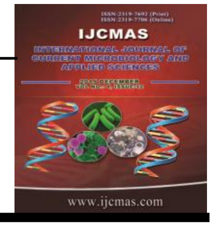

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Review Article

A Comprehensive Review on Pharmacological Properties of *Cuminum cyminum* (Cumin)

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A B S T R A C T

Cumin (*Cuminum cyminum* L.) is an annual plant that is not only one of the most popular seed species but also one of the oldest and most cultivated aromatic and herbaceous natural products with numerous medicinal, nutraceutical, and pharmaceutical properties. It is widely used in the beverage, food, liquor, medicine, perfume, and toiletry industries. Cumin is a traditional and much used spice from middle ages because it was an icon of love and fidelity. Cumin is available in different appearances such as anise, fennel and black cumin and the difference between them is their characteristics. Cumin has proved several benefits with the help of availability of nutrients. It is an important element of iron for energy, immunity systems, lactation and skin diseases. Cumin also shown various pharmacological effects but has some side effects. So, volatile plants generally come out as a complex mixture of less molecular weight lipophilic compounds that derived from different biosynthetic pathways and also contribute to a variety of physiological functions. The medicinal and health potential of cumin is mainly attributed to its antioxidant, antibacterial, antifungal, anti-inflammatory, antidiabetic, insecticide, and immunomodulatory properties.

Keywords

Cumin, Antidiabetic, Anti-inflammatory, Hypotensive, Hypolipidemi

Introduction

An annual herb, Cumin (*Cuminum cyminum Linn*.), is a member of the *Umbellifereae* plant family. It is well renowned for its preventive, medicinal, and dazzling scent qualities. It is one of the popular spices regularly used as a flavoring agent. Cumin is an annual cultivated herb, with an erect, round, slender, branched stem, about a foot high (Figure 1). (Rebey *et al.*, 2012) Although cumin was initially grown in Egypt, it is currently grown throughout much of Asia, including China, India, and other Middle Eastern nations. Cumin has reportedly had significant culinary and therapeutic purposes throughout history in a variety of Middle Eastern cultural contexts. The reason for its popularity, pervasiveness, and wide acceptability was due to its peppery and spicy flavour, which has made it a suitable substitute for black pepper, which is typically expensive and hard to come by. Cumin has fantastic medicinal and aesthetic properties and can be used to fake pallor.

Cumin is a small hairy, brownish in color, boat shaped seed plant that have a spicy sweet aroma property and powerful slightly bitter and pungent flavor (Figure 2) (Rebey *et al.,* 2012). Cumin is an aromatic plant having hollow stems and the well-known members of this family are anise, asafoetida, caraway, carrot, celery, coriander, cumin, dill, fennel, parsley, parsnip, and sea holly. Cumin is still a key ingredient in many Asian dishes, despite the fact that the majority of people classify the seed as a spice. In addition to the seeds' use as a culinary additive and spice, researchers have discovered specific uses for them inconventional and pharmaceutical medicine (Abu-Nahoul and Ismail, 1995). The plant's increasing relevance can be observed in its persistent demand and low production and supply levels (Abu-Nahoul and Ismail, 1995). Farmers incur crop losses every year as a result of insect and disease effects, with Fusarium wilt disease being the most common of these diseases (Omer *et al.*, 1997). There have been reports of the plant's use in the creation of traditional and indigenous medicine. For instance, the plant has long been used in India by the Ayurvedic medical system to cure a variety of illnesses, including dyspepsia, diarrhoea, and digestive abnormalities (Srinavas, 1986).

Oil from Egyptian cumin seeds has reportedly been found to have 39.2% cumin aldehyde (Srinavas, 1986). Probably as a result of cumin aldehyde's presence, cumin oil possesses excellent antifungal capabilities. According to research, the seeds promote bile acid elimination and activity (Platel and Srinivasan, 2000). In addition, it has been observed to stimulate pancreatic activity in laboratory rats and to increase the activity of digestive enzymes in the small intestine, including amylase, trypsin, and lipase (Milan *et al.,* 2008). Rats allegedly had a much shorter time for food to pass through their digestive tracts after ingesting roughly 1.25% of cumin seeds (Platel and Srinivasan, 2001). Broiler weight gain was dramatically accelerated by adding cumin seeds to the diet. Additionally, the presence of significant amounts of dietary fibre resulted in improved absorption of meals (Mansoori *et al.,* 2006).

