Cumin (Cuminum cyminum L.): A review of its ethnopharmacology, phytochemistry

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ABSTRACT

Introduction: 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. The objective of this work was to provide a precise and up-to-date review of the ethnopharmacology, phytochemistry, and biological activities of cumin. Methods: Information was gathered from the review of relevant literature obtained from various databases, such as Science Direct, Springer, PubMed, Google, and Google Scholar. Results: The various parts of the cumin plant (leaves, shoot, root, and flowers) contain similar and different chemical compounds. Conclusion: The medicinal and health potential of cumin is mainly attributed to its antioxidant, antibacterial, antifungal, anti-inflammatory, antidiabetic, insecticide, and immunomodulatory properties. More studies are, however, required to unravel novel components and applications of cumin.

Key words: Cuminum cyminum, Cumin, Ethnopharmacology, Phytochemistry, Biological Activities

INTRODUCTION

The usage of herbal and other natural products for disease management, whether for prevention or treatment, has been known for ages1–5. Some edible herbal plant species, such as cumin (Cuminum cyminum L.), are also commonly used as food additives owing to their accessibility, safety, and usefulness6. Cumin belongs to the Apiaceae family, tribe Ammineae, and subtribe Carinaceae, and has 2n = 14 chromosomes6,7. Cumin is the second most popular seed species after black pepper8. It is an annual plant and is also one of the oldest and most cultivated aromatic and herbaceous natural products with numerous medicinal, nutraceutical, and pharmaceutical properties. Cumin also has wide usage in the beverage, food, liquor, medicine, perfume, and toiletry industries7. It is native to and cultivated extensively in several places, mainly in arid and semi-arid climates, such as China, Egypt, Saudi Arabia, and the Mediterranean, as well as India and Iran. However, the largest consumer of cumin seed in the world is India while China is the largest exporter and producer. Cumin has remarkable antioxidant properties and is traditionally used as an astrigent, carminative, coagulant and stimulant, as well as remedy against diarrhea, dyspepsia, epilepsy, toothache, whooping cough, flatulence, indigestion, and jaundice6,7,9–11. Cumin grows to about 30–60 cm tall, with a glabrous, branched, and slender stem. It has compound leaves with thread-like leaflets. It has terminal umbel inflorescence. Each cumin branch has 3–9 umbels with 5–7 umbellets, consisting of small hermaphrodite flowers which are either white or pink. It has schizocarps, i.e. fruits containing two mericarps, and about 6 mm long seeds which are oblong but thicker in the middle. It is mostly planted in the winter or autumn with the emergence of seedlings occurring after about 14 – 50 days. Cumin seed germination usually occurs at low temperatures (< 20 °C) and is arrested at high temperatures12. Cumin has a weak vigor owing to its increased sensitivity to environmental stresses and because its seeds contain 10% oil11. The seeds of cumin are characterized by abortifacient, antispasmodic, diuretic, emmenagogic, carminative, and stomachic properties. Oleoresin from the seeds is commonly applied in crackers, sauces, meat, and sausages. The distinct and strong aroma of the seeds are responsible for its use as spices as well as other medicinal uses. The aroma is mainly due to cuminol which makes up 2.5 – 4.0% of the seed. The essential oils of cumin seeds primarily contain hydrocarbons and aldehydes8.

The objective of this work is to provide a precise and up-to-date review of the ethnopharmacology, phyto-
chemistry, and biological activities of cumin. The information was gathered from the review of relevant literature obtained from various databases, such as Science Direct, Springer, PubMed, Google, and Google Scholar.

