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MULTIFARIOUS ACTIVITIES IN MAIN COMPONENTS OF ARQ-E-ZEERA I.E, *CUMINUM CYMINUM, BUNIUM PERSICUM, ZINGIBER OFFICINALE* AND *TRACHYSPERMUM AMMI*

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Keywords:

Arq-e-zeera, *Cuminium cyminum*, *Bunium persicum*, *Tachyspermum ammi*, *Zingiber officinale*, Phytoconstituents, Antimicrobial, Anti-inflammatory, Anti-oxidant, Anti-diabetic

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ABSTRACT: Arq-e-zeera, a distillate preparation of mainly *Cuminum cyminum* (Safed zeera), *Bunium persicum* (Shahi/kala zeera), *Trachyspermum ammi* (Ajwain) seeds, and *Zingiber officinale* (Adrak) rhizome isclinically used for declining obesity. Numerous trace elements, including calcium, magnesium, manganese, iron, zinc, and salt, are abundant in these herbs. These herbs have been observed to have diverse activities, notably antioxidant, antimicrobial, antidiabetic, hepatoprotective, anti-inflammatory and against gastrointestinal disorders. Major compounds of Arq-e-Zeera, as identified by GCMS and GC analysis, include thymol, limonene, terpinene, Cuminaldehyde, carvacrol, cymene, 1-phenyl-propanol, and 4-ethyl-3 non-5 yne, among other chemical components. Furthermore, because no or less evidence of their toxicity has been found in the literature, these are employed as aromatic ingredients and to enhance the taste, flavor, texture, and therapeutic benefits of many traditional cuisines. This review provides updated information on the morphological and taxonomical classification, chemical structures, experimental models, and methodologies employed in investigating the numerous activities and chemicals identified from the four primary constituents of Arq-e-zeera.

INTRODUCTION: Arq-e- zeera, a hydro-distillate product of four major herbs namely i.e, seeds of *Trachyspermum ammi L.*, (Ajwain), Family Apiaceae; *Cuminum cyminum*, (cumin), Family Apiaceae; *Bunium persicum*, (kala zeera), Family Apiaceae; and rhizome of *Zingiber officinale Roxb.*,(ginger) Family Zingiberaceae is being used in the control of clinical obesity [1].

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These four herbs cumin, caraway seeds, ajwain, and ginger, are also widely used in Southeast Asian indigenous medical systems, including Siddha, Ayurveda, and Unani systems of medicine either alone or in combination with other herbal products.

These have multifarious activities and have been claimed for anti-inflammatory, carminative, eupeptic, antispasmodic, antidiabetic, anti-hyperlipidemic, antioxidant, hepatoprotective, astringent and many others. These are also believed to enhance the absorption of other herbs [2]. Many of the herbal formulations to treat mild gastrointestinal problems, diarrhoea, morning sickness, dyspepsia, flatulence, colic, dyspeptic

headaches, bloating, and obesity contain these as one of their constituents. Nearly 37 chemical components were identified in Arq-e-zeera by GCMS and GC analysis. **Table 1** Out of 37 chemical constituents, the major ones arecumin aldehyde (21.13 %), thymol (44.40 %), 1-phenyl propanol (14.234 %), and 4-ethyl-3-non en-5-yne (11.29 %) that sums up to approximately 91%[1]. Thymol, amonoterpenicphenolic component of *Tachyspermum ammi*, hinders the action of 3hydroxy3-methylglutaryl coenzyme A reductase, which in turn hashypocholesterolemic properties [3, 4, 5, 6]. It has been revealed that cumin aldehydeis present in *Carum carvi L*. and *Cuminum cyminum L*. and possesses anti-oxidant, anti-inflammatory, anti-hyperglycemic, and anti-hyperlipidemic properties [7, 8, 9]. In obese rats given a high-fat diet, arq zeera and its constituents demonstrated a strong anti-obesity impact. This effect was partially attributed to pancreatic lipase inhibition and hypolipidemic, hypoglycemic, hypoinsulinemic, and hypolipidemic actions [1].

TABLE 1: CHEMICAL PROFILE OF ARQ-E-ZEERA FORMULATION [1]

S. no.	Compound	Molecular formula	Molecular weight (g/mol)
1.	2-Methyl-propane-1-one	C8H20O	132.24
2.	N-Pentadecanoic Acid	C15H30O2	242.39
3.	D-Limonene	C10H16	136.238
4.	1,8-Cineol	C10H18O	154.25
5.	O-Cymene	C10H14	134.22
6.	2-Heptanol	C7H16O	116.201
7.	alpha -Terpinene	C10H16	136.23
8.	p-Cresol	C7H8O	108.14
9.	Limonene epoxide	C10H16O	152.23
10.	4-Terpineol	C10H18O	154.25
11.	α-Terpineol	C10H18O	154.25
12.	4-Thujanol	C10H18O	154.25
13.	Borneol	C10H18O	154.25
14.	4-Isopropyl-1-methyl-2-cyclohexen-1-ol	C10H18O	154.25
15.	4-p-Menthadien-7-ol	C10H16O	152.23
16.	Sabinyl-acetate	C12H18O2	194.27
17.	β-Citronellal	C10H18O	154.25
18.	p-Cumic aldehyde	C10H12O	148.205
19.	Hexan-2-ol	C6H14O	102.174
20.	Trans-Citral	C10H16O	152.23
21.	Cuminol	C10H14O	150.221
22.	Nerol	C10H18O	154.25
23.	1-Phenylpropanol	C9H12O	136.19
24.	Geraniol	C10H18O	154.25
25.	4-Ethyl-3-Nonen-5-Yne	C11H18	150.26
26.	4-(Isopropyl phenyl) Methanol	C10H14O	150.22
27.	Thymol	C10H14O	150.22
28.	Carvacrol	C10H14O	150.217
29.	2-Heptanol	C7H16O	116.201
30.	4-Isopropyl-2-cyclohexen-1-yl) methanol	C10H16O	152.23
31.	β-Linalool	C10H18O	154.25
32.	α-Curcumin	C21H20O6	368.4
33.	Zingiberene	C15H24	204.187
34.	β-Bisabolene	C15H24	204.35
35.	β-Sesquiphellandrene	C15H24	204.35
36.	Farnesene	C15H24	204.36
37.	Nerolidol	C15H26O	222.37

TABLE 2: MORPHOLOGICAL CHARACTERISTICS OF COMPONENTS OF ARQ-E-ZEERA [10, 11, 12, 13]