The oil, derived from cumin by steam distillation, is used to flavor alcoholic beverages, desserts, and condiments. It is also used as a fragrant component of creams, lotions, and perfumes. Cumin has been used as anti-inflammatory, diuretic, carminative, and antispasmodic, treatment of toothaches and epilepsy and also as an aid for treating dyspepsia, jaundice, diarrhea, flatulence, and indigestion. Cumin powder has been used as a poultice and suppository and has been smoked in a pipe and taken orally.

Traditional uses of *C. cyminum*

Cumin is a multipurpose plant that is used both as medicine and food in many different parts of the world. In the creation of other cuisines, such as soup, bean dishes, pickles, cheese, and liquors, it is also employed as an additive and spice (Gohari and Saeidnia, 2011; Thippeswamy and Naidu, 2005). For instance, cumin is a highly well-liked spice all across the world and is a key condiment spice in India (Dhandapani *et al.,* 2002). After black pepper (*Piper nigrum*), cumin-based spices are thought to be the second most consumed spices worldwide (Zohary and Hopf, 2000). *C. cyminum* seeds are traditionally used for the treatment of a wide range of illnesses, including toothaches, dyspepsia, (Dhandapani *et al.*, 2002) diarrhoea, epilepsy, and jaundice (Nostro *et al.,* 2005). Strong bioactives and biochemicals like terpenes, phenols, and flavonoids are what give them such a significant therapeutic potential. Cumin seeds are used in traditional medicine as a carminative and appetite stimulant, as well as a stomachic, astringent remedy for diarrhoea and to enhance taste (Romagnoli *et al.*, 2010).

The powder or decoction of cumin seeds has been used in many Maghreb nations, including Algeria, Morocco, and Tunisia, to curem digestive issues. As a stomachic, carminative, antispasmodic, and anthelmintic, it is advised. Additionally, cumin has frequently been applied externally as a poultice to treat acute viral inflammations like neck mumps (Mazars, 1998). Additionally, Indian herbalists frequently recommend cumin for the treatment of fever, colds, and sleeplessness.

The fruit of the plant has been used extensively in ancient Iranian medicine to treat a variety of ailments, including treatment of toothaches and epilepsy (Janahmadi *et al.*, 2006). Cumin has also reportedly been used frequently to cure dyspepsia, diarrhoea, and jaundice in Ayurvedic medicine (the traditional Indian medicine). Growing research suggests that the plant material has beneficial anti-inflammatory, diuretic, and hypoglycemic properties (Wang and Jones, 2004). Colic, gas, and diarrhoea are also relieved by the tonic and stimulating effects of cumin (Berrai and Zibouche, 2016). It has been demonstrated to improve lactation, lessen morning sickness while pregnant, and can be used as a poultice to alleviate breast or testicularedoema (Jalali-Heravi *et al.*, 2007).

C. cyminum L. are extensively used as a spice because of their characteristic aroma, but they are also frequently used in traditional medicine to cure a number of illnesses. The biological and medicinal effects of cumin are well documented in the literature, and are typically attributed to its bioactive ingredients such terpenes, phenols, and flavonoids (Mnif and Aifa, 2015).

Pharmacological effects of *C. cyminum*

Cumin and its active constituents used as a antibacterial, antifungal, anti-inflammatory, antioxidant, astringent, atherosclerosis (hardening of the arteries), blood thinner, bone loss, cancer, cardiovascular disease, carpal tunnel syndrome, cataracts (eye disease), cavities, dental plaque, diabetes, digestion, diuretic (improves urine flow), ear infections, food uses (flavoring and preservative), gas, gastrointestinal disorders, general health maintenance, general stimulant, high cholesterol, immune modulation (affects the immune system), insect repellant, insecticidal, low blood sugar, menstrual flow stimulant, promoting flow of breast milk, relaxation, seizures/epilepsy, ulcers, weight loss. Numerous pharmacological benefits of *C. cyminum*, including anti-inflammatory, anti-diabetic, antioxidant, neuroprotective, and chemopreventive properties, have been identified.

