Nigella Sativa’s role in augmenting immunity

Introduction

The role of natural health products (NHPs) in modifying immunity has been widely reviewed. Research has found that many plants/plant extracts contain active ingredients that accelerate, prolong, or enhance both innate and adaptive immune responses. Hence, their inclusion in diet is being encouraged in order to reduce the risk, severity, and duration of infections. Additionally, these NHPs are believed to have relatively less adverse effects on the body as compared to the synthetic preparations (1).

Among various medicinal plants, *Nigella sativa* (*N. sativa*) belonging to the family Ranunculaceae is gaining attention for its pharmacological potential, and general well-being. *N. sativa* has found to be predominantly beneficial as an antihypertensive, antidiabetic, and anticancer agent. *N. sativa* consists of four main active ingredients; namely thymoquinone, dithymoquinone, thymohydroquinone, and thymol. However, most of the therapeutic properties of this plant are due to the presence of thymoquinone (TQ), which is a major active chemical component of the *N. sativa*’s essential oil. (2,3)

Although thymoquinone has gained a significant amount of attention for its anti-cancer activity, this paper is attempting to explore thymoquinone’s immunomodulatory function through a review of studies done on human volunteers. Past research has suggested that if used on an ongoing basis, thymoquinone can play an important role to enhance human immunity, particularly in immune-compromised patients (9,10).
**Thymoquinone and Immunity**

1) **Cell-mediated immunity**

The predominant way by which Thymoquinone exerts its immuno-stimulant action is by increasing the number of helper T-cells (Th cells). Th cells are a type of T-cells that aid immune response by recognising foreign antigens and secreting substances called cytokines. The latter activates B-cells to secrete antibodies and macrophages to destroy ingested microbes, as well as cytotoxic T-cells to kill infected target cells. These T-helper cells have CD4 markers on their surface.

When a naïve helper T-cell comes in contact with an antigen, it differentiates into either a Th1 or Th2 effector helper cell. Th1 cells produce several inflammatory and immunomodulatory mediators like interferon-gamma (IFN)-γ, Interleukin (IL)-2 and 12, and tumor necrosis factor (TNF)-alpha. (4)

Thymoquinone plays a major role in this type of cell-mediated immunity by increasing the concentrations of interferon-γ and IL-2 and IL-12. This process not only maximises the killing efficacy of macrophages but also enhances the proliferation of cytotoxic CD8+ T cells (5).

CD8+ T-cells play an important role in the control of viral infection and eliminating cells with malignant potential. Studies have shown that even low concentrations of TQ can result in enhanced functional activity of CD8+ T cells, thereby leading to a better cellular immune response. (6)

2) **Immunoglobulin class switching**

Immunoglobulin class switching is a biological mechanism that changes a B-cell's production of immunoglobulin (antibodies) from one type to another, such as from the isotype IgM to the isotype IgG. Th1 cells participate in isotype switching by releasing interferon (IFN)-γ, which preferentially induces switching to IgG2a and IgG3. Thymoquinone leads to improved levels of IgG, which is a key player in the humoral immune response. IgG augments immunity by activating the complement system and causing phagocytosis of microorganisms. (7)
**Effect of Thymoquinone on an immunocompromised state**

An immunocompromised state is the hallmark of HIV infection and AIDS. It makes the body vulnerable to opportunistic infections by causing pronounced depletion of activated as well as memory CD4+ T-cells. Additionally, an imbalance in the Th1-type and Th2-type responses contributes to this immune dysregulation, which is dependent on a Th1 > Th2 dominance. It has been found that many seronegative, HIV-exposed individuals generate strong Th1-type responses. Additionally, progression to AIDS is characterised by loss of IL-2 and IFN-γ production concomitant with increases in IL-4 and IL-10 (8).

Two studies have indicated that Nigella sativa has an important role in treatment of HIV/AIDS by improving CD4+ T-cell count and inhibiting viral replication.

1. Nigella sativa had been documented to cause sero-reversion in HIV infection which is very rare despite extensive therapy with highly active anti-retroviral therapy (HAART). At the end of the study, the patient had complete recovery
and sero-reversion after treatment with a Nigella sativa concoction. The patient had presented with a history of chronic fever, diarrhea, weight loss and multiple papular pruritic lesions of 3 months duration with moderate weight loss. ELISA and western blot confirmed HIV infection and CD4 count of 250-cells/mm$^3$. The patient was commenced on Nigella sativa concoction 10 ml twice daily for 6 months. Fever, diarrhea and multiple pruritic lesions disappeared on $5^{th}$, $7^{th}$ and $20^{th}$ day. Additionally, there was a significant reduction in viral load ($\leq$1000 copies/ml) on $30^{th}$ day. Repeated EIA and Western blot tests on $187^{th}$ day were sero-negative. The post therapy CD4 count was 650cells/mm$^3$ with undetectable viral load. Repeated tests for HIV remained sero-negative, with aviraemia and normal CD4 count (9).

2. In another human clinical trial conducted at the Department of Biological and Medical Research Center in Riyadh, Saudi Arabia, the results showed that seeds of N. sativa enhanced helper T-cell by 55% with a 30% enhancement of Natural Killer cell activity (10).

The above trials provide good evidence that Nigella sativa enhances T-cell mediated immunity, thereby decreasing the susceptibility of these patients to opportunistic infections.

**Conclusion**

Research has indicated that Nigella sativa and its active components, particularly Thymoquinone has immense potential in enhancing immunity in an immunocompromised state.

Since limited studies have been done on human volunteers, further research is needed to substantially improve the immunotherapeutic application of Thymoquinone in clinical settings.

*Authors: Dr Yashaswi Gupta; Dr Michael Shleifer*
References