Parts	*Bunium persicum*	*Cuminum cyminum*	*Zingiber officinale*	*Trachyspermum ammi*
Plant	A perennial herb, compact, moderately to highly branched, tuberous,	It is an annual plant, small 30 cm to 50 cm tall, slender, and herbaceous with finely dissected	An upright, thin, herbaceous plant with a maximum height of 1.8 meters.	An upright, up to 90 cm tall that is branching, glabrous or slightly pubescent, annual herb

	and ranges in height from 30 cm to 80 cm.	leaves.		
Flower	Compact umbels of white, small, flowers with five stamens, sepals and petals, that are easily symmetrical, are present.	The tiny, pink or white blooms are carried in umbels. There are five to seven umbellets each umbel.	Pink and white clusters of flower buds which on maturity grow into yellow flowers.	The flowers are white and actinomorphic
Fruit	The schizocarp comprises two mericarps, frequently joined to a central stalk (carpophore) that is elongated or spherical and has oil tubes called vittae.	The fruit is slender, oval-shaped, and yellowish brown, about 4-5 mm (1⁄6–1⁄5 in) in length. Has two mericarps, with a single seed. Eight ridges with oil canals are seen on its seeds.	Fruit consists of a red, three-valved capsule with a thin wall. Small, black seeds have an aril on each one.	The plant produces tiny, fragrant, egg-shaped fruits that are greyish-brown in color.
Stem	hollow in the internodal area that contains secretory canals filled with resins and ethereal oils	slender, glabrous, grey or dark green, branched stem with a diameter of 3–5 cm (1+1⁄4–2 in), height of 20–30 cm (8–12 in). There are 2-3 subbranches for every branch. Every branch grows to the same height, and the plant's canopy is consistent.	stem that is shallowly rooted underground and grows horizontally. The flesh is pale yellow with a spicy smell, and the epidermal layer is dark and corky, covered in deciduous thin scales that create ring-like scars. This layer is normally removed before use.	The plant's stem, which can reach a height of 90 cm, is striated and upright, with glabrous or faintly pubescent characteristics.
Leaves	The leaves are filiform, freely dissecting, pinnate (2–3), and finely divided.	The leaves are pinnate or bipinnate, 5–10 cm (2–4 in) long, and have leaflets that imitate threads.	The leaves are long and elongated in nature, and they grow alternately. The pseudostems consist of a sequence of tightly wrapped leaf bases, or sheaths, around which are grouped alternating long (up to 7 cm) and thin (up to 1.9 cm) mid-green leaf blades.	It has feathery 2.5 cm long leaves with 16 umbellets that bear 6–16 blooms near the head section.
Bract	Bracts are linear and sometimes divided	Bracts often as many as primary rays, sheathing at base.	Series of greenish or yellowish bracts with translucent margins.	Bracts are 3 to 8, linear-subulate and are 5 to 7 mm.
Bracteoles	Bracteoles are absent with asymmetrical rays	bracteoles 3-5 per umbellet	bracteoles ovate-oblong.	Bracteoles are 5 to 10, linear and is 2 to 3 mm
Gynaecium	Bicarpellate, having two united styles at the base and an inferior ovary.	the ovary is below the point of petal and/or sepal attachment. All the flowers at the final division of the umbel have both carpels and stamens	The gynoecium is syncarpous, having an inferior ovary, 3 carpels (including the median carpel anterior), 1 or 3 locules, and a terminal style that is positioned between the anther thecae and in the filament's furrow. Placentation is axile or parietal, the ovules are bitegmic, anatropous, and ∞ per carpel.	The gynoecium consists of two carpels fused into a single, bicarpellate pistil with an inferior ovary.

TABLE 3: TAXONOMICAL CLASSIFICATION [28, 141, 142, 143]

	Bunium persicum	***Cuminum cyminum***	***Zingiber officinale***	***Trachyspermum ammi***
Kingdom	Plantae	Plantae	Plantae	Plantae

Sub kingdom	Tracheobionta	Viridiplantae	Tracheobionta	Tracheobionta
Super division	Spermatophyta	Embryophyta;	Spermatophyta	Spermatophyta
Division	Magnoliophyta	Tracheophyta	Magnoliophyta	Magnoliophyta
Class	Magnoliopsida	Magnoliopsida	Liliopsida	Magnoliopsida
Subclass	Rosidae	Rosidae	Zingiberidae	Rosidae
Order	Apiales	Apiales	Zingiberales	Apiales
Family	Apiaceae	Apiaceae	Zingiberaceae	Apiaceae
Genus	Bunium	Cuminum	Zingiber	Trachyspermum
Species	Persicum	*C. cyminum*	*Z. officinale*	Ammi
Botanical name	*Bunium persicum*	*Cuminum cyminum*	*Zingiber officinale*	*Trachyspermum ammi*
Common name	Shahi zeera, kaala zeera	Zeera	Ginger, adrak	Ajwain, ajowan

***Bunium persicum* Seeds:** *Bunium persicum*, also known as Zireh Kermaniand *Carum persicum* in Iran, Kala Zira in India, and Zeera in Central Asian nations (Tajikistan, Uzbekistan, Kyrgyzstan, and Pakistan), is native to Iran, Afghanistan, Pakistan, and some other Central Asian nations [8]. In Jammu and Kashmir, it is popularly known as siah zeera, kala jeera, and shahi zeera; in some areas of Himachal Pradesh as kali zeeri; and in some regions of Iran as zirehkuhi[14]. This crop has a high value and costs between 1200 and 2800 Indian rupees per kilogram [15]. The seeds of *B. persicum* are reported to have medicinal value as they are frequently used to treat various illnesses, including diarrhoea, dyspepsia, fever and stomach problems [16-21]. Considering their multifunctional antioxidative, anti-inflammatory, antifungal and antibacterial, properties, essential oils of *B. persicum* seeds are considered natural food additives [22, 23].

Phytochemistry: Several populations of dried fruits of *B. persicum* produced an average range production of essential oil of 1.92-9.1% v/w. Sesquiterpenes, phenyl propenes, oxygenated monoterpenes, and hydrocarbon monoterpenes are the primary components of the essential oil of *B. persicum*. Major components of essential oils include cumin aldehyde (5.96-40.66%), γ-terpinene-7-al (8.3-26.91%), caryophyllene (0.08-27.81%), γ terpinene (0.8-46.1%), limonene (0.5-15.7%), α terpinene-7-al (0.4-37.2%), β-pinene (0.2-15.62%), cuminyl acetate (0.09-14.57%), ρ-cymene (2.8-19.15%), α-terpinene (0.1-11.3%), cumin alcohol (0.21-7.4%), camphor (1.75-10.43%), terpinolene (0.05-8.27%), and 2-carene-10-al (2.69-6.92%) [24]. Variations in the meteorological, seasonal, and geographic variables impact the chemical composition of *B. persicum* essential oil [25, 26].

