The History of Black Cumin Oil, its use in Traditional Medicine and some Pharmacological Properties

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ABSTRACT
Black Cumin (Nigella sativa) is a herbaceous plant which belongs to the Ranunculaceae family. The seeds of black cumin have been used in some foods such as confectionery, drinks and bakery products. It’s widely used in traditional and modern medicine to treat and prevent a high number of diseases. The seeds of this plant contain fixed and essential oils as well alkaloids, proteins, saponin, and other chemical components. Most biological properties result from thymoquinone, a major component of the essential oil and present in fixed oil. Many researchers are interested in studying the pharmacological properties of this oil, and have shown its effect against inflammation, cancer, hepatic disorders and other diseases. A huge number of studies support the potential use of this plant in human therapy.

ÖZET

INTRODUCTION
The Ranunculaceae family is composed of around 1,500 to 2,000 species grouped into around 60 genera. Some genera like Anemone, Aconitum, have already shown an interesting effect in medicine (1) (Figure 1).

It is a small genus widely used as a condiment in Mediterranean and Asian producing countries, but some species also extending across most of Europe, western Asia and Northern Africa (Figure 2).

Nigella (Nigella Sativa) also called black cumin, pepper, black sesame has been used for nearly 2000 years as a spice and natural remedy in the East, in Egypt where it is called “gold of the Pharaohs ”, and more particularly among Muslims influenced by the prophetic word. The plant is traditionally used to treat bronchopulmonary and gastrointestinal disorders (1).

The seed of N. sativa has been used traditionally in food as well as in medicine. In tea, coffee, the seeds are used as a flavoring; they are part of the composition of bread and serve as a preservative. The plant is considered as a drug for digestive and hepatic disorders, it is also indicated in chronic headaches and migraines. In dermatology, the seed treats alopecia and eczema. The fixed oil of black seed has many pharmacological properties and can be considered as an anti-inflammatory, anti-tumor, anti-diabetic and it plays a significant role in the cardiovascular and gastrointestinal systems (2).

In this review, it will be shown firstly a short overview about the history of this plant, its use in traditional medicine and its effect on some pharmacological properties.

HISTORY
The use of plants for therapeutic purposes dates to very ancient times. Fossils from the early Cretaceous (~250 million years old) prove the existence of black cogs at the end of the Secondary Era (3). Firstly, the Sumerian civilization, the first truly “urban” civilization that marked the end of prehistoric times in the Middle East, is at the origin of the use of plants as sources of “medicine” (2). Moreover, Egyptian civilization is no slouch in terms of medicinal plants. Indeed, the papyrus discovered by Edwin Smith in 1862 in the ruins of Louksor, written between 1500 and 1600 BC and deciphered by the German...
Egyptologist Georg Ebers, constitutes one of the oldest medical treatments. Archaeologists have discovered a vial of black cumin oil in the tomb of Pharaoh Tutankhamun. This “miracle” oil would have been used by Cleopatra and Nefertiti as a beauty product thanks to its calming, regenerating, vitalizing and anti-inflammatory effects for the face and to treat skin problems (1,2).

The Greco-Roman civilization also excelled in terms of herbal therapy, notably thanks to Hippocrates (460-377 BC). Claude Galien (born circa 131 A.D.), Emperor Marcus Aurelius’s official physician, the originator of “galenic pharmacy”, improved in terms of precision and quality the knowledge provided by Hippocrates. He advises burning black seed to kill midges and mosquitoes; and Tragus used them as anthelmintics (4).

The Arabs’ excellence in medicine is credited with expanding the scope of this plant in therapy. “Heal yourself using black seed, it is a cure for all ills except death,” such is the recommendation made by the prophet Muhammad in the 7th century (2) One of his disciples, Ibn Atîq, used the seeds of N. sativa macerated in olive oil. Three drops of this oil were instilled into each nasal opening to treat the flu that was accompanied by bursts of sneezing (2,5).

Born near Bukhara in Persia (present-day Uzbekistan), Abu Ali Al-Hussein Ibn Abdallah Ibn Sina, known as Avicenna (980-1037) deals with black seed in his work “The Book of the Healing of the soul or “Kitab Al-Chifâ” (2,5) (Figure 3).

He advised roasting the seeds and reducing them to powder, then placing this preparation in a cloth bag and inhaling daily to unclog the nasal passages, following the same principle as a spray. Avicenna also advocated black seed for dyspnea and in the treatment of asthma and bronchitis (6).

This same preparation, taken with boiled water, has diuretic and renal stone dissolving actions (7). On the other hand, taking black seed oil with olive oil was very well known as an aphrodisiac.

**Using Nigella Sativa in Traditional Medicine**

In Unani medicine, nigella seed is considered as a diuretic, it is used for cough, eye pain, paralysis, hemorrhoids, and fever.

In Malaysia, the seeds are used for headaches, nasal ulcers, and rheumatism. Arab women use the seed of N. sativa as a galactogen (8).

In Turkey, Seed oil is used orally for its carminative, antihypertensive, diuretic, diaphoretic, stomachic properties. In friction, it is recommended against muscle spasms, and rheumatism (9).

Black cumin seed and oil, taken alone or in addition to other medications, is effective against alopecia and other skin conditions (8). A figure summarizes all the traditional medical indications (10) (Figure 4).
PHARMACOLOGICAL PROPERTIES OF N. SATIVA AND THEIR EFFECTS ON HUMAN HEALTH

During the last 20 years, several works have focused on the study of Nigella sativa, on the effects due to the extracts of the seed of this species as well as to the main constituents called “thymoquinone” on various systems in vitro and in vivo (Figure 5).

