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Review

# Immunomodulatory and therapeutic properties of the *Nigella sativa* L. seed

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**Abstract**

A larger number of medicinal plants and their purified constituents have been shown beneficial therapeutic potentials. Seeds of *Nigella sativa*, a dicotyledon of the Ranunculaceae family, have been employed for thousands of years as a spice and food preservative. The oil and seed constituents, in particular thymoquinine (TQ), have shown potential medicinal properties in traditional medicine. In view of the recent literature, this article lists and discusses different immunomodulatory and immunotherapeutic potentials for the crude oil of *N. sativa* seeds and its active ingredients. The published findings provide clear evidence that both the oil and its active ingredients, in particular TQ, possess reproducible anti-oxidant effects through enhancing the oxidant scavenger system, which as a consequence lead to antitoxic effects induced by several insults. The oil and TQ have shown also potent anti-inflammatory effects on several inflammation-based models including experimental encephalomyelitis, colitis, peritonitis, oedama, and arthritis through suppression of the inflammatory mediators prostaglandins and leukotriens. The oil and certain active ingredients showed beneficial immunomodulatory properties, augmenting the T cell- and natural killer cell-mediated immune responses. Most importantly, both the oil and its active ingredients expressed anti-microbial and anti-tumor properties toward different microbes and cancers. Coupling these beneficial effects with its use in folk medicine, *N. sativa* seed is a promising source for active ingredients that would be with potential therapeutic modalities in different clinical settings. The efficacy of the active ingredients, however, should be measured by the nature of the disease. Given their potent immunomodulatory effects, further studies are urgently required to explore bystander effects of TQ on the professional antigen presenting cells, including macrophages and dendritic cells, as well as its modulatory effects upon Th1- and Th2-mediated inflammatory immune diseases. Ultimately, results emerging from such studies will substantially improve the immunotherapeutic application of TQ in clinical settings.
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*Keywords:* *Nigella sativa*; Thymoquinone; Colitis; Encephamolyelitis; Arthritis; Anti-diabetic; Anti-oxidant; Toxicity; Anti-histaminic; Anti-inflammatory; Anti-tumor; Anti-microbial; Bacteria; Virus; Fungus; Schisosoma; Immunity

*Abbreviations:* Abs, antibodies; CCL4, carbon tetrachloride; Con A, concanavalin-A; DCs, dendritic cells; DOX, doxorubcin; EAE, experimental allergic encephalomyelitis; FS, Fanconi syndrome; HHcy, hyperhomocysteinemia; i.p., intraperitoneal; i.v., intravenous; PBMC, peripheral blood mononuclear cells; PHA, phytohemagglutinin; LPS, lipopolysaccharide; ROS, reactive oxygen species; STZ, streptozotocin.

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## 1. Introduction

Interest in medicinal plants has burgeoned due to increased efficiency of new plant-derived drugs and the growing interest in natural products. Because of the concerns about the side effects of conventional medicine, the use of natural products as an alternative to conventional treatment in healing and treatment of various diseases has been on the rise in the last few decades. The use of plants as medicines dates from the earliest years of man's evolution [1,2]. Medicinal plants serve as therapeutic alternatives, safer choices, or in some cases, as the only effective treatment. People in separate cultures and places are known to have used the same plants for similar medical problems. A larger number of these plants and their isolated constituents have shown beneficial therapeutic effects, including anti-oxidant, anti-inflammatory, anti-cancer, anti-microbial, and immunomodulatory effects [1,3–9].

## 2. *N. sativa*: botanical and historical background, and folk medicine

Among the promising medicinal plants, *N. sativa*, a dicotyledon of the Ranunculaceae family, is an amazing herb with a rich historical and religious background [10]. *N. sativa* is found wild in southern Europe, northern Africa, and Asia Minor. It is a bushy, self-branching plant with white or pale to dark blue flowers. *N. sativa* reproduces with itself and forms a fruit capsule which consists of many white trigonal seeds. Once the fruit capsule has matured, it opens up and the seeds contained within are exposed to the air, becoming black in color [11]. The seeds of *N. sativa* are the source of the active ingredients of this plant. It is the black seed referred to by the prophet Mohammed as having healing powers [10]. Black seed is also identified as the curative black cumin in the Holy Bible and is described as the Melanthion of Hippocrates and Discroides and as the Gith of Pliny [12].

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