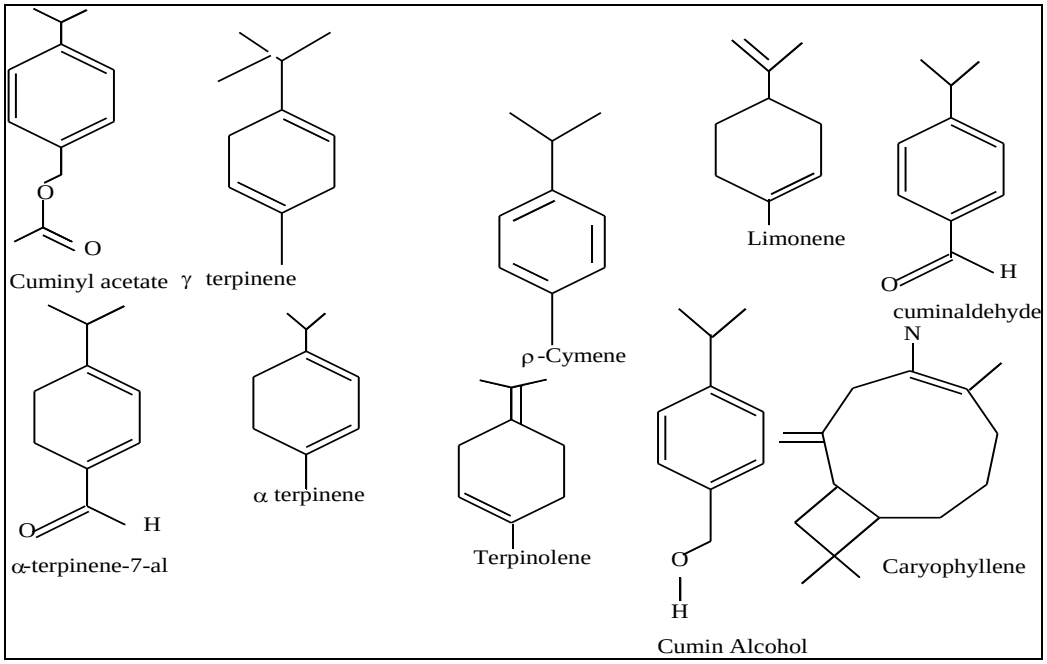

FIG. 1: THE STRUCTURE OF SOME OF THE PRIMARY ACTIVE COMPONENTS IN *B. PERSICUM* ESSENTIAL OIL [14]

Trace Elements: A study done by Moghaddam on micro and macro elements of different herbs of Iran found the presence of trace elements Fe, Zn, Cu, Mn, and Na in the highest concentration [144].

Pharmacological Properties:

Antioxidant Activity: Elevated levels of antioxidant and free radical scavenging activity were observed in experiments conducted on *B. persicum* essential oil and extracts [27, 19]. The carotene bleaching assays and 2,2-Diphenyl-1-picrylhydrazyl (DPPH) scavenging were studied by Shahsavari *et al* [29] to investigate the antioxidant activity and chemical composition of essential oils. The antioxidant activity of the BPEO oil was evaluated by testing the oil substrate's peroxide and thiobarbituric acid levels under fast conditions at 60°C. The outcomes demonstrated that BPEO decreased the rate of soybean oil oxidation. Essential oil and differential extracts of black cumin were assessed by utilising β-carotene bleaching, DPPH, and ammonium thiocyanate techniques. The maximum antioxidant activity was found in the methanolic extracts and essential oil of black cumin, with IC_{50} values of 45.7± 3.6 g/ml and 23.4±1.6 g/ml in the DPPH assay, respectively [30]. According to Zangiabadi *et al.* [31] thiobarbituric acid (TBA) and peroxide value (PV) tests, *B. persicum* can be utilised as a reliable and affordable natural antioxidant supplement in daily meals. Different *B. persicum* extracts had antitoxic and anti-oxidative properties, and they might prevent the hematotoxicity caused by reactive oxygen species (ROS) in rats with leukemic blood [32].

Antimicrobial Activity: Gram-positive bacteria like Listeria monocytogenes responded strongly to *in-vitro* antibacterial testing essential oil of *B. persicum* [33]. Bacillus cereus and Escherichia coli, as well as the relative sensitivity of other gram-negative bacteria including *Salmonella typhimurium* and *Staphylococcus aureus. B. persicum* essential oil's main components that are thought to be responsible for its antibacterial properties include monoterpenes such as cumin aldehyde [34, 35]. Additionally, *B. persicum* extracts showed notable inhibitory efficacy against several pathogenic microorganisms, including *Staphylococcus aureus, Candida albica, Pseudomonas aeruginosa* and Escherichia coli [36, 37]. By using the agar well diffusion method, Amber *et al.* [38] evaluated the antibacterial activity of *B. persicum* against *Staphylococcus aureus, Escherichia coli,* and *Klebsiella pneumonia* at a concentration of 50 mg/ml. They verified that alkaloids of plants created noticeably high inhibitory zones against bacteria compared to saponins and flavonoids. Crude methanolic extracts and phytochemicals' lowest inhibitory and bactericidal concentrations against the investigated bacterial strains were respectively, 25–50 mg/ml and 12.5–50 mg/ml [38]. Also, in an *in-vivo* study, a strong inhibitory effect against Listeria monocytogenes was reported during a 12-day, 4C investigation of *B. persicum* on a fish model system [39].

Antidiabetic Activity: *B. persicum* seed extract may result in insulin-dependent hypoglycemia. According to Eddouks *et al.* [40], the hypoglycemic effect of these plants may be caused by their ability to either stimulate or inhibit the consumption of glucose in peripheral tissues, particularly in fat and muscle tissues. In renal tubes, its extract has been shown to block the reabsorption of glucose [41].

On diabetic rats, a study was conducted and found that the *B. persicum* seed ethanolic extract, at different doses, substantially lowered the rats' blood glucose and insulin levels as compared to healthy rats [42]. Black zeera components have excellent antioxidant properties in aqueous extract, particularly carvone and flavonoids, which offer protection against diabetes and associated consequences. Rats with diabetes-induced kidney impairment have exhibited protective effects from *B. persicum* water extract **[43].** Black Zeera has been demonstrated to have strong hypolipidemic effects in several experiments on animals [44].

Anti-inflammatory Activity: Rat's ear oedema induced by croton oil and paw oedema induced by carrageenan was utilized to evaluate the anti-inflammatory properties of *B. persicum* fruits. According to the findings, essential oil (100-400 l/kg, i.p.) and hydro-alcoholic extract (200-800 mg/kg i.p.) both significantly reduced inflammation. Essential oil and Hydro-alcoholic extract both included flavonoids and polyphenolic substances that prevented mast cells from releasing histamine and had anti-inflammatory properties [45].

Gastrointestinal Protection: In a double-blind, randomised, crossover clinical trial, 93 breast cancer patients with refractory chemotherapy-induced nausea and vomiting with outpatient high emetogenic treatment took part. For seven days, the patients were administered Persumac, which is a combination of Rhus Coriaria and semi-ground *B. persicum* fruits. Their study found that persumac greatly reduced the frequency and intensity of nausea and vomiting [46].

Dyslipidaemia and Weight Loss: The treatment of *B. persicum* extract combined with endurance training for 6 weeks significantly raised cardiorespiratory capacity and HDL levels in research on forty male hypercholesterolemic mice. Additionally, there was a substantial decrease in LDL, TG, and total cholesterol, concentrations, however, the groups' differences in body weight were not statistically significant [44]. According to Saber Jafari-Maskouni *et al.,* 2020 [47] in their study, compared to the control group, *Bunium persicum* considerably decreased weight and BMI; however, waist circumference reduction was negligible.