**Previous studies on C. cyminum**

According to literature, the quality and quantity of the compounds commonly identified in cumin vary in the various parts of the plant, such as the leaves, shoots, roots, and flowers. Though both the shoots and flowers have relatively similar terpene compounds, their concentrations are higher in the flowers. Furthermore, α-pinene and β-pinene were not found in the roots, α-phellandrene was notably the only detected terpenoid compound in the leaves while the flowers had the highest concentration of α-pinene. Cumin fruits mainly contain cellulose, fixed oil content (about 10%), mineral elements, protein, sugar, and volatile oils (1.5%), as well as appreciable amounts of phenolic compounds. Formulated C. cyminum essential oil in oil-in-water nanoemulsions have demonstrated successful incorporation of lipophilic bioactive agents into functional food gels. Natural deep eutectic solvents have also been used to significantly enhance cumin essential oil extraction with a higher yield and premium quality, as an eco-friendly and economical extraction technique.

An increase in enzymatic (amylase, lipase, protease, and phytase) activities and antioxidant activity were achieved with saline and hot aqueous cumin extracts, as well as its oleoresin and essential oil. Water-soluble C. cyminum polysaccharides possess lower molecular weight and effectively stimulate RAW264.7 and NK-92 cells to express interleukin (IL)-1β, IL-6, IL-12, and tumor necrosis factor (TNF)-α inflammatory cytokine, and release nitric oxide. Kedia and colleagues have also reported the fumigant, larvicidal, oviposition deterrent, ovicidal, repellent, and pupaeidal activities of C. cyminum seed essential oil, as well as its 4 main components (cymene, cumin aldehyde, γ-terpinene, and (−)-β-pinene) against Callosobruchus chinensis and Sitophilus oryzae. Cumin is considered a very useful eco-friendly alternative for the management of insect infestation in food commodities. C. cyminum also has a remarkable antibiofilm and quorum sensing inhibitory potential against Gram-negative bacterial pathogens. The essential oils of cumin have also demonstrated strong fumigant effects and toxicity against Anopheles gambiae.

**Ethnopharmacology of Cumin**

The common ethnomedicinal uses of cumin are summarized in Table 1. Traditionally, cumin is commonly used as a remedy against gastrointestinal, inflammatory and neurological disorders, as well as toothaches. In Iranian traditional medicine, cumin fruits are also used as a medication for colic, diarrhea, dyspepsia and flatulence, and for stimulation of breast milk production. It is used in Morocco for the flavoring of foods and soft dates. It is also commonly used in Tunisia as aromatic herbs and culinary spices, as well as in Italy for various gastrointestinal and neurological diseases.

**Phytochemistry of Cumin**

The various parts of the cumin plant (leaves, shoot, root, and flowers) contain similar and different chemical compounds. The most important chemicals which have been identified from cumin essential oils are shown in Table 2.

**Biological activities of Cumin**

The most important biological activities of cumin found in literature are summarized in Table 3. They include antioxidant, antibacterial, antifungal, anti-inflammatory, antidiabetic, insecticide, and immunomodulatory properties.

**Antioxidant activity**

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 (2018) 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.

**Antimicrobial activity**

The antibacterial activity of ethanolic extracts of C. cyminum against Staphylococcus aureus has been reported. 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.
Table 1: Ethnomedicinal uses of cumin

| Region     | Plant part used (Iran) | Traditional uses and ethnobotanical reports                                                                 | References                                      |
|------------|------------------------|-------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| Iran       | Spice                  | Antispasmodic, lactagogue and carminative ingredient.                                                        | Tabarsa, et al. (2020)                           |
| Iran       | Cumin seed (zire in Iran) | Treatment of mild digestive disorders as a carminative, euphetic, astringent in bronchopulmonary disorders, cough remedy, as well as an analgesic. | Minooeianhaghighi, Sepehrian and Shokri (2017)  |
| Iran       |                        | Ramin, Sattari and Ghavamzadeh (2017)                                                                     |                                                 |
| Tunisia    | Seed                   | Aromatic herbs and culinary spices, stimulant, carminative, astringent, and anti-diabetic properties.      | Rebey et al. (2017)                             |
| Italy      | Seeds                  | Aromatic herbs for toothaches, gastrointestinal, and neurological diseases.                                 | Benelli et al. (2018)                           |
| Morocco    | Seeds                  | Flavoring of foods especially soft dates.                                                                   | Petretto et al. (2018)                          |

Antidiabetic activity
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.

