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A panoramic view on phytochemical, nutritional, ethanobotanical uses and pharmacological values of *Trachyspermum ammi* Linn.

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ABSTRACT

Trachyspermum ammi Linn. (*T. ammi*) is an aromatic, grassy, annual plant belonging to Umbelliferae family which grows in the east of India, Pakistan, Iran, and Egypt. *T. ammi* has been used traditionally to treat arthritis, colic, diarrhea and gastrointestinal problems. In addition to these medicinal uses, *T. ammi* continues to be valued around the world as an important cooking spice and is believed to relief the common cold, flu-like symptoms, headaches, and even painful menstrual periods. These multiple uses can be explained by its several active compounds. The phytochemical studies on *T. ammi* seeds have revealed the presence of alkaloids, steroids, fixed oils, glycosides, tannins, saponin and flavonoids, cumene, thymene, amino acids and dietary fiber essential oils like thymol, c-terpinene, p-cymene. Several pharmacological studies on anti-tussive effect, inhibitory effect on histamine (H1) receptors, antihypertensive, antispasmodic, bronchodilator, hepato-protective, analgesic, anti-inflammatory, antioxidant and anti mutagenic activities of *T. ammi* seed extracts have been reported in the literature. The present review is therefore, an effort to give a detailed survey of the literature on traditional, phytochemical and pharmacological properties of *T. ammi*.

1. Introduction

Trachyspermum ammi Linn. (*T. ammi*), belonging to Umbelliferae family, is an Ayurvedic plant with important medicinal properties. It is known by various vernacular names such as Bishop's weed (Sanskrit), Carom seed (English name) and Ajowan or Ajwain or Omum (Indian name)[1,2], Kammun or Al-Yunan (Arabic), Hounastan (Armenian), Xi Ye Cao Guo Qin (China), Ajwan (Dutch), Adiowan, Ajowan, Agyptischer (German)[3]. Ajowain is native of Egypt and grows widely around Mediterranean Sea and in Southwest Asia. It is cultivated in India, Iran, Afghanistan, Pakistan and Iraq[4]. *T. 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, ovary inferior. Leaves pinnate, upper leaves are smaller and shortly petiolate while lower leaves have long petioles (Figure 1). Fruit is grayish brown, ovoid, consisting of two mericarps with prominent ridges. Fruit is 2 mm long and 1.7 mm wide[5].

Transverse section of *T. 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[6].

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2. Panoramic view

2.1. Synonyms

Ammi copticum L., *Ammi glaucifolium* Blanco, *Ammios muricata* Moench, *Apium ammi* (L.) Urb. (illeg.), *Selinum copticum* E.H.L. Krause, *Trachyspermum copticum* (L.) Link., *Ptychotis coptica* (L.), *Athamanta ajowan* Wall., *Bunium copticum* (L.), *Carum ajowan* Benth. & Hook. f., *Carum aromaticum* Druce, *Carum copticum* (L.) Lag., *Daucus copticus* (L.) Pers., *Helosciadium ammi* (L.) Oken, *Helosciadium ammi* (L.) Britton, *Ligusticum ajawain* Roxb. ex Fleming, *Ligusticum ajawain* Spreng., *Ptychotis coptica* (L.) DC[3].

2.2. Adulteration

T. ammi seed is available as whole and in ground form (Figure 2). It is adulterated by addition of spent seed (from which oil or oleoresin has been extracted) excess stems, chaff and earth or dust. The oil is also adulterated with ajowan chaff oil in which the range of essential oil is 2%-4% and it should contain thymol in the range of 35%-60%. In addition to the chaff oil, the thymol content will reduce to less than 35%. By gas chromatography or by thin layer chromatography coupled with high-performance liquid chromatography can be done for the detection of these adulterants[7]. The seeds are mostly adulterated by ban ajwain [*Seseli diffusum* (Roxb. ex. Sm.)] or randhuni [*Apium graveolens* (Linn.) Sprague]. The adulteration can be detected by thin layer chromatography using benzene: petrol (1:7).