Nigella being an aromatic spice, it regulates the appetite and has digestive properties.

a) Gastrointestinal properties:
The seed of N. sativa is widely used in disorders of the gastrointestinal system. The oil has a cytoprotective effect (11).

In aspirin-induced ulcer in rats, aqueous extract of black cumin seed showed anti-ulcer activity. The volume of gastric acid secretion, total and free acidity decreased markedly (12).

Black cumin vegetable oil and thymoquinone had a protective effect against lesions of the gastric mucosa (13). Another study showed the effects of thymoquinone in acidic acid-induced colitis in rats. At low doses, 5 mg/kg, thymoquinone had a partial protective effect, and at higher doses, the protection was greater than with sulfasalazine (intestinal anti-inflammatory drug used in ulcerative colitis). The protection would be partly due to the antioxidant properties of the nigella (14).

b) Hepatoprotective properties:
Studies have demonstrated the antioxidant effect of thymoquinone. Liver damage produced by carbon tetrachloride in mice was inhibited by a single dose of thymoquinone at 100 mg/kg. The slowing down of lipid peroxidation explains the effect of thymoquinone antioxidant (15).

c) Antitumor properties:
Thymoquinone potentiates the detoxifying functions of the liver, thereby increasing glutathione levels and reducing tumors. In addition, with dithymoquinone and ethanolic seed extracts, it is cytotoxic to cytostatic-resistant tumor cells. Extracts of black cumin seeds reduce the development and growth of tumor cells (16).

Fixed oil, thymoquinone and dithymoquinone were tested for their cytotoxicity on multi-drug resistant human tumor cells. Thymoquinone and dithymoquinone were cytotoxic on pancreatic adenocarcinoma, uterine sarcoma, and leukemia cells, while fixed oil had no effect (16).

The incubation of two prostatic tumor cell lines in the presence of thymoquinone promotes an inhibition of their growth. Indeed, Thymoquinone created oxidative stress, the level of reduced glutathione decreased while that of reactive oxygen species increased. As a result, tumor growth was stopped. In addition, Thymoquinone would stimulate the expression of certain apoptotic genes, at the same time as it would inhibit the expression of anti-apoptotic proteins linked to Bcl2 (17).

d) Antidiabetic properties:
Treatment with various preparations of Nigella sativa L. consistently results in lowered blood glucose levels in different animal models.

A mixture of five plants including N. sativa has been used in Kuwait on rats with streptozotocin-induced diabetes and on normal rats. Glucose tolerance was improved in both groups (11).

Subsequently, it was thought that this mixture would inhibit hepatic gluconeogenesis. On hyperglycemic and normal rabbits, the essential oil of black seed was injected intraperitoneally at a dose of 50 mg/kg. Four to six hours after administration, a decrease in blood sugar was observed (15-23%). As the improvement in glycaemia is not accompanied by a change in Insulinaemia, this effect of nigella would be independent of insulin mechanisms (18).

An Egyptian team has demonstrated the protective effect of nigella on kidney and spleen tissue. In fact, in rats with alloxaan-induced hyperglycemia, producing a selective necrosis of the beta cells of the islets of Langerhans, a mixture of plants containing nigella normalizes glycaemia.

In the control group having no treatment with plants, after 10 days, an alteration of the hepatic, renal and pancreatic tissues is observed, while in the group treated even after 20 days, no pathological abnormality was visible (19).

e) Effect on the kidneys:
The nigella with its antioxidant and anti-inflammatory properties would effectively fight against kidney damage. Nigella sativa seed extract administered at 50 mg/kg thirty minutes before cisplatin, a DNA alkylating cytotoxic agent used in cancer chemotherapy, restores the biochemical and physiological indicators of nephrotoxicity (11).

Thymoquinone and other known antioxidants such as vitamin E and C, lycopene, and curcumin, have been tested on mice with cisplatin or ciclosporin A-induced nephrotoxicity. Thymoquinone had the best results, these are its properties microsomal lipid peroxidation inhibitors and polymorphonuclear stimulants which would protect against the action of free radicals. Its anti-inflammatory effect, inhibition of COX and LOX, would also fight against the inflammatory state induced in the kidney (20).

f) Neuroprotective properties:
To measure the pharmacological activities of nigella on the central nervous system (CNS), the aqueous and
methanolic extracts of the seed oil of N. sativa L. were used. The results were such that the two extracts had a CNS depressant effect, and a central analgesic effect (21). In a study performed on rats with induced spinal cord trauma, the effects of N. sativa on the protection of spinal cord neurons were compared to those of the anti-inflammatory corticosteroid called “methylprednisolone”. In the placebo group, thickening of the nerves followed by their degeneration were visible, while the treated groups retained neuronal morphology. Nigella sativa could be beneficial in spinal cord trauma and be used clinically (22).

**CONCLUSION**

We have seen that Nigella sativa L., a plant used first as a spice and then as a remedy for more than 2000 years in Eastern culture, has a wide spectrum of activity, and more particularly its main constituent, thymoquinone which acts on many targets to treat different conditions.

At present, the mechanisms of action of thymoquinone still remain unclear, but it would protect against cancer, metabolic and infectious diseases, cardiovascular, neurological, gastrointestinal, hepatic, nephrological diseases, by antioxidant and anti-inflammatory.

Indeed, we have seen the multitude of work carried out on laboratory animals, and the number of pathologies that this plant can treat is considerable. In the perspective of use as a drug on humans, clinical trials should be carried out with thymoquinone initially, then with the other molecules derived from the nigella seed. It takes several years before putting a new molecule on the market, still a lot of work is needed to consider thymoquinone as a drug.

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