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Pharmacological activities of *Carum carvi* L.

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ABSTRACT

Carum carvi L. Cultivated in many regions of the world including Iran and India, states of Gujarat and Rajasthan. This plant is used in Iranian folk medicine for therapeutic purposes. The aim of this study was to overview its therapeutic effects than its nutritive and industrial effects. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and Iran Medex databases. The initial search strategy identified about 128 references. In this study, 113 studies was accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of *Carum carvi* L. and dated mainly from the year 1964 to 2016. The search terms were “ *Carum carvi* L.”, “therapeutic properties”, “pharmacological effects”. The results of this study was shown that this plant possess Appetite- suppressing activity, Oral mucositis, Irritable Bowel Syndrome, Hypothyroidism, Blood pressure lowering, vasodilator and cardiac-modulatory, Antitubercular activity, Anti-cancer, Anti-colitis activity, Cardiovascular disease, Anti-obesity activity, Antimicrobial activity, Hyperlipidemic effect, antihyperglycemic and hyperlipidemic activity, Anti-oxidative stress activity. This plant is useful for treatment and prevention of many diseases with few (if any) side effects.

Keywords: *Carum carvi* L., Phytochemicals, Therapeutic effects, Pharmacognosy, Alternative and complementary medicine.

INTRODUCTION

Caraway [*Carum carvi*] [black zeera] belongs to Apiaceae family [1, 2] is a biennial plant grown in western Asia, Europe and Northern Africa [3]. It is also known as Persian cumin. It is a biennial, aromatic, umbelliferous plant. The plant grow 20–30 cm [4, 5]. The main flower stem is small white or pink flowers in umbels. Caraway fruits are crescent-shaped achenes, around 2 mm long.

Caraway is useful for digestive problems including heartburn, bloating, gas, loss of appetite, and mild spasms of the stomach and intestines [6, 7]. Caraway oil is also used to help people cough up phlegm, improve control of urination, kill bacteria in the body, and relieve constipation. Women use caraway oil to start menstruation and relieve menstrual cramps; nursing mothers use it to increase the flow of breast milk [8-10]. Caraway is used in mouthwashes and in skin rubs to improve local blood flow. The seeds of *Carum carvi* [caraway] are considered as antispasmodic, carminative, astringent and used in the treatment of stomatitis stimulant, diarrhea, dyspepsia, hysteria, flatulent indigestion, colic, dyspeptic headache and improve liver function, for gastrointestinal problems

and obesity, anticonvulsant, Reno-protective effect ,anti-hyperglycemic and antimicrobial effects[6, 11-18] Carumcarvi is a widely available herb that has been used as a food additive[19] and as a medication in traditional medicine for many years. Its potential biological effects include anti-obesity, analgesic, anti-inflammatory, anti-anxiety and antispasmodic, hypothyroidism activities [20-24].

Carumcarvi L. [Apiaceae family] or caraway is a common household plant grown around the world including Iran. Caraway fruits are used as flavoring agent in foods and beverages, and have various traditional uses in ethnomedicine. Anti-inflammatory, spasmolytic, antimicrobial, antioxidant, carminative and immunomodulatory properties of caraway suggest that it might exert beneficial effects on inflammatory bowel disease [IBD][8, 25-28].

Chemical compound

Major Phytochemicals reported in *C. carvi* seeds are limonene, carvacrol, carvone, carvenone, γ -terpinene, α -pinene, linalool, and p-cymene[29].The essential oil compositions of the different plant parts of wild growing caraway a high proportion of limonene [61-83%], and those from inflorescences limonene [39-62%] and germacrene D [23-41%][30]. Leaves and stems, low in volatiles, were dominated by germacrene D and germacrene [31].the essential oils extracted under SFE conditions had high carvone and limonene contents[30] .The oils from young fruits had a high proportion of limonene [61-83%], and those from inflorescences limonene [39-62%] and germacrene D [23-41%]. The carvone contents of fruits, inflorescences and leaves varied greatly. Leaves and stems, low in volatiles, were dominated by germacrene D and germacrene A[31]

Appetite- suppressing activity

In an *in vivo* study, the appetite-suppressing effects of caraway aqueous extract (CAE) on 70 aerobically trained, overweight, and obese women were examined. Subjects were randomly allocated into placebo and experimental groups and consumed either 30 mL/day of CAE or placebo without changing their diet or physical activity over a period of 90 days. The results showed a significant reduction in appetite levels and carbohydrate intake of the experimental group compared with the placebo group ($p < 0.01$). These preliminary outcomes suggest that a dietary CAE might be effective in weight management of physically active, adult females, reducing their body size and hunger level. (32)

Oral mucositis

In an animal study, The effects of hydroalcoholic extract of caraway in 5-fluorouracil -induced OM was investigated. It showed that the caraway was more powerful against *Staphylococcus epidermidis* and *Streptococcus intermedius*. The main constituent of its essential oil was identified as γ -Terpinene .Thus topical use of this extract is to reduce intensity of MO due to its antibacterial activity and terpinene contents.(1)