2.3. Phytochemistry

Analysis of *T. ammi* seeds shows that it contains fiber (11.9%), carbohydrate (38.6%), tannins, glycosides, moisture (8.9%), protein (15.4%), fat (18.1%), saponins, flavones and mineral matter (7.1%) like calcium, phosphorus, iron and nicotinic acid[8]. Essential oil present in the ajwain (2.5%-5.0%) contains the major constituent thymol (35%-60%)[9]. The remainder non-thymol fractions called thymene contains p-cymene (50%-55%), β-pinene (4%-5%), limonene with γ-pinenes and β-pinene (30%-35%)[10]. Alcoholic extract contains highly hygroscopic saponin. It has been reported that minute amount of camphene, myrcene and D3-carene is also present. A yellow crystalline flavone and steroid like substance have been isolated from the fruit of ajwain and it also contains a glucoside 6-O-β-glucopyranosyloxythymol[11]. The major constituents of *T. ammi* are carvone (48%), limonene (38%) and dillapiole (9%)[12].

From the water-soluble portion of the fruit methanol extract of *T. ammi* 25 compounds, together with five new monoterpenoid glucosides, two new aromatic compound glucosides, and two new glucides were obtained. Their structures were identified by spectral analysis. A monoterpenoid 3,7-dimethyloct-3(10)-ene-1,2,6,7-tetrol (a mixture of two stereoisomers) were recognized. Monoterpenoid glucosides A, B, C, D, E, F, G and H were known as (2S,6Z)-3,7-dimethyloct-3(10)-ene-1,2,6,7-tetrol 1-O-β-D-glucopyranoside; 6-hydroxythymol 6-O-β-D-glucopyranoside; 6-hydroxythymol 3-O-β-D-glucopyranoside[13], $C_{16}H_{24}O_7$ as 7-hydroxythymol 3-O-β-D glycopyranoside; $C_{16}H_{28}O_7$ as (4R,6S)-p-menth-1-ene-4,6-diol4-O-β-D-glucopyranoside; $C_{22}H_{34}O_{12}$ as 6-hydroxythymol 3,6-di-O-β-D-glucopyranoside; $C_{16}H_{28}O_7$ as (4S)-p-menth-1-ene-4,7-diol 4-O-β-D-glucopyranoside; $C_{16}H_{28}O_7$ (4R,6S)-p-menth-1-ene-4,6-diol 4-O-β-D-glucopyranoside; $C_{16}H_{26}O_7$ as 3β-hydroxy-p-menth-1-en-4β, 5β-oxide 3-O-β-D-glucopyranoside, respectively. Among them D, E, F, G and H are latest monoterpenoids glucoside. A new monoterpenoid was recognized and its structure was well-known as p-menth-3-ene-1β,2β,5β-triol[9]. Alkyl glucoside and aromatic compound were known as 2-methyl-3 buten-2-ol-β-

Figure 1. The photo of *T. ammi*.

Figure 2. *T. ammi* seeds.

D-glucopyanoside,benzyl-β-D-glucopyranoside and 19-(3-hydroxy-4,5 dimethoxyphenyl)-propane-29,39-diol, respectively. A new aromatic compound glucoside $C_{15}H_{22}O_8$ was recognized as 3,4-dihydroxyphenylpropanol-3-O-β-D-glucopyranoside. Nucleosides were known as adenosine and uridine and glucides were recognized as (2S,3R)-2-methylbutane-1,2,3,4-tetrol) and (3R)-2-hydroxymethylbutane-1,2,3,4-tetrol, respectively[14]. Two new glucosides were isolated and identified as 1-deoxy-L-erythritol ($C_4H_{10}O_3$) and 1-deoxypentitol ($C_5H_{12}O_4$)[9]. Ajwain fruit contains several minerals like aluminium, calcium, cadmium, copper, iron and lithium[15]. Riboflavin, thiamine, nicotinic acid, carotene, calcium, chromium, cobalt, copper, iodine, iron, manganese, phosphorus and zinc were also found in fruit[16].