Hepatoprotective Activity: The results of the liver histology in the research revealed a variety of abnormalities in the experimental groups, including necrosis, phagocytic cell accumulation, haemorrhage, and hepatic sinusoidal dilatation. The degree of lesions was notably greater in control fish compared to fish supplemented with *B. persicum* essential oil (BEO), especially in fish treated with 3% BEO [48].

Toxicity: Iranians use *B. persicum's* fruits and essential oil in a variety of ways and found that the plant has not been associated with any hazardous effects [49, 50]. However, sustained fruit-eating has been linked to weight loss and a yellow discolouration of the skin in the traditional medical literature. During pregnancy, *B. persicum's* emmenagogue characteristics should raise a few concerns [51, 52]. BEO has a large margin of safety in rats, according to an acute toxicity investigation, and its LD_{50} was 375 mg/kg/b.wt [53].

Traditional Uses: Because of its strong antioxidant and antibacterial properties, *B. persicum* has a great potential for use in food to prevent food-borne illnesses as well as the microbiological and chemical degradation of food.

Numerous experiments were done in this area to increase the shelf life of foods. In addition to having a major impact on consumer health, *B. persicum* essential oil (BPEO) can be utilized as a preservative against microbial contamination in products like Gouda cheese [54]. It can also be used as a natural flavouring. Due to the significant antioxidant impact shown in the starch film, this plant's essential oil can be employed as a natural preservative in the food business [55].

Additionally, biodegradable starchy films with BPEO can be employed as an active ingredient in food industries to improve safety and extend the shelf life of goods because they have a potent inhibitory effect on food pathogens [56]. According to research [57], adding BP extract can significantly increase the shelf life of fresh silver carp fish in refrigerator storage conditions for a period of 6 to 9 days. Additionally, it was demonstrated in a different study that the Hurdle system, which combines BPEO, low temperature, NaCl, and smoking, significantly inhibits the growth of L. monocytogenes in fish model systems [39].

Apart from its noteworthy influence on enhancing the colour, texture, flavour, and overall acceptability of this product, the BPEO has exhibited favourable inhibitory effects on food pathogens throughout the process of producing, maturing, and preserving Iranian white cheese [24]. The deterrent impact on the causative agents of chemical and microbiological deterioration has been demonstrated by adding various quantities of BP essential oil to chicken flesh [58]. According to (Talebi, 2017) [59], products can be packaged using polylactic acid films containing BPEO to increase their shelf life and guarantee their safety. Research on the preservation and oxidative stability of various edible oils, including linseed, olive oil, and soybean oil has demonstrated that *B. persicum* essential oil can be used as a food additive and a naturally occurring antioxidant to increase the oils' shelf life and oxidative stability [60, 29, 31].

***Cuminum Cyminum* Seeds:** The family Apiaceae includes *Cuminum cyminum*, or cumin, which is indigenous to South Asia and the East Mediterranean. It is also known as cumin seeds which are yellow-grey in colour and oval in shape. Since time, cumin seeds have been widely utilised

in many different cuisines of various food cultures, both whole and pulverised. Cumin seeds have been a staple element in many Indian dishes for thousands of years, including kormas and soups. They are also a component of many other spice blends [140].

India is the world's highest cumin seeds consumer, while China is the primary producer and exporter [61, 62]. It also possesses excellent antioxidant qualities [63]. It has numerous uses in conventional medicine and is used as food. Cumin seeds have plenty of medicinal benefits in the Indian Ayurvedic system of medicine, especially for digestive issues. It is a traditional cure for various ailments, including epilepsy, diarrhoea, dyspepsia, toothaches, indigestion, flatulence, whooping cough, and jaundice [64, 65]. People often identify the fruits of *B. persicum* as those of other Apiaceae plants, such as Carum carvi and *Cuminum cyminum*.

Phytochemistry: Several minerals, including iron, magnesium, calcium, zinc, potassium, selenium, manganese and copper, are abundant in *C. cyminum*. It also contains high levels of the B complex vitamins, such as vitamin B-6 (0.40–0.47 mg/kg), thiamin (0.60–0.68 mg/kg), niacin (4.50–4.57 mg/kg), and riboflavin (0.30–0.35 mg/kg), as well as some other critical vitamins like vitamin C (7.67–7.72 mg/kg) and vitamin E (3.30–3.35 mg/kg) that function as antioxidants. The seeds of this herb are a well-known source of many flavonoids and phenolics [66]. As well as cumin aldehyde (4-isopropyl benzaldehyde), pyrazines, such as 2-ethoxy-3-isopropylpyrazine, 2-methoxy-3-methylpyrazine and 2-methoxy-3-secbutylpyrazine, cumin seed has been acquired with a variety of additives. Additionally, cumin seeds include many phytochemicals that are well-known for their antiflatulent, carminative, and antioxidant properties [67]. Cumin aldehyde, p-mentha-1,3-dien-7-aL,b-pinene, g-terpinene,p-mentha-1,4-dien-7-aL, p-cymene, myrcene, limonene, linalool, a-farnesene, a-phellandrene, terpinolene, a-terpinene, a-terpineol, b-farnesene, safranaland camphene are all present in the steam-distilled essential oil of cumin seeds [68].

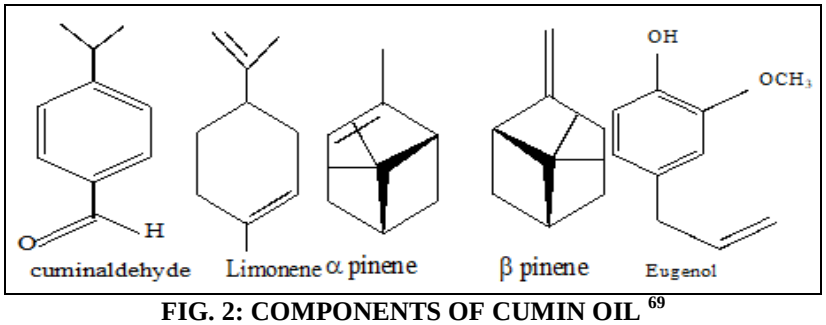

FIG. 2: COMPONENTS OF CUMIN OIL [69]

Trace Elements: Nearly 22 elements have been identified in *Cuminum cyminum* using instrumental neutron activation analysis. These elements included 8 essential chemical elements, or "micronutrients," present in the order Potassium (K) >, Calcium (Ca) > Sodium (Na) > Iron (Fe) > Zinc (Zn) > Chromium (Cr) > Cobalt (Co) and > Selenium (Se). The toxic elements present can be arranged in descending order of content Bromine (Br) > Arsenic (As) >Antimony (Sb). The findings indicate that the elements Iron (Fe), Potassium (K), Calcium (Ca), Strontium (Sr), and Sodium (Na) are at the major level. At the same time, zinc (Zn), Chromium (Cr), Bromine (Br), barium (Ba), and Rubidium (Rb) are present at the minor level. Cobalt (Co), Selenium (Se), Arsenic (As), Antimony (Sb), Cerium (Ce), Cesium (Cs), Europium (Eu), Lanthanum (La), Neodymium (Nd), Scandium (Sc), Samarium (Sm), and Thorium (Th) are discovered to be present at trace levels. While chromium is a necessary element as an insulin cofactor and a component of the glucose tolerance factor (GTF), the other five essential dietary elements Chromium (Cr), Cobalt (Co), Sodium (Na), Selenium (Se), and Zinc (Zn) are found in seeds in a high concentration[70].

