REVIEW ARTICLE

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Black Seed (Nigella Sativa) and Immunomodulatory Effect

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Abstract
Nigella (Nigella sativa) plants and oil for centuries in Africa, Asia and the Middle East today is by the United States and millions of people in Europe "to promote health" was a plant used and has been a material referenced in terms of health. As a result of scientific research, it was suggested that the seeds of vitamins, active substances and essential fatty acids should be consumed by scientists due to acid. Nigella sativa has significantly increased the total lymphocyte amount and has been supported by studies that have an immunomodulatory effect on both humans and animals. Healthy life support issues to the forefront of popular Cumin seed, which is an important component of thymoquinone (TQ) has been preferred due to potential medicinal properties as a source of healing. In the scientific researches, seedlings of black seed, vitamins, active substances and essential fatty acids may be useful to be consumed due to the products.

Keywords: Nigella sativa, immunomodulatory, thymoquinone

INTRODUCTION

Medicines derived from plants and plant extracts have traditionally been used for many years in the treatment of diseases. In the field of science, the mechanisms and active components of plants are tried to be understood in recent years (Abuharfeil et al., 2001). In many studies, herbal medicines have been shown to have many beneficial effects including antioxidant, anti-inflammatory, anti-carcinogen, antibacterial and immunomodulatory (Abuharfeil et al., 2001; Al-Ali et al., 2008; Al-Asoom et al., 2014). There are many plants used for traditional treatment purposes; one of them is *Nigella Sativa* (Nigella) plant, which belongs to the family Ranunculuceae (Al-Asoom et al., 2014; Al-Gaby, 1998; Al-Ghamdi, 2001).

Today, health problems due to technological advances have led researchers to seek different solutions. The most important tendency in this field is alternative medicine and traditional methods with products of natural origin. These products have become very popular around the world due to the benefits they provide to human health. Recently, the daily use of plant-based food products has increased, which does not carry a health risk and has no excessive side effects. In addition, these products are used as therapeutic and supportive food. Since ancient times, various plants have been used to treat different ailments. Similarly, today, plants are treated and the related industry is growing rapidly from year to year (Al-Kushi, 2013). In developing countries, the majority of the population uses herbal medicines to treat different basic medical problems (Alshatwi, 2013). One of the underlying causes of this; according to chemical drugs, herbal treatments are more effective, safer, less toxic, easily usable and affordable (Baytop, 1984). For this reason, serious research is carried out on the therapeutic potentials and medical uses of plants in medicine.

It is known that *Nigella sativa* seeds are used to support healthy living, active and healthy aging, improve quality of life, and most importantly to help prevent diseases, i.e. preventive medicine. Thymoquinone, an important component of *Nigella sativa* seed oil, which is at the forefront of supporting healthy life, is preferred due to its potential medical properties. As a result of the researches, the active ingredient found in the plant seed is one of the products that may be beneficial to be consumed due to vitamins and fatty acids. Thanks to the clinical findings, the scientifically proven of pharmaceutical activities of the *Nigella sativa* seed have also been a preferred plant for treatment purposes. One of the important features of Nigella is the immunomodulatory effect of the substances in its composition (thymoquinone). (Al-Asoom et al., 2014; Boskabady et al., 2011; Cheikh-Rouhou et al., 2007; Çelik et al., 2014; Elkadi and Kandil, 1987). Many years ago, studies have started to be done that black seed can increase immune response in humans. Recently, the immunomodulatory effect and protein structure of all extracts of black seed has been analyzed in vitro (Ghosheh et al., 1999). As a result of the examinations, the black seed oil increases T cell proliferation and therefore triggers cellular immunity; on the other hand, it has been reported that it suppresses B cells, i.e. humoral immunity (Al-Asoom et al., 2014). These findings, obtained through *in vitro* studies, were also supported as *in vivo* (Abuharfeil et al., 2001; Gholamnezhad et al., 2014; Girgin et al., 2008). Based on recent in vitro and *in vivo* data, it is possible to say that black seed can increase cellular immunity while suppressing humoral immunity. However, more experimental studies are needed to confirm this hypothesis. Thanks to the studies to be carried out in this way, the immunomodulating effects of black seed can be measured based on the natural immune reaction mediators in diseases.