Antimicrobial Activity

A drug that kills or prevents the growth of microorganisms like bacteria, fungus, or protozoa is known as an anti-microbial (Aberoumand and Deokule, 2009). According to technical definitions, antibiotics are only those chemicals produced by one bacterium that may either kill or stop the growth of another (Wang and Jones, 2004). Of fact, in modern parlance, the term "antibiotic" refers to practically any medication that aims to clear your body of bacterial infection. Antimicrobial substances include both synthetically created compounds and antibiotics (Hajlaoui *et al.*, 2010). Plant essential oils are renowned for their antibacterial properties and may be able to prevent plant illnesses brought on by bacteria, especially those that originate in seeds (Matsubara *et al.,* 2000). Due to their accessibility, lack of side effects or toxicity, and superior biodegradability in comparison to currently available antibiotics and preservatives, natural products have recently attracted increasing interest (Abbas and Ahmed, 2010). Due to public interest in natural food items and growing worries about microbe resistance to conventional preservatives, the study of naturally-occurring antimicrobials for food preservation is receiving more attention (Agrawal, 1996). Besides having an antibacterial action, cumin includes fatty oils. There are many inhibitory effects of cumin in powder suspension (Skrinjar *et al.*, 2009). A cumin seed oil extract improved cell shape, capsule expression, and reduced urease activity while inhibiting the development of *Klebsiella pneumoniae* and its clinical isolates (Razzaghi-Abyaneh *et al.,* 2009). In contrast, limonene, eugenol, α-pinene, and a few other minor elements have been proposed to contribute to the antibacterial action of cumin oil (Sheikh *et al.,* 2010). This feature was linked to cumin aldehyde, carvone, limonene, and linalool. Numerous antibacterial activities of cumin seed oil have been discovered (El-Sawi and Mohamed, 2002). According to reports, *Escherichia coli*, *Bacillus brevis*, and *Enterobacter aerogenes* are all susceptible to the cumin hydrosols. Additionally, rosemary essential oil was found to have weaker antibacterial properties than cumin essential oil against *Listeria monocytogenes*, *S. aureus*, and *E. coli* (Gachkar *et al.,* 2007). A natural resistance plasmid DNA from *K. pneumonia* as well as planktonic and biofilm cells have all been tested against the essential oil from cumin seeds (Derakhshan *et al.,* 2010). The findings showed that the essential oil reduced biofilm formation, slowed strain development, and worked synergistically to increase ciprofloxacin's effectiveness against *K. pneumoniae*.

The antibacterial activity of ethanolic extracts of *C. cyminum* against *Staphylococcus aureus* has been reported (Srivastava and Mustafa, 1994). The essential oils of *C. cyminum* also possess antimicrobial properties. Coronatine elicitation reportedly enhanced the yield and level of chemical components, as well as antibacterial, antifungal, antioxidant and *in vitro* cytotoxic activities of the cumin essential oil. The antifungal effects of *C. cyminum* essential oils against *Candida albicans* have also been reported. According to literature, cumin has demonstrated a broad-spectrum antifungal effect against several pathogenic *Candida* and other fungal species.

The antimicrobial action of cumin both oil and aqueous has assessed against a wide range of valuable and pathogenic gram-positive and gram-negative microbial strains. Cumin seed oil and alcoholic extract inhibited the growth of *Klebsiella pneumoniae* and its clinical isolates and caused improvement in cell morphology, capsule expression and decreased urease activity. Cumin has also found the biofilm-formation preventive properties against *Streptococcus mutans* and *Streptococcus pyogenes*. Cumin has shown the anti-fungal activity against food, soil, animal and human pathogens, yeasts, aflatoxins and mycotoxin producers (Skrinjar *et al.,* 2009).

The in vitro examination of cumin hydrosols against a variety of phytopathogenic fungi revealed encouraging antifungal properties (O'Riordan and Wilkinson, 2008). In contrast to other commercial items, commercial samples of cumin were uncontaminated by aflatoxin, a toxin made by *Aspergillus flavus*, according to O'Riordan and Wilkinson (2008). Cumin oil, which is notably high in α-pinene (29.2%), has been shown by Mnif and Aifa (2015) to have positive inhibitory effects on the growth of Aspergillus strains from several species. Additionally, fluconazole-resistant fungi have been tested against using cumin essential oil (Mnif and Aifa, 2015).