Pharmacological Properties:

Antioxidant Activity: Cumin oils, as well as their solvent and aqueous extracts, have demonstrated strong antioxidant activity in a variety of test protocols. These effects' capacity to considerably

squelch hydroxyl radicals, 2,20-diphenyl-1-picryl hydrazyl (DPPH) radicals, and lipid peroxides is well-known and well-documented. Other investigations included ferric-reducing ability, ferric thiocyanate method in the linoleic acid system, soybean lipoxygenase-dependent lipid peroxidation, and ascorbate-induced rat liver microsomal lipid peroxidation (LPO) [71]. Mainly because of the presence of flavonoids, other polyphenolic components, and monoterpene alcohols, cumin oil displayed excellent antioxidant activity [72].

Antimicrobial Activity: A fatty oil found in cumin (*Cuminum cyminum*), primarily composed of petroselinic acid and linoleic acid, has demonstrated antibacterial action. Cumin powder suspension inhibits the growth of mycelium, as well as the formation of toxins or a-toxins in *Caribena versicolor*, *Aspergillus ochraceus,* and *Cantharellus flavus*. The antibacterial properties of cumin oils, as well as their solvent and aqueous extracts, have been revealed by several studies. A variety of harmful and beneficial gram-negative and gram-positive bacterial strains were used to test the antibacterial effect [73].

It has been discovered that the alcoholic extract and oil made from cumin seeds suppress the growth of clinical isolates of *Klebsiella pneumoniae. Eugenol*, *pinenes*, Limonene, and other minor components have also contributed to the antibacterial action of cumin oil, which is linked to the cumin aldehyde and linalool [74]. According to Behbahani, (2010) [75], the antifungal properties of cumin have been observed against pathogens found in food, soil, animals and humans as well as producers of mycotoxin and aflatoxins and vibrio species.

Antidiabetic Activity: Whereas, for the treatment of diabetic mellitus, cumin (*Cuminum cyminum*) supplements are more beneficial than glibenclamide [76]. According to Lee (2005) [9], cumin oil contains an active ingredient that inhibits the enzymes a-glycosidase and aldose reductase. A related consequence of diabetes mellitus is hyperlipidemia. In rats with STZ-induced diabetes, cumin was administered orally and resulted in decreased plasma and tissue cholesterol, body weight, free fatty acids, triglycerides and phospholipids. When cumin was introduced to a hypercholesterolemic diet for rats, the liver and serum cholesterol levels dropped [77].

Anti-inflammatory Activity: Adiponectin, high-sensitivity C-reactive protein (hs-CRP), and TNF α (Tumor necrosis factor-alpha) are just a few of the inflammatory indicators that treatments supplemented with *C. cyminum* have been shown to have a significant impact on [78, 79]. A thorough description of *C. cyminum's* anti-inflammatory activities was also provided by Srinivasan (2018) [80].

Gastrointestinal Protection: Cumin *(C. cyminum)* is incredibly beneficial for digestive issues. Cuminaldehyde, an aromatic chemical molecule that is a key ingredient in essential oils and gives cumin its distinctive flavour, activates salivary glands in the mouth of humans and helps to speed up primary digestion of food [81]. The thymol in cumin has stimulating qualities that aid in the release of bile and the enzymes needed for thorough meal digestion in the intestines and stomach. Additionally, cumin aids in digestion because of its high magnesium and salt levels as well as essential oil content [82]. The lipase, phytase, amylase, and protease activities were enhanced by solvent and aqueous extracts of cumin [83].

Dyslipidaemia and Weight Loss: Randomized clinical research was carried out to investigate the effects of cumin powder on the lipid profile and body composition of women who are overweight or obese, while another study assessed the hypocholesterolemic effect of *Cuminum cyminum* (MCC) methanolic extract. The findings indicate that the powdered cumin lowered fasting blood levels of triglycerides, cholesterol, and LDL while raising HDL. Reductions in BMI, waist circumference, weight, and fat mass were also noteworthy. On the other hand, it had no impact on fat-free mass and FBS [84].

There are reports of how supplementing with cumin extract affected levels of paraoxonase 1 activity, oxLDL, FBS, triglycerides, total cholesterol, LDL-C, HDL-C, apolipoprotein A1 (Apo A1) and apolipoprotein B (Apo B) in patients with hypercholesterolemia. The outcomes showed that after receiving cumin, the level of ox-LDL

significantly decreased. The activities of arylesterase and paraoxonase in serum increased following the consumption of cumin extract. PON1 (paraoxonase 1) hydrolyzes lipid peroxides in human atherosclerotic lesions and plays a preventive function against the oxidative alteration of plasma lipoproteins [85]. Researchers examined how overweight patients' metabolic profiles and weight loss responded to consuming *Cuminum cyminum.* At baseline and eight weeks during the intervention, fasting blood samples and anthropometric measurements were obtained. The consumption of *Cuminum cyminum* led to a comparable and noteworthy reduction in weight [86].

Hepatoprotective Activity: In experimental research, 30 female albino mice were administered 25mg/kg body weight of Profenofos to induce hepatotoxicity. Oral administration of *C. cyminum* (cumin) showed significantly lower levels of marker enzymes SGPT and SGOT. The bilirubin level also decreased as a result [87].

Toxicity: Following the correct administration of prescribed therapeutic dosages of cumin, health concerns or side effects are not documented [88]. In mice, the LD50 for essential oils was 0.59 ml/kg [89]. For six weeks, male Wistar rats were fed fruits containing cumin cyminum at a rate of 2% or 10% of their usual diet. For a similar time, rats were also fed a combination that contained 5% *Cuminum cyminum* fruits and 5% *T. vulgaris* leaves. Diets containing 2% *Cuminum cyminum* fruits were not found to poison the rats. Rats given a diet containing 10% *Cuminum cyminum* fruits displayed developmental retardation and enterohepatic nephropathy. Rats fed the combination of the two plants also showed leukopenia, anaemia, increases in serum AST activity and urea, as well as reductions in total protein and albumin levels [90]. Cumin essential oil's acute and subchronic toxicity was examined in a 30-day oral toxicity study conducted on rats. WBC count fell by 17.38% but hematocrit, platelet count, and haemoglobin concentration rose by 25.77%, 14.24%, and 108.81%, respectively. Half of the LDL/HDL ratio was reduced [91].

