absence of this process can result in self-fertilization. Optimal sowing time is crucial for maximizing *T. ammi*'s genetic potential, impacting seed and oil productivity (Meena et al., 2018). The experiment using licorice aqueous extract at a concentration of 40 g/L and Moringa ethanol extract with a concentration of 100 g/l (L3 x M2) showed the most favorable essential oil content, L/g and L/area of the oil, and thus the favorable influence of these concentrations on the production of essential oils(El-Ghait et al., 2021). Indian studies affirm that seeding on October 30 th produces much better outcomes than colonizing on October 15 th and November 14 th due to the supporting climatic conditions. The sowing on the 1st of September in the Southern Telangana region of Andhra Pradesh one of the states of India has the highest yield, making it very important to sown at the right time. The best sowing time of Ajwain in different areas depends on various reasons such as weather, suitability of the soil and requirements of the variety. Ajwain is also spreading in Algeria and established itself in the Algerian agricultural setting. Algeria has a benefiting atmosphere to the growth of this aromatic plant since it is a great contribution to local agricultural practices. Hot and dry summer and warm and moist winter climatic conditions characterize the climate, similar to that of its original natural habitat. Realizing the gastronomic and medicinal importance of ajwain, Algerian farmers have devoted themselves to its growing.

Table 1. Ethnobotanical uses of *Trachyspermumammi L.*

Medicinal uses	Part(s) used	Traditional preparation	Region of use	Reference
Digestive aid, relieving stomach discomfort	Seeds	Ground seeds, infused in tea	India, Pakistan	(Siddiquie et al., 2024)
Antispasmodic, stimulant, carminative	Seeds	Fruits mixed with milk or water	Mauritius	(Mahomoodally et al., 2019)
Respiratory ailments	Leaves	Fresh or dried leaves, brewed into tea	Middle East, Egypt	(Chahal et al., 2017)
Relief from indigestion, gas, and bloating	Essential oil	Inhalation, massage oil	Ayurveda (Indian subcontinent), Middle Eastern cuisine	(Moein et al., 2015)
Diuretic	Root	-	India, Pakistan	(Asif & Hashmi, 2021)
Anti-helminthic	Leaves	Infusion	Middle East, Egypt	(Bagherivand et al., 2024)
Epilepsy	Leaves, Roots	-	Middle Eastern cuisine	(Monfared et al., 2020)
To regain strength after delivery	Fruits	Ajwain is mixedwith jaggery and ghee	India	(Johari, 1994)
Piles	Fruits	Seed balls made along with jaggery	India	(Vharamble et al., 2023)
Dipsomania	Leaves	Aqueous leaf extract	India, Egypt	(Mahale et al., 2022)
Tonsillitis	Leaves, Roots	Aqueous Extract of roots and leaves	India	(S. A. Jan et al., 2015)

Ethnobotanical uses

In traditional medicine, every part of the plant is employed to address various health conditions. Using ethnobotanical survey, *T. ammi* L. was found to be a significant culinary herb with exceptional application in the management of primarily colic, and gastrointestinal disorders. It has been reported to act as a galactagogue, uterine tonic, diuretic, and antiemetic, and possesses wound-healing properties (Goyal et al., 2022). Most of the tribes in India have been using this plant for treating various gynecological problems(H. A. Jan et al., 2020)and

used to treat boils and epilepsy and acts as a powerful vermifuge (Kaushik et al., 2023). Other nations' ethnomedicine also recognizes the significant contributions *T. ammi*, or ajwain, has made to conventional medical procedures. Ajwain is extensively used in Indian and Pakistani ethnomedicine to treat digestive problems such as gas, bloating, and acidity. Furthermore, due to Ajwain's expectorant qualities, traditional healers in Pakistan frequently suggest it as a treatment for respiratory conditions like bronchitis and coughs (Siddiquie et al., 2024) and is also used in Bangladesh to treat a variety of illnesses, such as irregular menstruation, discomfort following menstrual irregularities, postpartum discomfort, and lactation aid for breastfeeding moms(Das, 2023). Ajwain's alleged antibacterial and antifungal properties are beneficial for treating wounds and various skin ailments. In traditional ethno-veterinary practices, the seeds are employed to relieve diarrhea, indigestion, and constipation. They are given orally to enhance strength and improve milk yield (Sharma et al., 2024).