Irritable Bowel Syndrome

the efficacy of caraway oil poultices for treating IBS was assessed and it was found that Hot caraway oil poultices is effective without any side effect, although it may be useful because of its heat therapy. Thus, it is helpful and appropriate in the self-management of IBS.(33)

Hypothyroidism

In a case study, a patient with papillary thyroid carcinoma was reported who were under treatment with levothyroxine and experienced an elevated TSH level by ingestion of Carumcarvi. The result of this study was suggested the effect of consumption of Carumcarvi in increasing TSH level in hypothyroid patients treating with levothyroxine.(34)

Blood pressure lowering, vasodilator and cardiac-modulatory

In an animal study, blood pressure-lowering, endothelium-dependent, and independent vasodilator and cardio-modulatory actions of Caraway was investigated. results indicated that cardiovascular effects of its seed extract are mediated possibly through combination of Ca^{++} antagonist, nitric oxide modulating and phosphodiesterase inhibitory mechanisms. However, its mechanism of action is yet unknown.(35)

Antitubercular activity

In a human study, the efficacy of Carumcarvi on pharmacokinetics of rifampicin, isoniazid, and pyrazinamide in fixed dose combination was evaluated and it showed that its additions result in increasing in plasma levels of

rifampicin, isoniazid, and pyrazinamide and consequently, it can act as a bioenhancer and modifies the kinetics of antitubercular treatment favorably.(12)

Anti-cancer

In an animal study, the effect of dietary caraway oils on the progression of cancer, with emphasis on β -catenin expression in the colon during DMH-induced colonic carcinogenesis was examined. It was indicated that the Wnt/ β -catenin signaling pathway is activated during colon cancer promotion and that the expression of colonic β -catenin is altered in long-term caraway oil feeding, leading to suppression of DMH-induced premalignant lesions in rat colon.(36)

The growth inhibitory effect of TQ on 2 TNBC cell lines with mutant p53 was investigated. Cell metabolism assays showed that TQ inhibited TNBC cell growth without affecting normal cell growth and TQ enhanced cisplatin- and docetaxel-induced cytotoxicity. Thus, it is suggested that TQ could be useful in the management of TNBC, even when functional p53 is absent. (37)

Anti-colitis activity

The effects of caraway hydroalcoholic extract (CHE) and its essential oil (CEO) in an immunological model of colitis in rats induced by trinitrobenzene sulfonic acid (TNBS) was investigated. It was found that caraway fractions are both effective and possess anti-colitis activity irrespective of the dose and route of administration (3).

Cardiovascular disease

In an animal study, the effects of caraway plant on blood levels of glucose, lipid profile, and C-reactive protein in diabetic rats was investigated. It was suggested that caraway can exhibit blood glucose and lipid lowering activities in diabetes, without any effect on C-reactive protein level (38).

Anti-obesity activity

The weight-lowering effects of caraway extract (CE) on physically active, overweight and obese women was investigated and. Participants received either 30 mL/day of CE or placebo without changing their diet or physical activity. No changes were observed in lipid profile, urine-specific gravity, and blood pressure of subjects. The results suggest that a dietary CE with no restriction in food intake, when combined with exercise, is of value in the management of obesity in women wishing to lower their weight, BMI, body fat percentage, and body size. Results of this study suggest a possible phytotherapeutic approach for caraway extract in the management of obesity. (39).

Antimicrobial activity

The antimicrobial efficacy of pullulan films containing caraway essential oil was evaluated against *Salmonella enteritidis*, *Staphylococcus aureus*, *Saccharomyces cerevisiae*, or *Aspergillus niger*. It showed that *S. enteritidis* was the most resistant among the tested species. Results of this study suggest the feasibility of applying a pullulan film with incorporated CEO to extend the microbiological stability of minimally processed foods (40).

Hypolipidemic effect

The effect of aqueous extract of *Carum carvi* seeds in diet induced hyperlipidemia in rats was assessed and it found that aqueous seeds extract of this plant reduce lipid levels in diet induced hypolipidemic rats(6).

Antioxidant activity of this valuable herb have been revealed(41).

Antihyperglycemic and hypolipidemic activity

The effect of oral administration of caraway on the blood glucose level, lipid profile, and the weight of diabetic rats was evaluated. The results showed that oral administration of caraway caused a significant decrease in blood glucose level of treated rats ($p = 0.001$) and alleviated their body weight loss. Caraway has both antihyperglycemic and hypolipidemic activity in diabetic rats. However, more studies are needed in vivo to be able to use it in real life.(14).

Anti-oxidative stress activity

In an animal study, the effects of caraway extracts on preventing sepsis induced by oxidative tissue injuries have been investigated. Sepsis induction caused a significant increase in kidney but not heart LP, indicating that kidney was more affected by sepsis induction than heart. Kidney LP and plasma urea/creatinine ratio levels were readily reversed in rats treated with essential oils but not in those treated with hydroalcoholic extract. Thus, it showed that

caraway oils probably have a protective role in kidney tissue against oxidative injury in advanced stages of sepsis (42).

Potential side effects

The oral intake of CAE found to be safe at a dosage of 30 ml daily for a period of 12 weeks (11).

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