Traditional Uses: Cumin is typically used to treat diarrhoea and dyspepsia. A teaspoon of roasted cumin seeds is boiled in three cups of water to create hot cumin water, which is regarded as an effective treatment for colds and fever. Also, it is a carminative, astringent, abortifacient, and tonic for the intestines. It is reportedly used to boost lactation and lessen pregnant sickness. The seeds of cumin are used to treat skin conditions, asthma, bronchitis, leprosy, cough, ulcers, etc., and they also increase appetite. Veterinary workplaces continue to use cumin [92]. Cumin is utilised to strengthen nails and make hair glossy and lustrous. It is also useful for the treatment of carpal tunnel syndrome. The stomach's functions are strengthened by cumin, and any bleeding is stopped. Its oil is beneficial for the treatment of cholera and diarrhoea as it is a wonderful bactericide. Cumin oil's anti-septic qualities prevent cuts and wounds from becoming infected, and they also work as a circulatory, excretory, and nervous system tonic. Additionally helpful for massage and aromatherapy, cumin oil extract can be used to treat dandruff on the scalp. Its seeds can be ground to avoid bleeding gums, and the seeds can be massaged into the gums to treat sinusitis [93].

To remove toxins from the body, cumin seeds support the liver by stimulating the creation of the enzymes needed to break down lipids, starches, proteins, and sugars in the body. This herb's antiseptic qualities have been discovered to boost the immune system's resistance to the flu and the common cold. It is utilised to keep the respiratory system from developing a cough. According to Thippeswamy and Naidu (2005) [63], cumin contains a substantial amount of vitamin C and is a good source of iron. Cumin is a strong source of dietary fibre that can be used to treat piles and constipation. It also functions as an organic laxative that can speed up digestion and help heal injuries or infections in the digestive and excretory systems. Thymol promotes the secretions of acids, bile, and enzymes from the pancreas, and cumin contains a staggering level of calcium in secretions that can be accurately measured. While thymol is in charge of completing food digestion in the stomach and intestine, saliva aids in primary digestion [89].

***Zingiber officinale* (GINGER) Seeds:** The perennial herb ginger (*Zingiber officinale Roscoe*), which is native to Southern Asia, is one of the spicy spices in the Zingiberaceae family.

Due to its advantageous qualities, including pungency, nutrients, aroma, and pharmacological activity, has been utilized for more than 3000 years in traditional medicine, supplements, spices, cuisine, and flavouring agents in places like the Arab countries, Germany, Burma, Congo, Greece, Tibet, China, India, Japan, Indonesia, Sri Lanka, and the United States of America [94, 95].

As a carminative, antiflatulent, and digest ant, ginger has been used in traditional medicine to treat various ailments and symptoms, including colds, headaches, nausea, diarrhoea, upset stomach, rheumatism and arthritis. Additionally, ginger has been shown to have pharmacological activity against chemical, natural, and radiation-induced toxins, including hepatoprotective, neuroprotective, radioprotective, gastroprotective, nephroprotective, and reproductive-system-protective effects. Its molecular mechanism of action has also been investigated [96].

Phytochemistry: The ginger rhizome is composed primarily of 60–70% carbohydrates, 3–8% crude fibre, 9% protein, 8% ash, 3–6% fatty oil, and 2-3% volatile oil. Zingerone, shogaols, gingerols, and volatile (essential) oils, which make up to 3% of the fresh weight of ginger, are what give it its distinctive flavour. The sesquiterpenoids a-zingiberene (30–70%), b-sesquiphellandrene (15–20%), b-bisabolene (10–15%), and a-farnesene, as well as monoterpenoids (b-phellandrene, cineol, geraniol, camphene,citral, etc.), make up the majority of the volatile fragrant essential oil of ginger. Ginger also includes ginger glycolipids and diterpenes [97]. The gingerols that make [6]-gingerol (1-[40-hydroxy30-methoxyphenyl]-5-hydroxy-3-decanone), an oily liquid and the most prevalent component of the gingerols, are what give fresh ginger rhizomes their flavour. The non-volatile phenylpropanoid-derived chemicals from gingerols, particularly shogaols, are responsible for the bitter taste of cooked or dried ginger. During the drying process, the less aromatic zingerone is also created from gingerols; it has a spicy-sweet scent. Acrid resinous compounds are also present in ginger (5-8%) [98].

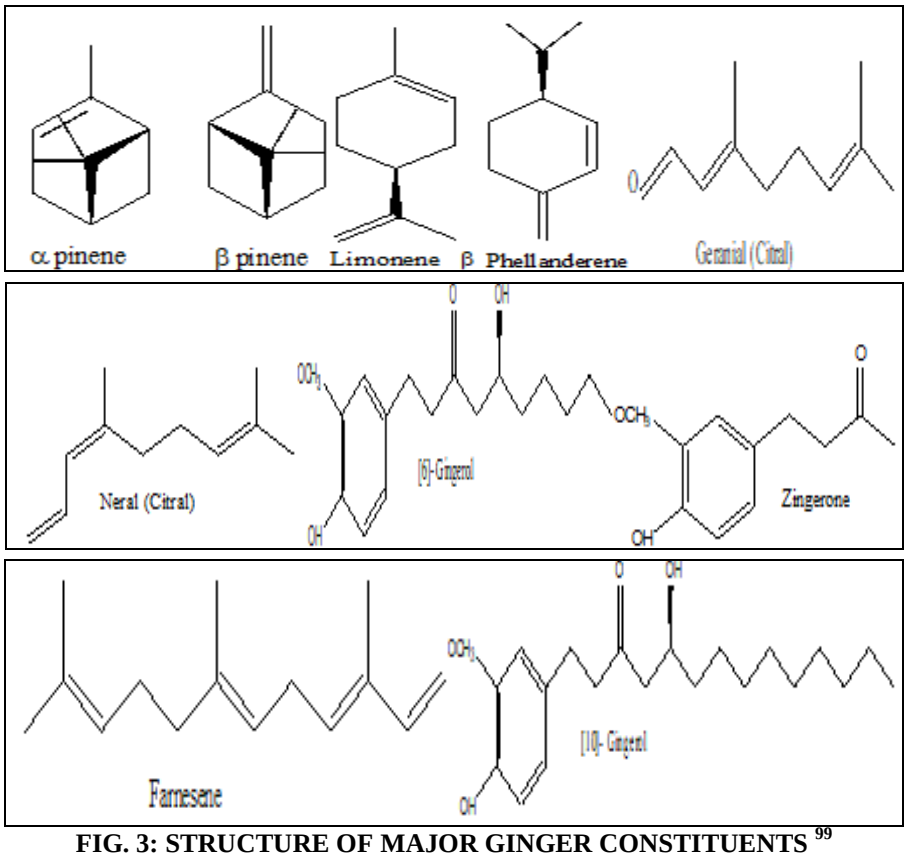

FIG. 3: STRUCTURE OF MAJOR GINGER CONSTITUENTS [99]

Trace Elements: Trace metal analysis in *Zingiber officinale* (Adrak) could be put in the following order Magnesium (Mg) (2700– 4090 mg/kg) > Calcium (Ca) (2000–2540 mg/kg) > Manganese

(Mn) (184– 401 mg/kg) > Iron (Fe) (41.8–89.0 mg/kg) > Zinc (Zn) (38.5–55.2 mg/kg) > Chromium (Cr) (6.02–10.8 mg/kg) > Nickel (Ni) (5.61–8.40 mg/kg) > Cobalt (Co) (2.04– 7.58 mg/kg) > Cadmium (Cd) (0.38–0.97 mg/kg).It was discovered that the potentially hazardous non-essential heavy metal lead (Pb), was below the method's detection limit. The findings of this study show that, among the identified macro- and micronutrients, ginger officinalis accumulates comparatively larger quantities of magnesium and manganese, respectively [100].