Nutritional Uses

The nutritional analysis of seed indicated to have energy value of 314.55%, carbohydrates (47.57%), protein content (20.23%), fat content (4.83%), moisture content (11.6%), fiber (4.3%), ash (11.5%) (Javed et al., 2012)].*T. ammi* leaves exhibiting high anti-oxidant activities are consumed by the local people(H. A. Jan et al., 2020). The leaves of the plant are identified as the rich source of phenolic compounds, flavonoids and carotenoids and terpenoids (Saraswat et al., 2020). Seeds of the plant contain Vitamin B and Vitamin C and also include various minerals like cobalt, manganese, and iron.

Phytochemistry

Ajwain seeds comprises carbohydrates (38.6%), fat (18.1%), protein (15.4%), fiber (11.9%), and various phytochemicals such as tannins, glycosides, moisture (8.9%), saponins, flavones, and mineral matter (7.1%). Further, contain important minerals like calcium, phosphorus, iron, cobalt, copper, iodine, manganese, thiamine, riboflavin, and nicotinic acid (Zarshenas et al., 2014). Gas chromatography and mass spectrometry (GC-MS) analysis of hydro distilled volatile oil showed the presence of 17 constituents in the oil of which thymol (39.36%) and γ-terpinene (30.97%) were the major constituents. The total percentage of identified compounds was 99.20%. The GC analysis of distilled volatile oil indicated p-cymene 18.49% - 22.82%, γ-terpinene 22.44%-33.50%, and thymol 37.42%-48.42% as major constituents (Shahrajabian & Sun, 2024). In the study conducted on Ajwain seeds of 23 ecotypes from the gene bank of RIFR, Iran, P-cymene, γ-terpinene, and thymol were found to be in higher concentration (Mirniyam et al., 2022). Flavonoids, terpenoids, and polyphenols are found in various plant extracts and the results revealed how these phytochemicals' abundance changes with the seasons (Saxena, 2015). Interestingly, it has been discovered that one specific phytochemical was seen in large quantities during specific seasons, suggesting seasonal changes in the chemical composition of the plant. In addition, it is found some important compounds that ajwain contained in both its vegetative and flowering stages, suggesting insights into many stages of the plant's growth and development and how they affect the chemical composition of the plant. This study sheds important light on the bioactive elements of ajwain, which may have consequences for both its culinary and medical applications. Hydro-distillation process from the aerial parts of the plant (leaves and Inflorescence) shown to contain isothymol (51.1%), p-cymene (14.1%), thymol (13.0%), limonene (11.8%) and γ-terpinene (6.8%) as major constituents (Kambouche & El-Abed,

2003). Another study by Singh et al., 2004, related to Ajwain essential oil has been found to contain 26 identified components, which collectively account for 96.3% of the total composition. The major component is thymol (39.1%), followed by p-cymene (30.8%) and γ-terpinene (23.2%), along with α-pinene (1.7%) and terpinene-4-ol (0.8%). The highest phenolic content in *T. ammi* was noted with microwave-assisted extraction (MAE), while the highest total phenolic content (TPC) of 1860 ± 31.2 mg GAE 100g DW−1 was achieved using 100% methanol with ultrasonic-assisted extraction (UAE) for 20 minutes. R3Og was subsequently encapsulated within whey protein isolate (WPI) using heat gelation and characterized by FT-IR and SEM. A kinetics study indicated a pH-independent release behavior of R3Og from the WPI matrix, suggesting that the release was controlled by the Pharmacological activities of *T. ammi*