Chemical Structure of Thymoquinone

Nigella sativa, commonly bred in middle eastern and West Asian countries and popularly known as Nigella, used for bronchial asthma, cough, headache, toothache, nasal congestion, infections, obesity, back pain, is used in the treatment of hypertension, diarrhea, digestive system problems and numerous types of cancer (Güzelsoy er al., 2018). In addition, Black Seed is used as a food additive and spice (Abuharfeil et al., 2001; Grover and Yadav,2004; Guyton and Hall, Haq et al., 1995; Haq et al., 1999; 2001; Hawsawi et al., 2001).

The part of the Nigella sativa species of the Ranunculacea (Buttercups) family, which is used as food, is the seed. Nigella seeds; It consists of 36-38% fats, proteins, alkaloids, saponins and 0.4 -2.5% fatty acids. The majority of fats are unsaturated fatty acids. Although it contains many components in its structure, the main factor is thymoquinone (27.8% 57%) (Çelik et al., 2014). Black seed seeds are especially rich in oleic acid, linolenic acid, linoleic acid, arachidonic acid, palmitoleic acid and stearic acid, which are fatty acids (Hosseinzadeh and Parvardeh, 2004). The biologically active compounds of black cumin include thymoquinone, thymohydroquinone, ditimokinone (Kanter, 2009; Kaya et al., 2003). The nitroseutic substance in the seeds is considered to be thyroxinone (Figure 1). Seeds also contain carotene and potassium, phosphorus, calcium and iron, which are converted into vitamin A in the liver (Kenawy et al., 2014). It has been shown in studies that cytotoxic effect against various cancer cells (Mills and Bone, 2010) increases cellular activation and tumor-specific antibodies production. Salemi and Hossainb (2000) have shown that seed extract and seed oil have an antiviral and antimicrobial effect in their work (Mohammed et al., 2010).

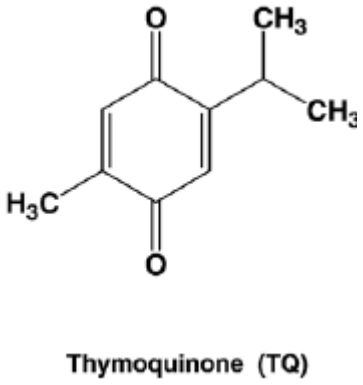

Figure1. Molecular structure of thymoquinone

In many studies, it has been tried to show certain neuropharmacological effects of the active substance and it has been revealed that thymoquinone can be used as an anticonvulsant in mild epilepsy (Çelik et al., 2014; Haq et al., 1999). It is also reported to have a healing effect in neuropathic pain (Haq et al., 1999).

Today, gastrointestinal system problems are quite common and play a role in the pathogenesis of most diseases. There are various causes of stomach problems such as stress, smoking, malnutrition, infections and nonsteroidal anti-inflammatory drugs. Studies have shown that black seed and its active ingredient, thymoquinone, play an important role in preventing gastric mucosa damage by decreasing the increased stomach acidity. It is reported that this protective effect may be achieved by increasing the arachidonic acid bioavailability of the gastric mucosa (Al-Ghamdi, 2001).

Physicochemical Properties of Nigella Sativa Seed

When the physical properties of black seed oils were examined, there was no significant difference between the oils obtained by the cold press method and the physical properties of the oils obtained by solvent extraction. In the studies conducted, it has been stated that black seed oil has high UV absorption due to its color composition and can provide sun protection effect with this feature. Regarding oxidative stability, studies carried out with rancimat device showed up to 55 hours of durability. It can be stored for long periods of time due to its high amount of natural antioxidants and low amounts of unsaturated fatty acids. Thanks to this feature, it prevents many vegetable oils. (Ojha et al., 2015).

Considerations in the Hand of Nigella Sativa Seeds

It has been reported that the environmental conditions, climate, light, sea height, distance from the equator, soil condition, soil reaction, condition of water and minerals that are effective in the development of plants such as black seed. At the same time, factors such as the age of the plant, physiological development, harvest time, processing and drying operations have a positive or negative effect on the normal development of the plant and the synthesis of valuable substances, the quantity and quality of the essential oil obtained. Therefore, the number of essential oils such as nigellone and thymoquinone, which are active ingredients in the composition of black seed grown in different geographical regions, may also vary. In studies on the chemical composition of black seed seeds grown in different regions of our country, it is reported that the amount of essential oil varies between 0.09% and 0.36% (Alshatwi, 2013).