Pharmacological Activity:

Antioxidant Activity: The mammalian system spontaneously produces reactive oxygen species, which is offset by a sophisticated endogenous antioxidant defence system. Oxidative stress, which significantly impacts the onset of degenerative diseases, results from excessive free radical production outpacing the rate at which they are removed. Significant emphasis has been given to herbs and spices as natural antioxidants to support the body's defence mechanism. Spices like ginger include bioactive substances that have anti-inflammatory, antimutagenic, and anti-cancer properties. These substances are antioxidants [101].

10 ginger species utilised in Southeast Asia have had their flavonoid, phenolic acid, and polyphenol concentrations, as well as their overall antioxidant capacity, assessed. The relationship between total antioxidant capacity and inborn phenolic compounds was positive and linear. This study demonstrated that ginger rhizomes may be a source of free radicals. The spicy components of ginger, such as 6-gingerol and 6-paradol, have antioxidant and anti-inflammatory activities [102].

Antimicrobial Activity: Ajayi, 2017 [103] examined the dried ginger's antibacterial effectiveness against *Salmonella* spp., *Staphylococcus epidermidis*, and *Staphylococcus aureus*. The outcome demonstrated that every ginger extract exhibited antibacterial properties. According to the findings of other studies (Suhad, 2012) [104], compared to Gram-negative bacteria, ginger frequently works better against Gram-positive bacteria.

Antidiabetic Activity: Dietary ginger markedly reduced the HbA1c level in diabetic patients, according to a review of type 2 diabetes mellitus encompassing 454 participants in 8 trials [105].A meta-analysis of ten research including 490 participants found that ginger was equally efficient as adjuvant therapy for metabolic syndrome and type 2 diabetes mellitus [106]. Ginger produced this effect at doses between 100 and 800 mg/kg, considerably lowering fasting blood glucose after 1 hour in STZ-diabetic rats, with the highest effect being observed at 4 hours [107].

Anti-inflammatory Activity: In a meta-analysis of 8 studies with 734 participants, ginger was shown to be hypoalgesic in inflammation [108], and in an analysis of 5 trials with 593 participants, it was shown to be effective and reasonably safe for treating osteoarthritis [109].

Gastrointestinal Protection: It has also been shown that pungent spice ginger has gastrointestinal protective properties and favourable effects on mucosal glycoproteins, which reduces mucosal injury in experimental mice [110]. By investigating the uptake of iron, zinc, calcium, and beta-carotene by the intestines of rats pre-fed this spice, ginger has been investigated for a potential influence on the intestinal absorption of these nutrients. Higher *in-vitro* absorption of zinc, iron, b-carotene and calcium was observed in the intestines of animals fed ginger [111].

Dyslipidaemia and Weight Loss: There are a few findings on ginger's effectiveness in reducing the body's cholesterol and fat buildup. Dietary ginger's ability to decrease cholesterol helps people manage their weight, which lowers their chance of developing cardiovascular problems. After two to four weeks of treatment, aqueous ginger infusion on hypercholesterolemic rats resulted in a notable drop in blood total cholesterol, LDL cholesterol, and triglycerides as well as an improvement in the total cholesterol/HDL cholesterol ratio [112].

In addition, the fact Serum total cholesterol and triglycerides decreased in streptozotocin-induced diabetic rats after 20 days of oral administration of an ethanolic extract of ginger (200 mg/kg) and an increase in HDL-cholesterol, these findings demonstrate the potential of ginger in the treatment of diabetic dyslipidemia [113]. By promoting PPARd (peroxisome proliferator-activated receptor d), anti-

obesogenic phytochemicals are predicted to improve lipid metabolism. Ginger has been demonstrated to produce anti-obesity benefits in C57BL/6J mice by controlling the PPARg signalling pathway in adipocytes [114]. Weaning mice were used to assess key hepatic pathways that anti-obesogenic ginger phytochemicals target [115].

Hepatoprotective Activity: Ginger's antioxidant potential has also been linked to reports of hepatoprotective effects. Hepatic cancer and cirrhosis of the liver are linked to alcoholic fatty liver disease (AFLD).

Male C57BL/6 mice were given essential oil of ginger once a day orally for four weeks while they consumed a liquid diet containing significant amounts of alcohol, and they demonstrated hepatoprotective effect against AFLD as determined by histopathological examination, antioxidant enzyme activity, and serum biochemical analyses [116].

Toxicity: In general, ginger has been recognized as a reliable herbal remedy [117]. The usage of ginger in humans has been linked to a few modest negative effects. One participant in a clinical investigation with 12 healthy volunteers who got 400 mg of ginger orally three times daily for two weeks experienced minor diarrhoea during the first two days of the ginger pre-treatment.

In doses greater than 6 g, ginger may serve as a stomach irritant and produce heartburn. Ginger dust inhalation may result in IGE-mediated allergies. Though it has been suggested that ginger may be a safe and effective alternative to traditional anti-emetic medications, it may be wise to avoid using ginger or compounds derived from it when a woman is pregnant, at least until more research has been done [118].

Traditional Uses: Ginger is a stimulant, carminative, and spicy herb that is frequently used to treat stomach aches malaria, and fevers. It is mostly used to treat illnesses brought on by Kapha and Vata morbidity.

Ginger enhances the release of stomach fluids and boosts hunger when combined with lime juice and rock salt. Anorexia, atonic dyspepsia, arthritis, bleeding, cancer, chicken pox, diarrhoea, cholera, chest congestion, cold extremities, colitis, colic, common cold, cough, cystic fibrosis, difficulty breathing, dropsy, bleeding, fever, flatulent, indigestion, disorders of the gallbladder, nausea, rheumatism, morning sickness, sore throat, throat ache, and stomach pain are among the conditions for which it Many pharmacopeial Ayurvedic medicines contain ginger as a key ingredient [119].

***Trachyspermum ammi L* (AJWAIN) Seeds:** The common name for *Trachyspermum ammi L.* (Apiaceae) is Ajwain. The tall, annual herb known as ajwain, or *Trachyspermum ammi (L.)* Sprague is native to eastern Persia and India.

It is also a common home remedy used for a variety of health issues, including stomach pain, problems, acid reflux, stomach distension, retching, free stool, intestinal gas, diarrhoea, breathing difficulties, and heaviness in the abdomen after eating. Based on its historical uses, it typically grows across India, but mainly in Rajasthan and Gujarat [120].