Anti-inflammatory activity
According to literature, treatments supplemented with *C. cyminum* have a profound effect on several inflammatory biomarkers, such as adiponectin, high-sensitivity C-reactive protein (hsCRP), and TNF-α. Srinivasan (2018) has also reported a detailed anti-inflammatory activity of *C. cyminum*.

Insecticide activity
Cumin essential oils possess effective insecticide activity against adult *Myzus persicae* and *Musca domestica*.

Immunomodulatory activity
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.

CONCLUSION
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. The medicinal and health potentials of cumin are mainly attributed to its antioxidant, antibacterial, antifungal, anti-inflammatory, anti-diabetic, 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.

ABBREVIATIONS
- eNOS: Endothelial nitric oxide synthase
- hsCRP: high-sensitivity C-reactive protein
- IL-6: Interleukin-6
- TNF-α: Tumor necrosis factor-alpha
- TRX1: Thioredoxin 1
- TRXR1: Thioredoxin reductase 1

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AUTHOR’S CONTRIBUTIONS
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Table 2: Common important chemicals in cumin essential oils

| Compound              | Chemical category | Part/Extract | References                                                                 |
|-----------------------|-------------------|--------------|-----------------------------------------------------------------------------|
| Cumin aldehyde        | Essential oil     | Seed and fruit | Kedia et al. (2015)\textsuperscript{19}; Moghaddam et al. (2015)\textsuperscript{14}; Jafari, Sattari and Ghavamzadeh (2017)\textsuperscript{1}; Petretto et al. (2018)\textsuperscript{10}. |
| γ-Terpinine           | Essential oil     | Seed and fruit | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Kedia et al. (2015)\textsuperscript{19}; Moghaddam et al. (2015)\textsuperscript{14}; Jafari, Sattari and Ghavamzadeh (2017)\textsuperscript{1}. |
| α-Sabinin             | Essential oil     | Seed         | Jafari, Sattari and Ghavamzadeh (2017)\textsuperscript{1}.                      |
| α-Flandren            | Essential oil     | Seed         | Jafari, Sattari and Ghavamzadeh (2017)\textsuperscript{1}.                      |
| α-Kadinin             | Essential oil     | Seed         | Jafari, Sattari and Ghavamzadeh (2017)\textsuperscript{1}.                      |
| p-Cymene              | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Kedia et al. (2015)\textsuperscript{19}; Moghaddam et al. (2015)\textsuperscript{14}; Petretto et al. (2018)\textsuperscript{10}. |
| α-Pinene              | Essential oil     | Fruit        | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Moghaddam et al. (2015)\textsuperscript{14}; Petretto et al. (2018)\textsuperscript{10}. |
| (−)-β-Pinene          | Essential oil     | Seed         | Kedia et al. (2015)\textsuperscript{19}; Petretto et al. (2018)\textsuperscript{10}. |
| α-Phellandrene, α-Terpinene | Essential oil | Fruit        | Moghaddam et al. (2015)\textsuperscript{14}; Petretto et al. (2018)\textsuperscript{10}. |
| α-Terpineol           | Essential oil     | Fruit        | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Moghaddam et al. (2015)\textsuperscript{14}; Petretto et al. (2018)\textsuperscript{10}. |
| Safranal              | Essential oil     | Fruit        | Moghaddam et al. (2015)\textsuperscript{14};                          |
| Limonene              | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Petretto et al. (2018)\textsuperscript{10}. |
| 1,8-Cineole           | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Petretto et al. (2018)\textsuperscript{10}. |
| Linalool              | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23};                          |
| Linalyl acetate       | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23};                          |
| α-Terpineol acetate   | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23};                          |
| Geraniol              | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23};                          |
| Methyl eugenol        | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23};                          |
| Sabinene              | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Petretto et al. (2018)\textsuperscript{10}. |
| Terpinolene           | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Petretto et al. (2018)\textsuperscript{10}. |
| α-Thujene             | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Petretto et al. (2018)\textsuperscript{10}. |
| Myrcene               | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Petretto et al. (2018)\textsuperscript{10}. |
| γ-Terpineol           | Essential oil     | Seed         | Naeini, Naderi, and Shokri, (2014)\textsuperscript{23}; Petretto et al. (2018)\textsuperscript{10}. |
| Daucene               | Essential oil     | Seed         | Petretto et al. (2018)\textsuperscript{10}.                                  |
| d3-Carene             | Essential oil     | Seed         | Petretto et al. (2018)\textsuperscript{10}.                                  |
| Pinocarvone           | Essential oil     | Seed         | Petretto et al. (2018)\textsuperscript{10}.                                  |
| Caryophyllene         | Essential oil     | Seed         | Petretto et al. (2018)\textsuperscript{10}.                                  |
| Farnesene-(Z)-β       | Essential oil     | Seed         | Petretto et al. (2018)\textsuperscript{10}.                                  |
| Germacrene D          | Essential oil     | Seed         | Petretto et al. (2018)\textsuperscript{10}.                                  |
| α-Acoradiene          | Essential oil     | Seed         | Petretto et al. (2018)\textsuperscript{10}.                                  |
| Carotol               | Essential oil     | Seed         | Petretto et al. (2018)\textsuperscript{10}.                                  |
### Table 3: Most important biological activities of cumin