The phenols, thymol and carvacrol are responsible for the antiseptic, antitussive, and expectorant properties. Researchers investigated the oestrogenic content of some herbs including *T. ammi* that are traditionally being used to increase the yield of milk in dairy cattle. *T. ammi* has also been traditionally used as a galactogogue in humans. Thymol is usually known for its anti-microbial properties. It is commonly incorporated in mouthwashes, due to its antibacterial action against oral bacteria. It has harmful effects on both the cellular cytoplasmic membrane (perforation) and the generation of adenosine triphosphate. It is reported that, in Lamiaceae plants, thymol is always accompanied by its isomer carvacrol. Thymol also possesses antiseptic activity and carvacrol has antifungal properties. Research has been reported that thymol and carvacrol possesses inhibitory effects against the peroxidation of liposome phospholipids in a concentration dependent manner. Both isomers thymol and carvacrol were equally effective in the autoxidation of lard at 35 °C at a concentration of 0.1%[2].

2.4. Nutritional value

T. ammi seeds have higher energy value that is 314.55%. It is rich source of carbohydrates 47.54%. Protein, moisture, ash and fiber contents are present in the range of 4.30%-20.23%; fat contents were in the range of 4.83%[17]. From neutraceutical point of view, spices ajwain is served as important constituents of human diet supplying the body with sufficient amount of proteins, carbohydrates and energy. The presence of biologically active compounds also adds to its nutritive value and thus proved to be potential sources of useful foods[18].

2.5. Ethnobotanical uses

T. ammi is used to treat anorexia, arthrosis, ascites, asthma, atony, boil, bronchitis, cachexia, cancer of abdomen, cardiopathy, cholera, cold, colic, congestion, cough, cramp, debility, diarrhea, dipsomania, dyspepsia, edema, emphysema, enteritis, epilepsy, escherichia, fever, flu, fungus, hemorrhoid, hepatosis, hiccup, high blood pressure, hysteria, laryngitis mycosis, nausea, nematode, nephrosis, ophthalmia, pain, paralysis, pneumonia, rheumatism, salmonella, sinusitis, snakebite, sore throat, stone, syncope, toothache, and wounds. It is used as antiseptic antispasmodic, aphrodisiac bitter, cardio-depressant, carminative, diaphoretic, diuretic, emmenagogue, expectorant, fungicide, gastro relaxant, gastro-stimulant, hypotensive, lactagogue, laxative, litholytic, parasympathomimetic, sialagogue, spasmogenic, stimulant, stomachic, tonic and vermifuge[16].

3. Pharmacological screening

3.1. Antidiarrhoeal activity

Antidiarrhoeal activity of 95% total alcoholic extract (TAE) and total aqueous extract (TAQ) of *T. ammi* seeds at a dose of 100 mg/kg body weight was evaluated using experimentally induced castor oil diarrhoea, gastrointestinal transit of charcoal meal and enteropooling activity in male Wistar rats and compared to standard drugs. In the study, the TAE and TAQ extracts of seeds at a dose of 100 mg/kg exhibited a significant inhibition of castor oil induced diarrhoea in dose dependent manner in experimental rats. TAE and TAQ extracts significantly decreased the diarrhoeal droppings when compared to castor oil group. The results obtained for TAE and TAQ extracts were similar to that of the standard drug loperamide (3 mg/kg) intestinal fluids in the small and large intestines[19]. Antidiarrhoeal and anti-dysenteric properties of medicinal plants were found to be due to the presence of tannins, flavonoids, saponins, alkaloids, sterols, reducing sugars and triterpenes[20,21]. The phytochemical studies on *T. ammi* seeds have revealed the presence of flavonoids, tannins, saponins and sterols. Thus, the antidiarrhoeal activity might be due to these chemical constituents. Flavonoids have antidiarrhoeal activity, which have ability to inhibit intestinal motility and hydroelectrolytic secretions which are known to be changed in diarrhoea conditions[22]. Tannins and tannic acid denature the proteins in intestinal mucosa by forming the protein tannates, which make the intestinal mucosa more resistant to chemical alteration, and hence reduce secretion[23]. In conclusion, the results obtained in the present study suggest that *T. ammi* seed extracts have beneficial effect in controlling the diarrhoea in experimental animals.