Microbial Inhibitory Effects

The growing worldwide threat of multiple drug resistance (MDR) in bacteria and other pathogens and the occurrence of novel infectious diseases present the greatest challenges in the context of treatment that increases the mortality rates. In such desperate condition, the application of bioactive compounds isolated in medicinal plants has been considered to be a niche in counter-measuring the MDR without causal side effect (Moiketsi et al., 2023) It is in this context that medicinal plants have been effective as anti-microbial agents due to their diverse activity against the broad range of bacteria, fungi and viruses. *T. ammi* seed extract and oil were also discovered to have a potent antimicrobial activity against diverse bacteria, including*; B. subtilis*, *S. aureus*, Bacillus phage CP5, *P. aeruginosa*, *S. dysenteriae*, *E. coli* and S. *aureus(Shin et al., 2018)*. Thymol and Carvacrol are reported as the key active principles with this property (Ardestani et al., 2020). Thymol demonstrates capacity to fight multi-drug-resistant microbial pathogens and demonstrates the prospect of food safeguarding the food stuff against the food spoilage (Hajibonabi et al., 2023). The plant extracts were also more effective against antibiotic-resistant pathogenic bacteria such as two gram-positive bacteria; Bacillus cereus (ATCC 1298), Staphylococcus aureus (ATCC 1189), and four gram-negative bacteria; Pseudomonas aeruginosa (ATCC 27853), Escherichia coli (ATCC 35218), Acinetobacter baumannii (ATCC 1611). Only Thymol and Carvacrol showed good inhibitory effect against the multi-drug-resistant Acinetobacter baumannii isolate with a minimum inhibitive concentration less than 500ug/mL. The hexane fraction in the ethanolic extract and thymol which had a high in vitro and in vivo anti- candidal activity. The lowest concentration of hexanes fraction with an inhibitory effect was identified as 225 mg/mL, which exhibited the same strength as that of the standard drug amphotericin B (200 mg/mL)(Wahab et al., 2021). Thymol, g-terpinene and p-cymene found to be the chemical composition of the *Trachyspermumammi*seed oil. Ajowan volatile oil was sensitive to Streptococcus pneumoniae bacteria with a minimum inhibitory concentration (MIC) of 0.125 to 0.5mg/mL. Synergy was also noticed between thymol and ciprofloxacin, although this was only apparent against P. aeruginosa and the penicillin-resistant Streptococcus pneumoniae clinical isolate.

Digestive Stimulant

The traditional utilization of *T. ammi* in Mexican medicine, Chinese medicine, and Ayurvedic medicine for over a century has predominantly focused on reliving the bloating, indigestion flatulence and abdominal pain. The versatile property and distinctive flavor of

Ajwain contribute to its importance as both a culinary and medicinal ingredient in various cultures(Khan et al., 2010). According to Ayurvedic principles, *T. ammi* has a pungent taste and heating energy, making it valuable for balancing Kapha and Vata doshas(Das, 2023). It is as an effective remedy for Kapha-related digestive concerns, including slow digestion, stomach heaviness, and excessive mucus production. Ayurvedic practitioners commonly prescribe a combination of *T. ammi* with ginger and cumin to synergistically enhance its digestive benefits, and digestive stimulant action, a study on the influence of spices on digestive enzymes like lipase, amylase, and chymotrypsin of rat pancreas and small intestine was conducted. The enzymes enhanced the activity when the ajwain was at the site of action[(Goyal et al., 2022).

Gastroprotective Effects

Gastric hyperacidity and ulceration are characterized by a repetitive cycle of healing and re-exacerbation (Asaad et al., 2024).Traditionally, Ajwain seeds boiled in water have been used to treat indigestion, bloating, and dyspepsia. The mucus neck cells are responsible for the secretion of mucus in the stomach and acts like a first line of defense, protecting the gastric mucosa from physical damage and hydrogen ion back diffusion. Mucopolysaccharides present in the mucus secretion have been enhanced when the TA is given to the animals and may contribute to the ulcer-protective effects of *T. ammi* fruit(Kumar & Singh, 2021)].