The MeOH extract of cumin seed shown a considerable antiviral activity when the effects of aqueous, methanolic, and hydroalcoholic extracts of cumin seed on HSV-1 development in a Vero cell line were examined in vitro. For Vero cells, it has a CC_{50} value of 0.45, anIC_{50} value of 0.18, and a therapeutic index of 2.5 mg/ml, respectively (Mohamadein *et al.,* 2015). Cumin seed extracts in both aqueous and hydroalcoholic form hadno inhibitory impact on HSV-1 (Ani *et al.,* 2006).

Digestive stimulant

An animal study looked at whether cumin seeds had any stimulatory effects on the digestive enzymes in light of the fact that they are said to help with digestion in traditional medicine and home remedies. Particularly, the effects of continuous dietary consumption and one oral dosage of cumin seeds on the digestive enzymes of the rat pancreas and intestinal mucosa have been studied (Platel and Srinivasan, 2000). Dietary cumin's ability to speed up food transit time is roughly related to the positive effects they have on bile secretion or digestive enzymes.

Antidiabetic effects

It has been observed that giving diabetic rats treated with alloxan anaqueous extract of cumin for six weeks prevented body weight loss and significantly decreased blood glucose and glycosylated haemoglobin. Additionally, it has been noted that the treatment lowers the levels of triglycerides, free fatty acids, cholesterol, and phospholipids in the plasma and tissues of the experimental rats (Bairy and Rao, 2001). Cumin has also shown a promising potential for usage as a dietary supplement to guard against diabetic DNA damage and reduce diabetes complications, according to Mnif and Aifa (2015). Human diabetics have claimed that cumin seeds have an anti-diabetic effect (Karnick, 1991). In alloxan-diabetic rabbits, *Cuminum nigrum* seeds or their water or methanol extracts have been found to be hypoglycemic. The flavonoid chemicals found in *C. nigrum* seeds have been suggested to have an anti-hyperglycemic effect. When compared to quercetinas an aldose reductase inhibitor and acarbose as α-glucosidase inhibitor, cumin aldehyde, an isolated component of *C. Cyminum* seeds, exhibits more inhibitory efficacy against Sprague-Dawley ratlens aldose reductase and α-glucosidase. The supplementation of *C. cyminum* has reportedly improved fasting blood glucose level and glycosylated hemoglobin readings. *C. cyminum* essential oil was also reported to exhibit maximum antidiabetic inhibition activity of α-amylase (Mnif and Aifa, 2015).

Oral administration of cumin showed hypoglycemic effect in normal rabbit, resulting in significant decrease in the area under the glucose tolerance curve hyperglycemic peak. The biologically active constituent cumin aldehyde inhibited aldose reductase and alpha glucosidase isolated from rat (Lee, 2005). In hyperlipidemia, when administered cumin by orally to alloxan induced diabetic rats, reduced the body weight, plasma and tissue cholesterol, phospholipids, free fatty acids and triglycerides and also decreased aspartate transaminase (AST), alkaline phosphatase (ALP) and γ-glutamyl transferase (GGT) activities and decreased the tissue (liver and kidney) levels of cholesterol, triglycerides and phospholipids.

Anti-inflammatory and Antioxidant Activity

The anti-inflammatory properties of cumin essential oil inlipopolysaccharide (LPS)-stimulated RAW 264.7 cells and the underlying processes were examined. By employing Gas Chromatography-Mass Spectrometry (GC-MS), volatile components in essential oils were discovered, with cumin aldehyde (48.8%) being the most prevalent. Cumin oil's ability to reduce inflammation was demonstrated in LPS-stimulated RAW cells through its inhibition of NF-B and nitrogen activated protein kinases. Numerous studies have been done on the antiradical and antioxidant properties of cumin essential oils. Results from -carotene bleaching tests out performed those from free radical scan experiments using 2,2-diphenyl-1-picrylhydrazyl (DPPH) (Gachkar *et al.*, 2007).

Cumin essential oils have remarkable antioxidant activities and phenolic contents which increase with maturity. Both the pure extracts and active agents of the European cumin have also been evaluated and found to be highly effective.

Mohamed, Hamed and Fouda have reported that cumin extract contains 23.02 ± 0.045 mg GAE/g extract and 19 ± 0.132 mg QE/g extract for total phenolic and total flavonoids, respectively. (Qazi *et al.*, 2004) The cumin oils have high antioxidant activity due to presence of monoterpene alcohols, essential flavours, flavonoids and other poly-phenolicmolecules.