3.2. Antibacterial activity

Thymol obtained from the seeds of the plant *T. ammi* used in fourth generation antibiotic formulation for control of drug resistant bacteria. More particularly,

compound thymol isolated from the oil distilled from the seeds of the plant *T. ammi* kill the bacteria, resistant to even prevalent third generation antibiotics, multi-drug resistant microbial pathogens and thus useful as a plant based fourth generation herbal antibiotic. The Gram-positive bacteria such as *Bacillus cereus*, *Bacillus subtilis*, *Staphylococcus aureus*, and *Listeria monocytogenes* show good inhibition action compared to Gram-negative bacteria (such as *Escherichia coli* and *Pseudomonas aeruginosa*). Gram-negative bacteria generally have been reported to be more resistant than Gram-positive. The different antimicrobial effect of essential oils is due to differences in the lipopolysaccharide constitution of cell walls. A number of hypotheses have been put forward which involve hydrophobic and hydrogen bonding of phenolic compounds to membrane proteins, which causes the partition into the lipid bilayer membrane disruption, destruction of electron transport systems and cell wall perturbation. The high activity of the phenolic component might be due to alkyl substitution into phenol nucleus, which is known to enhance the antimicrobial activity of phenols. Depending on the concentration used phenolic compounds, such as thymol and carvacrol are known to be either bactericidal or bacteriostatic agents[24].

3.3. Gastroprotective activity

T. ammi fruit have traditionally been used as medicinal plant for the treatment of indigestion and dyspepsia and many other gastric disorders. Therefore, ethanolic extract of *T. ammi* fruit was used for investigation of antiulcer activity by using pylorus ligation, as antisecretory model and indomethacin induced ulcer model, ethanol induced ulceration model, cold restraint stress induced ulcer model as cytoprotective model. The extract at dose of 100 mg/kg and 200 mg/kg showed significant protection ($P<0.001$) by reducing ulcerative lesions when compared with control group of animals. The findings indicated that *T. ammi* fruit extract have significant antiulcer activity.

Mucus is secreted by the mucus neck cells, serves as first line of defense against ulcerogens and covers the gastric mucosa preventing its physical damage and back diffusion of hydrogen ions. In the present study, *T. ammi* increased mucus secretion. The major constituent of mucus is mucopolysaccharides which are responsible for viscous nature and gel-forming properties of the mucus. The gel is reported to be resistant to a number of ulcerogens including acid, NSAIDs, *i.e.* indomethacin, *etc*. Therefore, increase in the production of mucus may be one of the important contributing factors for ulcer protective role of *T. ammi* fruit[25].

3.4. Relaxant effect on intestinal motility in ileum of rats

It has been reported that *T. ammi* possesses bactericidal, anticholinergic and antihistaminic activities. In addition, it also has β-adrenergic stimulatory effects. In a previous report, specific effects of *T. ammi* on mechanical activity of ileum, both qualitatively and quantitatively were determined. Anaesthetized rats were used for mechanical recording through isolated organ bath and oscillograph in the study. The affect obtained on intestinal motility was also tested for receptors identification and differentiation with cholinergic and adrenergic agents. The results demonstrate the effective concentrations of acetylcholine causing 50% of maximum response (EC_{50}) obtained in the presence of 0.01 extracts in all five sets of experiments, were significantly higher than those of saline ($P<0.000$) and also the maximum response to acetylcholine obtained in the presence of extracts were lower ($P<0.000$). The results of the study therefore specified a competitive antagonism effect of *T. ammi* at acetylcholine receptors[26].