Antioxidant effects

T. *ammi* seed extract possessed a high DPPH radical scavenging activity and a moderate H_2O_2 radical scavenging activity (Goswami & Chatterjee, 2014). The presence of various phytochemicals in TA like alkaloids, phenols, phytosterols, and saponins is shown to exhibit free radical scavenging potential and oxidative DNA damage preventive activity (Saxena, 2015). The seed extract of *Trachyspermumammi* is highly regarded for its exceptional antioxidant prowess. Research findings indicate its proficiency in neutralizing hydrogen peroxide (H_2O_2) radicals with moderate efficacy and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals with a notably high capacity. This underscores its ability to effectively counteract harmful free radicals within the body, which are notorious for inducing oxidative stress and causing cellular damage. The antioxidant potency of TA is attributed to the presence of various phytochemicals, namely saponins, phenols, alkaloids, and phytosterols. These natural compounds collectively play a pivotal role in safeguarding cells against oxidative DNA damage, thereby upholding cellular integrity and mitigating the risk of debilitating conditions such as cancer and cardiovascular diseases. In light of its remarkable antioxidant properties, TA emerges as a valuable natural remedy for enhancing overall health and well-being. Its ability to combat free radicals effectively positions it as a promising intervention to support bodily health and mitigate the onset of oxidative stress-related ailments. Incorporating TA into one's wellness regimen may prove instrumental in fostering longevity and vitality(Ranjbaran et al., 2019). The effects of oral administration of TA extract in collagen-induced arthritis (CIA) rat models reduced oxidative stress markers and inflammation while enhancing enzymatic antioxidants (Umar et al., 2012). Thymol present in the hexane extracts demonstrated stronger antioxidants from leaves and fruits respectively (Suryawanshi et al., 2015).

Anti hyperlipidemic Properties

Ajwain water is traditionally used in reducing the high amounts of cholesterol(Grover, 2021). An *in vivo* study in the albino rabbit model and in hyperlipidemia rat modelsindicates that ajwain seed powder, methanolic and aqueous extracts of TA is highly effective in improving lipid profiles, leading to reductions in total cholesterol, LDL-cholesterol, triglycerides, and total lipids. Furthermore, the organic extract of the seeds was found to lower the atherogenic index while increasing HDL-cholesterol levels in albino rabbits (Javed et al., 2012) and induced when administered orally at 3g/kg and 5g/kg for 21 days (Saleem et al., 2017). Ajwain intake of hyperlipidemic patients reduced LDL cholesterol by 8.9% and increased HDL cholesterol by 13.1% and was found to be effective for primary hyperlipidemia. T.*ammi* is shown to possess the chemopreventive potential against carcinogenesis. The different concentrations of the seed extract have significantly reduced the DMBA induced skin, B (a) P induced for stomach papillogenesis compared to the control groups.(De La Chapa et al., 2018)

Anti-inflammatory Effect

Research has demonstrated that both the total alcohol and aqueous extracts of ajwain exhibit significant anti-inflammatory effects on carrageenan-induced edema in a rat model. Additionally, the aqueous extract of T. *ammi* seeds was shown to influence inflammatory gene expression in the cartilage tissue of rats with collagen-induced arthritis, resulting in a reduction of Cox-2 mRNA levels. No toxicity was observed in acute and sub-acute toxicity studies, which (El-Ahmady et al., 2021) included assessments of relative weight and histopathological analysis. The fruit extract of T. ammi displayed notable anti-inflammatory potential, with an LD50 exceeding 3000 mg/kg (Saraswat et al., 2020).

Abortifacient and Galactagogue Effect

A survey conducted in Uttar Pradesh, India, indicated that *T. ammi* is among the indigenous medicinal plants traditionally used for abortion, and studies on teratogenicity in rat fetuses suggest it carries a significant risk of fetotoxicity (Balkrishna et al., 2024). Traditionally, ajwain has also been employed as a galactagogue for both dairy cattle and humans. The total phytoestrogen content in dry *T. ammi* seeds was measured at 473 ppm, ranking as the second highest among eight herbs evaluated (Kaur & Arora, 2010)

Hepatoprotective and Antiplatelet- Aggregatory Activities

T. ammi was shown to provide 80% protection in mice against a normally lethal dose of paracetamol (1 g/kg) and successfully normalized elevated serum liver enzyme levels induced by CCl_4-related liver damage in rats (Balkrishna et al., 2024). In antiplatelet aggregation studies conducted *in vitro* using blood from human volunteers, a dried ethereal extract of *T. ammi* seeds inhibited platelet aggregation triggered by arachidonic acid, collagen, and epinephrine. This research aims to support the traditional use of *T. ammi* for women following childbirth (Dubey & Kashyap, 2015).