It is frequently believed to be safe because it has been used for a long time to treat inflammatory diseases and abnormalities of the digestive tract. Because it is readily available and affordable, it is preferable to other plant-based products that have antioxidant properties [121].

Phytochemistry: The primary active components of Ajwain essential oil (E. O. A.) are phenols, especially thymol (35–60%), which significantly contributes to its therapeutic qualities. P-cymene (50–55%), terpinene (30–35%), -pinene (4%–5%), limonene containing -pinenes and -pinene (30–35%), and some carvacrol, saponins, flavons, and mineral matter (7.1%) are among the remaining non-thymol components known as thymine [122, 123].

The phenolic glucoside 2-methyl-3-glucosyloxy-5-isopropyl phenol is found in seeds. Camphene, myrcene, and D3-care are also said to be present in very small amounts. The fruit of Ajwain includes a glucoside called 6-O-glucopyranosyloxythymol as well as a yellow, crystalline flavone that resembles a steroid. *T. ammi* mostly consists of carvone (48%) limonene (38%), and dillapiole (9%). Thymol and volatile oil are responsible for the drug's flavour and flavour [124].

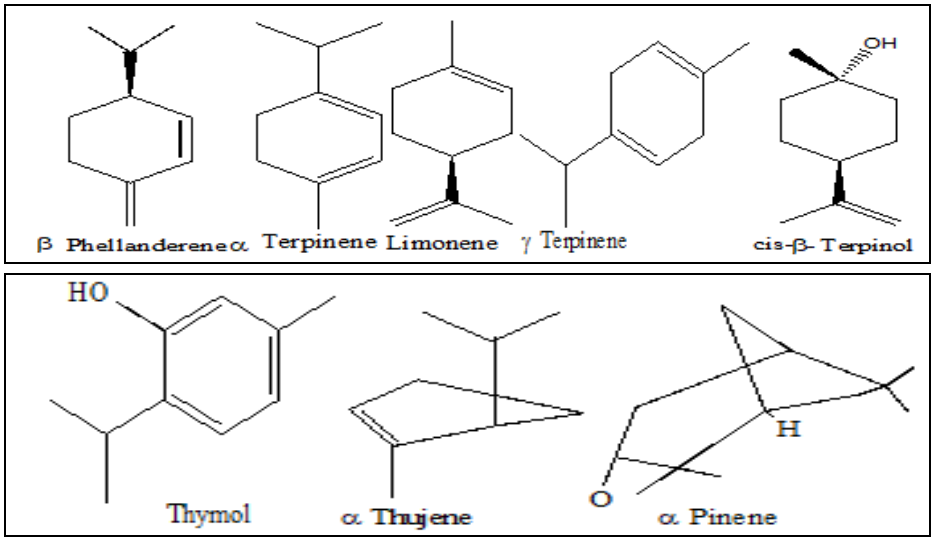

FIG. 4: CHEMICAL COMPOSITION OF PHYTOCHEMICAL COMPONENTS OF *TRACHYSPERMUM AMMI* [125]

Trace Elements: Calcium (1353.0±10.0 mg/kg), Magnesium (5.729±2.6 mg/kg), Sodium (228.47±2.0 mg/kg), Potassium (90.43±1.0 mg/kg), Iron (17.87±8.0 mg/kg), and Phosphorous (1764.0±16.0 mg/kg) have been determined to be the main constituents of *Trachyspermum ammi* (Ajwain) seeds. There are no reports regarding any heavy metals like As, Hg, Cd, Cr, or Pb in Ajwain spices [126].

Pharmacological Activity:

Antioxidant Activity: In an *in-vivo* experiment, ajwain extract's antioxidant and ameliorative properties were assessed on hexachloro cyclohexane-induced oxidative stress and toxicity. The findings indicated that dietary Ajwain extract consumption will reduce the toxicity caused by hepatic free radical stress [127].

Antimicrobial Activity: The antimicrobial activity of ajawain was examined against *Salmonella, S. aureus, E. coli* and *Shigella*, respectively. The result demonstrated the antibacterial activity of its seed extract against a variety of food spoilage microorganisms and pathogens [128].

Antidiabetic Activity: The antidiabetic activity of ajwain was investigated by using an α-amylase inhibitory assay. The high anti-diabetic properties of Ajwain essential oil can be attributed to the presence of the polyphenolic component thymol (50.43%), which is similar to the utilisation of thymol as a future natural, affordable, and prospective anti-diabetic precursor for medication formulation [129].

Anti-inflammatory Activity: Ajwain was examined for its potential to have an anti-inflammatory impact. As a result, both the complete alcoholic extract and the total aqueous extract have a noticeable anti-inflammatory effect *in-vivo* [130].

Gastrointestinal Protection: Traditional healers suggested the herb as a medication to stimulate the digestive system [131]. It has been discovered that ajwain increases the formation of digestive enzymes, gastric acid, and bile acids. It might also shorten the time food is in transit [132, 133]. As an enzyme modulator, ajwain enhanced the activity of pancreatic lipase and amylase, which may help the digestive stimulating function [83].

Dyslipidaemia and Weight Loss: The antihyperlipidemic function of ajwain is another activity that has been demonstrated. Ajwain seed powder is highly effective in lowering LDL cholesterol, total cholesterol, total lipids, and triglycerides, according to an in vivo investigation. Additionally, in albino rabbits, organic seed extract decreased the atherogenic index and raised HDL cholesterol levels [16]. Additionally, it contains a sizable number of fibres, which slow down the absorption of fat by the intestines and affect fat metabolism [122].

Hepatoprotective Activity: Methanolic extract of Ajwain has demonstrated *in-vivo* hepatoprotective action with 80% resistance againstlethal dose of paracetamol in mice, in addition to its powerful antioxidant activity. Additionally, the extract had

protective effects against CCl4-induced extension of pentobarbital sleep time as well as balancing the levels of hepatic enzymes such as aminotransferases (AST and ALT), alkaline phosphatase (ALP), and liver damage [134].

Toxicity: According to a report, ajwain was teratogenic to rat foetuses. Therefore, consuming it when pregnant may be dangerous [135].

Traditional Uses: Ajwain has been used internally as a common folk remedy for conditions such as cough, cold, asthma, diarrhoea, influenza, and cholera. It is also suitable for enhancing appetite, advised to treat stomach discomfort and ensure proper respiratory and kidney function [136]. The chilled fish product had the longest shelf life when made with a 3% Ajwain extract [137]. Ajwain essential oil and its main components are poisonous to Tuta absoluta larvae because they decrease the activity of AChE both *in-vitro* and *in-vivo* and greatly enhance the toxicity of -terpinene and p-cymene when combined with thymol [138, 139]. The putative cariostatic capabilities of *T. ammi* were revealed [122] and can be utilised as an alternate treatment to ward off caries infection.

CONCLUSION: Each of the four components (zeera, kala zeera, adrak, & ajwain) of arq-e-zeera has a unique set of pharmacological characteristics. All these plants possess phytochemicals responsible for treating different medical conditions. These components of arq-e-zeera may be employed in many of the therapeutic preparations considering their diverse range of activities.

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