3.5. Antihypertensive, antispasmodic and bronchodilating studies

The antihypertensive, antispasmodic and bronchodilating activity of aqueous and methanol extract of *T. ammi* seeds was studied to rationalize some of its traditional uses. It was observed that the extract causes dose dependent fall in blood pressure, inhibits the bronchoconstriction and has hepatoprotective effects and thus provides sound mechanistic basis for some of their folkloric uses[27].

3.6. Anti-inflammatory potential

Anti-inflammatory activity of the total aqueous extract and total alcoholic extract of the *T. ammi* seeds was evaluated and found by the result that total alcoholic extract and total aqueous extract exhibited significant ($P<0.001$) anti-inflammatory activity[28,29]. Its anti-inflammatory activity might be due to an increase in the number of fibroblasts and synthesis of collagen and mucopolysaccharides during granuloma tissue formation[30]. The anti-inflammatory activity exerted by *T. ammi* ethanol extract and *T. ammi* aqueous extracts suggest that they have effect on kinin, prostaglandin, bradykinin and lysozyme synthesis. Presence of terpenes, glycosides and sterols in plant has been found to exert active anti-inflammatory effects. Phytochemical analysis of *T. ammi* has revealed the presence of terpenes and sterols. The anti-inflammatory activity of the extract may be due to the presence of certain polar constituents such as flavonoids and glycosides that might be involved in the inhibition of prostaglandin synthtase[28].

3.7. Anti-lithiasis and diuretic activity

Anti-lithiasis and diuretic activity of *T. ammi* was evaluated and found by the result that the traditional use of *T. ammi* in the treatment of kidney stones was not supported

by their experimental evidence and also it was not effective in increasing the 24-hour urine production[30].

3.8. Antiplatelet-aggregatory activity

Antiplatelet activity of dried ethereal extract of *T. ammi* was evaluated and found by the result that the extract inhibited aggregation of platelets induced by arachidonic acid, collagen and epinephrine[31].

3.9. Abortifacient activity

T. ammi was commonly used as abortive plants from a survey in and around the villages of Uttar Pradesh. The *T. ammi* seed aqueous extract at a dose of 175 mg/kg in rats was 62.5% effective as an abortifacient. In cases where pregnancy was continued in spite of herbal drug administration, various skeletal and visceral defects were noticed. This shows the remarkable potential of the putative abortifacient herbal drugs to affect foetuses adversely[32].

3.10. 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[33].

3.11. Digestive stimulant actions

Study demonstrated that the addition of *T. ammi* to the diet reduced food transit time from 780 min (control) to 554 min, a 29% reduction ($P<0.05$) and 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 might be due to an acceleration of the overall digestive process as a result of increased availability and potency of digestive secretions[34].

3.12. Enzyme modulation activity

Acetyl cholinesterase, lactic dehydrogenase, succinic dehydrogenase and cytochrome oxidase activity in the nervous tissue of snails significantly changed by *in vivo* administration of *Lymnaea acuminata* to thymol and verified active molluscicidal. *T. ammi* also had significant activity against protease and also increased the activity of pancreatic lipase and amylase, which may hold its digestive stimulant activity[35].

3.13. Detoxification of aflatoxins

The seed extract of *T. ammi* exhibited the maximum degradation of aflatoxin G1[36].

3.14. Ameliorative effect

Ameliorative effect of ajwain extract was evaluated against hexachlorocyclohexane induced oxidative stress and toxicity in rats and it was concluded that hexachlorocyclohexane administration resulted in hepatic free radical stress, causing toxicity, which could be reduced by the *T. ammi* extract[1].