| Properties          | Model                  | Findings                                                                 | References                                                                 |
|---------------------|------------------------|--------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Antioxidant         | In vitro               | The antioxidant activities of cumin essential oils are positively correlated with their phenolic contents which increase at stages of intermediate and premature. | Moghaddam et al. (2015)\(^\text{14}\), Mohamed, Hamed and Fouda (2018)\(^\text{14}\). |
| Antibacterial       | In vitro               | Ethanol extracts of *C. cuminum* antibacterial effect have against *Staphylococcus aureus*. | Mostafa et al. (2018)\(^\text{25}\).                                       |
| Antifungal          | In vitro               | *C. cuminum* essential oils have a broad-spectrum antifungal effect against several pathogenic *Candida* species | Naeini, Naderi, and Shokri (2014)\(^\text{23}\); Minooeian-haghighi, Sepehrian and Shokri, (2017)\(^\text{24}\); Petretto et al. (2018)\(^\text{18}\). |
| Anti-inflammatory   | Animal model (rat)     | Nine weeks of intervention improved plasma nitric oxide, decreased the systolic blood pressure up-regulated the gene expression of eNOS, Bcl-2, TRX1, and TRXR1; and down-regulated Bax, TNF-α, and IL-6. | Kalaivani, Saranya and Ramakrishnan (2013)\(^\text{26}\); Srinivasan (2018)\(^\text{27}\). |
| Antidiabetic and anti-inflammatory | Human     | Eight weeks of intervention improved fasting blood glucose, glycosylated hemoglobin as well as serum levels of insulin, TNF-α, C-reactive protein, and adiponectin. | Jafari, Sattari and Ghavamzadeh, (2017)\(^\text{1}\). |
| Insecticide         | Insect vectors         | Cumin essential oils were very active against adults of *Musca persicae* (LC50=3.2 ml/L) and *M. domestica* (LD50=31.8 μg/adult). | Benelli et al. (2018)\(^\text{21}\).                                       |
| Immunomodulatory    | Animal (Swiss albin mice) | Cumin administration significantly increased CD4 and CD8 (T cells) count through the modulation of T lymphocytes expression and dose-dependently. | Chauhan et al. (2010)\(^\text{28}\); Srinivasan (2018)\(^\text{27}\); Tabarsa et al. (2020)\(^\text{18}\). |

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