Hypotensive Effect

In renal hypertensive rats, the standardized aqueous extract of *C.cyminum* seeds was tested for its ability to lower blood pressure as well as its effects on inflammation, the production of arterial endothelial nitric oxide synthase, and oxidative stress. Rats were subjected to the two-kidney, one-clip (2K/1C) technique to produce renal hypertension (Kalaivani *et al.*, 2013).

Hypolipidemic and weight reduction effects

Rats with removed ovaries [OVX] were used to assess the hypocholesterolemic effect of the methanolic extract of *C. Cyminum* (MCC). OVX rats received 10 weeks of oral administration of MCC1000 mg/kg and estradiol benzoate equivalent to 0.15 mg/kg of estradiol. The findings showed that whereas MCC was superior to estradiol in protecting OVX mice from elevated LDL levels broughton by ovariectomy. Taghizadeh *et al.*, studied the effects of *C.cyminum* intake on weight loss and metabolic profiles among overweight subjects by a randomized double-blind placebo-controlled clinical trial.

Cardio-protective influence through hypolipidemic

It was investigated how cumin seed aqueous extract affected arterial-endothelial nitric oxide synthase and its potential anti-hypertensive effects. In renal hypertension rats, expression, inflammation, and oxidative stress have been studied. Cumin seeds contain flavonoids, which are known to have antioxidant action and strengthen the antioxidant system. According to a study, cumin extract boosted the activities of paraoxonase and arylesterase in serum while considerably lowering the amount of oxidised low-density lipoprotein (OxLDL). Rats' liver and serum cholesterol levels were examined after cumin was introduced to diets that were both normal and hypercholesterolemia-inducing (Sambaiah and Srinivasan, 1991). When dietary cumin was consumed at a level that was about five times the average amount (1.25%), no cholesterol-lowering effects were observed.

Chemopreventive effects

When 2.5 and 5.0 percent dietary cumin were tested against benzo[a]pyrene-induced carcinogenesis in the stomach and 3-methylcholanthrene (MCA)-induced tumorigenesis in the uterine cervix in mice, it showed a substantial effect against the tumour. (Gagandeep *et al.,* 2003) Cumin exhibits chemopreventive properties. Cumin prevented lipidperoxidation, indicating that its capacity to modify may be responsible for its ability to prevent cancer.

Anticarcinogenic Effect

The protective mucins colon and glucuronide conjugates are hydrolyzed as a result of the activity of mucinases and glucuronidase being significantly elevated in the presence of the colon carcinogen 1,2-dimethylhydrazine (DMH). Toxins that are released by glucuronide hydrolysis increase the risk of colon cancer. Cumin can protect the colon by reducing mucinase and α-glucuronidase activities in the presence or absence of DMH, according to a prior rat model study.

A black cumin hexane extract was also shown by Bourgou *et al.,* (2012) to be effective against the colon cancer cell line DLD-1 and the tongue cancer cell line A-549, with IC50 values of 31.0 and 63.0 mg/ml, respectively. Two-ethyl-6-heptylphenol (EHP), a physiologically active substance isolated with benzene from Egyptian *C. cyminum* seeds, was shown to have good anticancer activity against six different tumour cell lines by Goodarzi *et al.,* in 2009 (HEPG2, HELA, HCT116, MCF7, HEP2, and CACO2). (Bourgou *et al.,* 2012) EHP had no cytotoxic effects when its action on the common fibroblast cell lines [BHK] was examined.

More recently, Daneshmandi *et al.,* (2010) showed that *C.cyminum* essential oil displayed appealing immuno-modulatory capabilities and might therefore be employed as a therapeutic or complementary drug in the treatment of tumours. (Daneshmandi *et al.,* 2010) In fact, it was found that *C. cyminum* essential oils strongly suppressed tumor-cell development when applied at dosages of 50 and 500 mg/ml. The ability of different cumin seed dosages in diets to prevent cancer has also been confirmed.