3.15. 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[37]. *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*[37].

3.16. Antioxidant activity

T. ammi methanol extract possesses strong antioxidant activity against DPPH, and could be used as natural antioxidants in food or pharmaceutical industry[38].

3.17. Blood pressure lowering action of active principle from T. ammi

The action of the thymol and the active principle of *T. ammi* on the blood pressure have been studied. Thymol (1-10 mg/kg) produced dose dependant fall in blood pressure and heart rate in anaesthetized rats. Atropine (1 mg/kg) did not block these effects and thymol did not change the pressure response of norepinephrine, which rules out the possibility of cholinergic stimulation or adrenergic blockade. Thymol caused decrease in force and rate of atrial contractions. In case of rabbit aorta, thymol caused relaxation of nor-epinephrine and potassium induced contractions in a concentration-dependent manner. These effects remained unaltered in the presence of atropine. These relaxant effects remained unchanged after the removal of endothelium. Moreover, atropine,

propranolol, indomethacine and glibenclamide did not alter the vasorelaxation by thymol. These results suggested that *T. ammi* contains a calcium channel blocker-like constituent (thymol) which may explain the hypotensive and bradycardiac effects observed in the *in vivo* studies[39].

3.18. A novel compound against dental caries

(4aS,5R,8aS) 5, 8a-di-1-propyloctahydro naphthalen-1-(2H)-one, a novel compound reported for the first time from the seeds of *T. ammi*, was examined for its activity against cariogenic properties of *Streptococcus mutans* (*S. mutans*). Purification of the active compound from the seeds was performed by silica gel chromatography, and spectroscopic methods (Fourier transform infrared spectroscopy, nuclear magnetic resonance and mass spectroscopy) were used for its structure determination and identification. Confocal microscopy was performed to visualize the effect of the compound on biofilm structure of *S. mutans*. Approximately 50% reduction was observed in adherence. It was found effective against adherent cells of *S. mutans*, decreased water-insoluble glucan synthesis by glucosyltransferases and hydrophobicity and inhibited the reduction in pH. Confocal microscopy revealed scattered cells at sub-minimum inhibitory concentration of the compound, resulting in distorted biofilm architecture in contrast to clustered cells seen in control. This study revealed a naphthalene derivative, isolated first time from *T. ammi* seeds with antibiofilm activity against *S. mutans*. *T. ammi* therefore represents an interesting source of a novel compound, (4aS, 5R, 8aS) 5, 8a-di-1-propyl-octahydronaphthalen-1-(2H)-one, with a great potential to be used as a therapeutic agent against dental caries[40].

3.19. Antiepileptic effect

Epileptic disorder is an important health-care issue, as about 30 000 people around the world suffered from epilepsy every year. The condition affects about one person in 20 sometime in their lives. There are about 20-70 new cases of epilepsy per 100 000 people per year[41]. Research reported that approximately 1% of the world's population is suffering from epilepsy, and this is the second most common neurological disorder after stroke[41]. Evidence has suggested that imbalance between inhibitory and excitatory neurotransmission in the brain is the most important contributor to seizure development in both clinical and experimental conditions[42]. The study was conducted to assess the potential of a methanol extract of *T. ammi* as an antiepileptic agent[43]. Tests were conducted with single- and multiple-dosing schedules of *T. ammi*, using a strychnine induced seizure model for epilepsy in experimental animals. A total of 21 animals were used which were divided into three groups; control (vehicle), standard (diazepam) and test (*T. ammi* extract). *T. ammi* showed antiepileptic effects, since there was a highly significant delay in the onset of convulsions as compared to the control, whereas the percentage of animals that survived or ignored seizure was also greater compared to the control. However, the duration of convulsions was significantly increased with both *T. ammi* extract and diazepam as compared to the control. *T. ammi* exert's anticonvulsant effect may be due to the presence of thymol, which might excites gamma-aminobutyric acid responses by stimulating human gamma-aminobutyric acid type A receptors and increasing the chloride ion channel opening, a mechanism followed by many sedative/hypnotics, CNS depressants and anticonvulsants[44]. Hence, it may be concluded that *T. ammi* possesses the antiepileptic effect similar to diazepam. However, further studies are required to evaluate the exact mechanism of action.