Nematicidal Activity and Antihelmintic Activity

Ajwain oil constituents, such as camphene, pinene, myrcene, limonene, terpinene, terpinen-4-ol, thymol, and carvacrol, have been demonstrated to have nematicidal activity

against pinewood nematode (PWN) *Bursaphelenchusxylophilus* which is known to cause Pine wilt disease. It has been postulated that amino and hydroxyl groups are target sites of methyl isothiocyanate in nematodes. Moreover, certain essential oils are also reported to alter the action of the neuromodulator octopamine or GABA-gated chloride channels in insect pests. Of these constituents, thymol and carvacrol are the most useful against PWN. These investigations show that the nematocidal properties of the ajwain oil are mainly triggered by the influence of thymol and carvacrol (Karvandi et al., 2023). The *T. ammi*antihelminthic has been proven to be active against certain helminths, including Ascaris lumbricoides in humans and *Haemonchuscontortus* in sheep. Such an anthelmintic action is thought to be the result of an inhibition of the energy metabolism of the parasites, an increase in ATPase activity, and a depletion of the energy stores of the parasites. Also, the plant has been reported to possess cholinergic effects, known to stimulate gut peristaltics and thus, help to expel intestinal parasites. This increased gut motility can also add to its total anthelmintic effects (Akhade& Jadhav, 2015).

Neuroprotective Effects

Medicinal plants have a long history of clinical use due to their increased tolerance and better therapeutic potential. Thymol, a major component of T. *ammi* seed extract, has neuroprotective effects. Oral administration of T.*ammi* seed extract (250 and 500 mg/kg), thymol (50 and 100 mg/kg), vehicle, and positive controls was given to pregnant mice. The supplementation markedly increased the expression of early neurogenesis markers and brain-derived neurotrophic factor (BDNF) in the postnatal day 1 in the pups' brains. Similarly, the P12 pups' brains had significantly higher levels of BDNF. Additionally, the P12 pups' brains had noticeably enhanced levels of BDNF. Further, in primary hippocampal cultures, TASE (75 and 100 μg/mL) and thymol (10 and 20 μM) increased the neuronal polarity, early neurite arborization, and maturation of hippocampal neurons in a dose-dependent manner. This reduction of TASE and thymol stimulation of neurite extension by the selective Tropomyosin receptor kinase B (TrkB) inhibitor ANA-12 (5 mM) suggested that the TrkBsignaling was involved (Timalsina et al., 2023). The bioactive principles within the TA offered neuroprotection to the cells by regulating pathways of oxidative stress, mitochondrial membrane potential, and it was also reported to be strong inhibitors of acetylcholine esterase enzymes by being competitive/mixed-type of inhibitors. The experiment had demonstrated to decrease the ROS and recovery of MMP (Mitochondrial Membrane Potential) in induced oxidatively stressed neuroblastoma cell lines.Furthermore, the extracts exhibited anti-acetylcholinesterase (AChE), anti-oligomerization, and anti-fibrilization activities. When comparing the two pure compounds, both demonstrated comparable effects in inhibiting Aβ-fibrilization, reducing reactive oxygen species (ROS), and providing neuroprotection. However, carvacrol was identified as a more potent inhibitor of AChE, being approximately ten times stronger than thymol. Carvacrol inhibited the enzyme through mixed-type inhibition, whereas thymol acted through competitive inhibition (Asangi et al., 2020).

Immunomodulatory Activity

T. *ammi* seed extracts possess immune stimulant and immune modulatory effects in altering skin thickness in rats. Additionally, studies have highlighted the presence of immunomodulatory components in T.*ammi*, such as ajowan glycoprotein (Agp), which induces proliferation of B-cell enriched murine splenocytes and activates macrophages to

release nitric oxide and promote phagocytosis, showcasing its immunomodulatory properties(Razzak, 2020).