For example, the effects of such diets have been examined in relation to 3-methylcholanthrene [MCA] and benzo[a]pyrene (BaP)-induced uterine cervix and stomach carcinogenesis, respectively. The findings showed that cumin significantly inhibited stomach tumour growth. The nutraceutical potential of spent cumin produced by the Ayurvedic industry was assessed and compared to that of raw cumin in terms of antioxidant (in terms of scavenging DPPH radical), antidiabetic [in terms of better α-amylase inhibition and glucose uptake activity in L6 cells), and anticancer properties. The findings indicated that cumin waste-derived nutraceutical food formulations might have a significant impact on the management or prevention of degenerative illnesses.

The dietary supplements of cumin have prevented the occurrence of rat colon cancer induced by a colon-specific carcinogen and also decrease the activity of β-glucuronidase and mucinase enzymes. In cumin-colon treated rats, the levels of cholesterol, cholesterol/phospholipids ratio and 3-methylglutaryl COA reducates activity were reduced.

The other inhibition activities of dietary cumin in mice are benzopyrene-induced for stomach tumorigenesis, 3-methyl-cholanthrene induced uterine cervix tumorigenesis, and 3-methyl-4-dimethy-aminoazobenzene induced hepatomas.

Ovicidal [Insecticidal] Activity

Cumin essential oil was proven to be an ovicidal agent by having the greatest impact on the destruction of *Tribolium confusum* and *Ephestia kuehniella* eggs. The *Ephestia kuehniella* TL99 (medianlethal time) value was 127.0 h at a concentration of 98.5 ml cumin essential oil/lair.

In adult male and female *Blattella germanica*, assessed the insecticidal and acetylcholine esterase (AChE) inhibitory activity of cumin and *Apicaceae* plant essential oils. At a dosage of 5mg/filter-paper, cumin demonstrated > 90% fumigant toxicity against German adult male cockroaches. Cumin essential oils possess effective insecticide activity against adult *Myzus persicae* and *Musca domestica* (Yeom *et al.*, 2012).

Miscellaneous nutraceutical effects

The seeds of cumin have historically and traditionally been used to alleviate diarrhoea. For instance, castor oil-induced diarrhoea in albino rats was tested against the aqueous extract of cumin seeds (100, 250, and 500 mg/kg). According to research on the inhibitory effects of *C. cyminum* essential oil on the fibrillation of -SN, cumin aldehyde contained incumin essential oils can control -SN fibrillation, demonstrating the potential therapeutic uses of such naturally occurring bioactive aldehydes in cumin. Fibrilliation of -SN is a crucial process in the pathogenesis of various neurodegenerative illnesses, including Parkinson's disease.

Central nervous system

The administration of cumin oil decreased the frequency of spontaneous activity induced by maximal electroshock and pentylenetetrazol (PTZ) in mice in time and concentration dependent and increased duration manner. Cumin aldehyde has tyrosinase inhibitor property that prevented the oxidation of l-3.5-dihydroxyphenyklalanine (l-DOPA) (Kubo and Kinst-Hori, 1998).

Estrogenic/anti-osteoporotic

The presence of phytoestrogens in cumin has shown the anti-osteoporotic effect of reduced the urinary calcium excretion, augmentation of calcium content and mechanical strength of bones (Malini and Vanithakumari, 1987).

Other biodynamic actions

Cumin has shown antitussive and produced relaxant effect by stimulating beta-adreno receptors and/or histamine H1 receptors. It has also shown antiaggregatory activity and inhibition of eicosanoid synthesis by inhibited arachidonic acid (AA)-induced platelet aggregation, thromboxane B2 production from exogenous AA and simultaneous increase in the formation of lipoxygenase (Srivastava and Mustafa, 1994).

Figure.1 Showing *Cuminum cyminum* plant

Figure.2 Showing seeds of *Cuminum cyminum*

Bioavailability enhancer

The bioenhancer flavonoid glycoside 3′, 5-dihydroxyflavone 7-O-β-d-galacturonide- 4′-O-β-d-glucopyranoside of cumin has shown a significant enhancement of rifampicin levels in rat plasma through the enhancement of peak concentration (Cmax) and area under the curve (AUC) of rifampicin by 35 and 53%, respectively, when co-dosed with this molecule (Sachin *et al.,* 2007).