3.20. Lithotriptic effect

It has been a well-known practice to use seeds and the essential oil of *T. ammi* as a strongly antiseptic, antispasmodic, aromatic, digestive, diuretic, expectorant and tonic. In one of the studies, the seeds of this herb were used as a urinary tract stone lithotripsy. The aim of the research was to use *T. ammi* seeds as a lithotripsy against different types of urinary stones and determine the efficiency of the preparation against which type of stone. A liquid solution was prepared from dissolving the seeds powder in cow milk and then concentrated. The preparation was done by boiling at 100 °C to reduce the volume of solution to the half. The treatment was given orally for 9 d before breakfast. A total of 350 patients with urinary stone of different type participated in this research. All patients were subjected to ultrasonography and intravenous pyelography examinations to determine the position and diameter of stone. The ultrasonography and intravenous pyelography examination and also biochemical tests for diagnosis of stones ingredients were repeated after the administration of treatment and excretion of stone fragments in urine. The results were so promising especially against pure ca oxalate stone[45]. The antilithiatic potential of *T. ammi* was confirmed by its ability to maintain renal functioning, reduce renal injury and decrease crystal excretion in urine and retention in renal tissue[46].

3.21. Analgesic effect

Pain is a universal complaint, which needs further investigations to search novel pain relieving agents. It is mentioned in the traditional literature that *T. ammi* has therapeutic effect on headache and joint pains. So, the study was conducted to design an experimental clinical trial study to assess and compare the analgesic effect of ethanolic extract of *T. ammi* fruit with morphine by using a tail-flick analgesiometer device. Results of the study indicate that the test drug produced significant increase in tail-flick latency

(TFL) during 2 h post-drug administration (P<0.05). The peak of the effect was observed at 45 min after drug injection, which was comparable to that of 1 mg/kg morphine. Positive results in this type of analgesiometric test indicate that the antinociceptive action may be of the opioid type. The study supports the claims of traditional medicine showing that *T. ammi* extract possesses a clear-cut analgesic effect. This effect may be due to its parasympathomimetic action on descending pain modulating pathways[47].

3.22. The therapeutic effect of T. ammi seeds on peptic ulcers

Non-steroidal anti-inflammatory medicines are extensively used today and of their side effects is gastric ulcer. A study was conducted to examine the effect of *T. ammi* aquatic extract on healing gastric ulcers inducted using ibuprofen in an animal[48]. A total of 30 adult Wistar female rats were used in this empirical study. The animals were divided into five groups. Then omeprazole or *T. ammi* plant extract was administered (125, 250 and 500 mg/kg doses) twice a day for 2 weeks. In the end, the number and area of the animals' gastric ulcers were examined. To assessed the side effects of the medicine on liver, the amount of liver enzymes aspartate transferase and alanine transferase was measured in the animals' serum. Plant aqueous extract had a significant effect on healing gastric ulcers comparing to the control group (P<0.05). The mean number and area of the gastric ulcers in the extract treating groups were significantly less compare to negative-control group. The amount of liver enzymes had also significantly (P<0.05) increased in the groups receiving the extract (250 and 500 mg/kg doses). The result of the study showed *T. ammi* plant seed extract is effective in healing gastric ulcers and its effect is comparable with omeprazole. Thus it can be commented that this extract perhaps had the similar effect as that of omeprazole in affecting the stomach acid secretion pump. However, to confirm this theory, future studies should be conducted to measure the amount of secretion of gastric acid after consumption of *T. ammi* seed extract, and thus to allow definitive comment on these mechanisms.