Toxicological effects

T.*ammi* is usually regarded as safe to consume in moderation. However, certain toxicological effects could result from overindulgence or allergic reactions. The side effects include gastrointestinal distress, which includes diarrhea, vomiting, and nausea - especially in people with sensitive stomachs. Ajwain can occasionally trigger allergic responses, including skin rashes or respiratory problems, particularly in people who already have allergies to related plants or spices. Furthermore, because ajwain seeds contain oxalate, taking significant amounts of them may result in severe issues like kidney damage. Overall, while ajwain offers various health benefits, it is essential to consume it in moderation and be mindful of any adverse reactions.

Conclusion

The purpose of the review was to bring into the limelight the research performed on the plant, and also to establish scientific loop holes. Interestingly, the research has been done on the nutritional and bioactive profiling of its different components very few times. Phytochemical screening of T. ammi has indicated that the plant contains a large number of monoterpenoid-based bioactive compounds such as thymol, g-terpinene, and p-cymene, and carvacrol which lead to the observed pharmacological properties. The *T. ammi* has been traditionally used in different systems of medicine (Ayurveda and Unani systems) and thus they have been well documented and have been among those used to treat digestive disorders, respiratory problems and even cancer related illnesses. Ethnopharmacological data about the plant has given a good platform to the study and the identification of its therapeutic properties. Studies, including in vivo and in vitro, have substantially shown the anti-inflammatory, analgesic, antitumor and antiviral effects. The pharmacological studies have demonstrated encouraging findings and the T. ammi could be used in the treatment of many conditions, such as stroke, rheumatoid arthritis, and cancer. Notwithstanding the achievements in the sphere of researching the therapeutic potential of the plant, there are certain aspects that should be explored further. Future studies ought to concentrate on the discovery of the active phytochemical constituents which impart the observed bioactivities. The interest in the new drug delivery systems of *T. ammi* (nanoparticles, microemulsions, liposomes) is increasing. These are superior formulations that intend to increase the bioavailability and therapeutic response of *T. ammi*. There is still need of further extensive research on the mechanisms of action of some of the bioactive components that are detected in the leaves, fruits, and flowers of the plant in the treatment of different disease conditions. The ability of the plant to reduce blood pressure in humans is one of the noteworthy ethnobotanical applications of the plant leaves. The effects of monoterpenoids were studied on different in vivo models as anticancer agents. Thymol and carvacrol were among the identified phytochemicals with anticancer properties; therefore, the potential therapeutic effects of the plant can be attributed to the synergetic action of these phytochemicals and others in the leaves. The studies have put emphasis on its high essential oil constituents, especially thymol, and many pharmacological effects including diuretic, antibacterial, antitussive, antiplatelet, antihypertensive, bronchodilator, and antihyperlipidemic. Also, Ajwain has been shown to have antiurolithic effect, diuretic effect, preventing aggregation of

calcium oxalate crystals, anti-oxidant effect, preserving the renal epithelial cells and also anti-spasmodic. Moreover, research has also investigated cytotoxic action of non-specific lipid transfer protein (nsLTP1) isolated in Ajwain in a range of cancer cell lines, thereby demonstrating its ability to provide anticancer action by inducing apoptosis and its structural stability under high-temperature environments and human serum.

Future Perspectives

Further studies on *Trachyspermumammi* (ajwain) have tremendous potential of extending its medicinal use. *T. ammi* has potential to be a useful natural therapeutic in the clinical scenario due to its antimicrobial, anti-inflammatory as well as anti-cancer effects caused by bioactive compounds that include thymol and carvacrol. Research in the future should be directed to explain the molecular processes of these compounds and do extensive in vivo experiments to ascertain their safety and effectiveness. In addition to that, the synergistic action of *T. ammi* when used with other natural compounds should be studied, which may lead to new formulations. Sustainable production, which would enable the provision of accessible health solutions, which are plant-based, on the global scale, could also be achieved through advances in biotechnology.

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