Protective effects

The impact of cumin on kidney exposure to profenofos was assessed in female swiss albino mice. According to the study's findings, cumin has a moderating influence on both the amount of creatine and uric acid. Rats given 500 mg/kg of paracetamol orally for 4 weeks showed growth retardation, hepatotoxicity, and nephrotoxicity. The impact of cumin on sperm quality and testicular tissue was investigated in mice after experimentally induced copper poisoning (copper sulphate100 mg/kg). The dosage of *C. cyminum* used was 1 mg/kg. The findings revealed that, in contrast to the control group, the copper group's sperm concentration, motility, and viability dramatically declined at weeks 4 and 6, and severe degenerative alterations were found in the testicular tissues. When compared to the copper group, the cumin-treated group showed a significant improvement in sperm count, motility, and viability as well as normal architecture in the majority of seminiferous tubules with ordered epithelium.

Bronchodilatory and Wound-Healing activity

Because previous studies have demonstrated the relaxing effects of 2-stimulatory, histamine H1 receptor inhibitory, and anticholinergic drugs, it is possible that the relaxing effects of various extracts from *C. cyminum* on the tracheal chains of guinea pigs result from a variety of different mechanisms, including stimulation of -adrenergic receptors, inhibition of histamine H1 receptors, or an anticholine. The effects of KCl on calcium channels have been demonstrated, and calcium channel blockers have been found to have bronchodilatory effects. Acute inflammation precedes the production of collagen and other intracellular macromolecules, which are then remodelled to form scars during the healing process of a wound.

On the wound models of granuloma, incision, and excision in albino rats, extracts and various fractions derived from cumin seeds were tested for their ability to heal wounds. Triterpenes were found to be the primary ingredient in wound healing, according to other investigations. The wound healing activity of cumin seeds can therefore be extrapolated to have been caused by terpenoids in the alcoholic extract and petroleum-ether fraction.

Immunological and Anti-amyloidogenic effect

Using flow cytometry and ELISA in healthy and immune-suppressed mice, *C. cyminum's* health-modifying impacts and immunomodulatory capabilities were assessed. In healthy mice, *C.cyminum* induced the production of Th1 cytokines and T cells. The findings indicated that treatment dramatically raised the number of T cells (CD4 and CD8) and the Th1-dominant immune response in adose-dependent manner, indicating immunomodulatory activity through modulation of T lymphocyte expression. The active amyloidogenic inhibitors in cumin oil were investigated. Two substances that had extremely similar chemical structures, terpinolene and limonene, prevented fibrillation. HEWL fibrils had an adverse effect on PC12 cells (derived from a transplantable rat pheochromocytoma), whereas inhibited forms of HEWL fibrils in the presence of terpinolene led to higher levels of viability, as shown by 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT), lactate dehydrogenase (LDH), and flow Terpinolene was predicted to interact with the protein's flexible cleft via molecular local docking studies. In the hot spot sections of the protein, this contact site was around the tryptophan residues 62 and 63 as well as two additional hydrophobic residues.

Cumin is an effective immunomodulatory agent whose administration significantly and dose-dependently increased the $CD4^+$ and $CD8^+$ T cell count and modulated T lymphocyte expression. The detailed immunomodulatory and other beneficial properties of *C. cyminum* have also been reported in literature. The oral treatment of cumin stimulated the T cells (CD4 and CD8) The cytokines' expression in normal and cyclosporine-An induced immune suppressed animal. Cumin also depleted T lymphocytes, decreased the elevated corticosterone levels and size of adrenal glands and increased the weight of thymus and spleen in stress induced immune suppressed mice (Chauhan *et al.,* 2010).

Contraceptive and Anti-osteoporotic effect

Male albino rats were used to test the effectiveness of *C. Cyminum* isolated fractions (CcFr) as a contraceptive. No significant changes in body weight were seen after oral administration of CcFr 50 mg/rat/day for 60 days, but there were clear anomalies in spermatogenesis, as seen by lower numbers in round spermatids, preleptotene spermatocytes, and secondary spermatocytes. A 100% negative fertility result was produced by sperm motility, density, and morphology. Significant declines were observed in testosterone levels. According to the authors' findings, *C. cyminum* can operate as a natural male contraceptive by inhibiting spermatogenesis in rats. Rats were used to test *C. cyminum's* anti-osteoporotic effectiveness. After receiving bilateral ovariectomies (OVX), adult Sprague-Dawley rats were randomised into 3 groups. More sham operations involved animals. The other two OVX groups received 0.15 mg/kg of estradiol and 1 g/kg of the methanolic extract of *C. cyminum* fruits (MCC) over the course of 10 weeks, whereas OVX and sham control groups received oral administration of vehicle. Animal bones, uteri, and blood were gathered at the conclusion of the study. In compared to OVX control, MCC (1 g/kg, po) considerably raised calcium content and mechanical strength of bones while dramatically reducing urine calcium excretion. In SEM examination, it revealed higher bone and ash densities and enhanced bone microarchitecture. It had no effect on body weight gain or the weight of the atrophic uterus in OVX animals, in contrast to estradiol. MCC had no anabolic impact on anatrophic uterus, but it reversed ovariectomy-induced bone loss in rats.