4. Medical indication supported by traditional experiences

4.1. Gastro-intestinal disorders

A teaspoonful of ajwain seeds with a little amount of rock-salt, mixed with water taken internally give relieve from flatulence, dyspepsia and spasmodic disorders.

Ajwain seeds, dry ginger and black salt ground together, the 3 g of this powder are taken along with warm water for colic.

Ajwain seeds and dried ginger in an equal quantity are soaked into two-and-half times the quantity of lime juice. After draining the water, they are dried and powdered with a little amount of black salt and about 2 g such powder mixed with warm water and taken internally, 2-3 times a day for relieving flatulence.

The volatile oil of ajwain seeds is given internally in a dose of 1-3 drops for cholera, flatulent colic, diarrhea, atomic dyspepsia and indigestion. Chewing ajwain seeds prevents bad breath.

4.2. Respiratory disorders

Ajwain seed powder mixed with buttermilk when given internally serves as an excellent expectorant even in difficult cases, such as when the phlegm is dried up. For pharyngitis in influenza, ajwain seeds mixed with clove and a pinch of common salt are chewed. For common cold, a tablespoonful of *T. ammi* seeds crushed and tied in a cloth as a bundle which is then inhaled by the patient. And such bundle can be used in nasal congestion; it is covered in the same blanket with the patient during sleeping hours. For the acute pharyngitis, sore and congested throat and hoarseness of the voice due to colds or making noise, infusions of the seeds with common salt are beneficial. In case of bronchial asthma, ajwain seeds are tied in the cotton cloth, heated in a frying pan and applied on the chest and neck when still warm.

4.3. Aphrodisiac

T. ammi seeds with the kernel of tamarind seeds act as a potent aphrodisiac; they are prepared by frying an equal quantity of both in pure ghee, dried and then powdered; then preserve it in airtight container. This is taken at bedtime to enhance virility.

4.4. Earache

For an earache, a half a teaspoon of seeds heated in 30 mL of milk and then strained on cooling used as ear drops. It decreases congestion and relieves pain.

4.5. Migraine

Seeds can be smoked or sniffed frequently to get relief from migraine and delirium.

4.6. Rheumatism

Oil extracted from the seeds resolves rheumatic and neuralgic pains when applied on affected parts[49].

4.7. 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, (integrillin) fondaparinux, (arixtra) heparin, (hepalean, hep-lock) indobufen (ibustrin) may increase the risk of bleeding and bruising[50,51].

4.8. Supplement interaction

T. ammi seeds may increase the risk of liver damage when taken with herbs and supplements that can cause hepatotoxicity (destructive effects on the liver), such as Bishop's weed, borage, chaparral, uva-ursi, and others. When used with herbs and supplements that might affect platelet aggregation, such as angelica, danshen, garlic, ginger, ginkgo biloba, red clover, turmeric and white willow, it may increase the risk of bleeding[50,51].

4.9. Safety information

Ajwain is generally regarded as safe when taken in the recommended doses, however, it can cause nausea and headache in some people. Safety in pregnant or nursing women, young children or those with severe liver or kidney disease is not reported[50,51].

5. 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. Recent years, ethnobotanical and traditional uses of natural compounds, especially of plant origin received much interest as they are scientifically tested for their effectiveness and generally believed to be harmless for human use. It is best conventional approach in the search of new molecules for management of several diseases. Detailed screening of literature available on *T. ammi* showed the fact that it is a popular remedy among the various ethnic groups and traditional practitioners for treatment of different types of ailments. Researchers are therefore, exploring the therapeutic potential of this plant as it has more therapeutic properties which are still not known. Although good scientists in many countries have been optimistic about the potentiality of *T. ammi*, more researches are required to upgrade the extraction and chemical analyses processes.

Conflict of interest statement

We declare that we have no conflict of interest.

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