Effect of Nigella Sativa on Immune System

In the study on humans, Nigella sativa seed oil has a CD4 (auxiliary lymphocyte) / CD8 (suppressive lymphocyte) rate of 55%; natural killer (NK) cells were found to increase by 30%. When nigella sativa seed's juicy extract was taken for a week, the amount of natural killer cells and cytotoxicity against YAC-1 tumor cells increased nearly twice (Osman et al., 2012). Black seed oil directly enhances immune resistance in the elderly. It has been reported that it prevents a decrease in the number of hemoglobin and total leukocytes caused by "cisplatin" in mice. The total number of leukocytes was increased by 3.2% in mice given black seed. Black seed has the effect of enhancing the effect of T cells in the immune system (Paarakh, 2010).

It is determined that black seed activates T lymphocytes for the IL-3 release while it has no activating effect in the IL-2 release and its proteins significantly increase the amount of total lymphocytes, and in this respect, it has an immune-modulating effect in both humans and animals (Randhawa and Alghamdi, 2011; Salama, 2010). In studies conducted, it was observed that black seed extract increased T cell population, CD3, CD4 and CD8 surface antigens and the number of immune system cells. As a reason for this increase, it was found that thymoquinone stimulates

hematopoiesis and thus the immune system-related cells are affected and the increase is shaped (Paul, 2003; Rahmani and Aly, 2015). In allogenic cell cultures and in vivo studies using black seed proteins, it causes large amounts of IL-1β and TNF-α expression. When activating the T lymphocytes of the black seed in the direction of IL-3 secretion, IL-2 has no activating effect towards release and their protein significantly increases the total amount of lymphocytes, in this respect, both in humans and in animals modulator (Randhawa and Alghamdi, 2011; Salama, 2010).

In another study on mice reported that black seed prevented decrease of hemoglobin amount and total leukocytes caused by Cisplatin (Mills and Bone, 2010). In this study, black seed seeds increased CD3 + T cells, CD4 + helper T cells, CD8 + suppressor to cytotoxic T cells and their ratio to each other (CD4 + / CD8 +) and increased the total leukocyte count.

A number of studies have been carried out to show the effects of Nigella and thymoquinone on the immune system. In previous studies, thymoquinone has been shown to have important effects on the immune system. This effect is defined by the active substance as suppressor or activation on T cells, B cells, and cytokines involved in the immune system (Salem, 2005).

Based on recent in vitro and in vivo data, it is likely to say that black seed can increase cellular immunity while suppressing humoral immunity. However, more studies are needed to confirm this hypothesis. Thus, the immunomodulatory effects of black seed can be measured based on the natural immune reaction mediators in diseases. In the literature studies, different application methods (orogastric, intraperitoneal, subcutaneous, inhalation etc.) of the active substance were and their effects were observed in order to investigate the immunomodulatory effects of black seed (Salemai and Hossainb, 2000; Swamy and Tan, 2000; Woo et al., 2000; Zohary et al., 2012).

CONCLUSION

In most of the studies on thymoquinone obtained from black seeds and seeds; It is reported that black seed has many beneficial pharmacological activities and can show toxic effects only in very high doses. It is reported that thymoquinone maybe contact allergen. Since the reliability of oral and dermal exposure is not sufficient, it is not recommended to use it during pregnancy and breastfeeding. It has been shown by studies that black seed significantly increases the total amount of lymphocytes; in this respect, it has an immunomodulatory effect in both humans and animals. However, more studies are needed to better understand its effects on metabolic pathways. In addition to use the black seed seeds and its effective components as medicines determined they are determined and standardized to have more advanced research methods, including clinical and toxicological studies to pass; quality, effectiveness and safety should be evaluated. It has been reported that the daily use of black seed seeds 30 mg / kg in humans can activate the immune system, but more studies are needed on this subject.

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