Drug Bioavailability-Enhancing Activity

Recently, interest in herbal drug interactions has grown. The research offers compelling evidence that these interactions could result in positive outcomes, with drug bioavailability standing out as the most significant one. An approach known as herbal drug synergism has shown cumin to increase the bioavailability of rifampicin, which is very intriguing. In fact, Sachin *et al.,* (2007) researched the pharmacological approach in which a drug's bioavailability may be influenced by the synergism of herbal drugs (Sachin *et al.,* 2007). A pure component isolated from *C. cyminum* and some herbal items were shown to interact pharmacokinetically with RIF in the investigation. The flavonoid glycoside 3',5-dihydroxyflavone 7-O-D-galacturonide 4'-O-D-glucopyranoside, present in aqueous cumin seed extract, was responsible for significant increase in rat plasma levels of RIF action(CC-I). The Cmax and AUC [area under the curve] of RIF were found to be improved by 35 and 53%, respectively, by CC-I. The changed bioavailability profile of RIF was determined to be due to the glycoside's capacity to increase permeability. (Sachin *et al.,* 2007) Recent research has demonstrated the critical functions that drug efflux pumps, including P-gp, play in preventing drug entry into the systemic circulation. P-gp is an energy-dependent trans-membrane drug efflux pump that is an ATPase and a member of the ABC transporter family. Its molecular weight is around 170 kDa and it contains 1,280 amino acid residues (Juliano and Ling, 1976). Given that it is distributed at the drug absorption site and has a selectivity for substrates, P-gp is becoming increasingly important in the improvement of absorption; however, additional work needs to be done to examine its modulation.

Additionally, it has been shown that the bioactive fraction of *C.cyminum* increases the bioavailability of drugs like erythromycin, cephalexin, amoxicillin, fluconazole, ketoconazole, zidovudine, and 5-fluorouracil. (Qazi *et al.*, 2004) Various volatile oils, luteolin, and other compounds have been implicated in *C. cyminum's* bioavailability and bioefficacy. Luteolin proved to be a potent P-gp inhibitor (Boumendjel *et al.*, 2002).

Cumin has reportedly had vital culinary and therapeutic purposes throughout history in a variety of cultural contexts. Cumin is mostly cultivated for its numerous medicinal, nutraceutical, and pharmaceutical properties. It also has a wide use in beverage, food, liquor, medicine, perfume, and toiletry. Cumin seeds are highly nutritious and have a high nutritional value. The medicinal and health potentials of cumin are mainly attributed to its antioxidant, antibacterial, antifungal, anti-inflammatory, antidiabetic, insecticide, and immunomodulatory properties. The various parts of the cumin plant (leaves, shoot, root, and flowers) also contain similar and different chemical compounds. More studies are, however, required to unravel novel components and applications of cumin. They offer significant levels of protein, dietary fibre, and fat, particularly monounsaturated fat. Cumin seeds also include a number of minerals, particularly iron, as well as other vitamins like vitamins B and E. Aldehyde, derivatives of methane, terpinene, p-cymene, and pinene make up cumin essential oil. In the current review, additional pharmacological activities including anti-hypertensive, hypo-cholesterolemic, wound healing, and chemo prevention have been reported. The effectiveness of contraceptives and immune-modulating medications was also covered. The current analysis offers compelling evidence of cumin's positive effects and reports and discusses experimental studies that confirm the results that have been claimed. Finally, cumin has a place in supplementary medicine. As a phyto-constituent in the cosmetic business, it can also be used due to its broad spectrum of biological qualities. But in order to make greater use of this plant, mechanisms and modes of action of cumin still need to be clarified.

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