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Research Article

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Nigella Sativa (Black Seed) Oil and Its Role in Vitiligo Management: A Review of Potential Mechanisms and Clinical Evidence

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Abstract

Vitiligo, characterized by the progressive loss of skin pigmentation, remains a challenging condition with limited treatment options. This review explores the role of Nigella sativa (black seed) oil in vitiligo management, focusing on its potential mechanisms and clinical evidence supporting its use. The novelty of this review lies in its comprehensive analysis of black seed oil's bioactive compounds, particularly thymoquinone, and the possible influence on melanocyte function and skin repigmentation. Evidence from clinical trials and experimental studies suggests that black seed oil may exert therapeutic effects through anti-inflammatory, antioxidant, and immune-modulatory actions, which could contribute to stabilizing and promoting repigmentation in vitiligo lesions. Future research should address the optimal formulation and dosage, investigate long-term efficacy and safety, and compare its effectiveness to current standard treatments. In summary, Nigella sativa oil presents a promising adjunct therapy for vitiligo, offering a novel approach with potential benefits that warrant further exploration to fully understand and integrate its role in clinical practice.

Introduction

Vitiligo is an autoimmune disease in which the cells that create pigment, melanocytes, are destroyed by the immune system [1]. The loss of melanocytes leads to the loss of pigmentation of the skin. Often, these sites of vitiligo present as small depigmented macules and can grow progressively larger over time. This disease equally affects all skin types and can affect any area of the skin, including the scalp. Unfortunately, this autoimmune skin disease is chronic and once melanocytes are destroyed, it is difficult to achieve repigmentation. This condition affects approximately 0.5-2% of the population and is most noticeable in people with skin of color [2]. Current treatment options for vitiligo include topical and oral immunomodulating agents, phototherapy, and a recently approved topical JAK inhibitor [2]. In addition to these approved treatments, the severity of the condition, and varying treatment outcomes, adjuvant treatments are of interest to both patients and clinicians.

A recent survey reported that out of 625 respondents with vitiligo, 203 of these participants have explored the use of complementary and alternative medicine. Of these 203 respondents, 53 reported using topical *Nigella sativa (N. sativa)* oil [3]. *N. sativa* is a well-known medicinal plant from which oil rich in thymoquinone can be extracted [4]. This beneficial bioactive ingredient in the oil is known to interact with the immune system providing anti-inflammatory and immunomodulating effects [5]. Due to the immune dysregulation present in patients with vitiligo, this oil has potential utilization in this patient population.

The purpose of this paper is to explore the efficacy of *N. Sativa* oil as a treatment option for patients struggling with vitiligo. This condition can be extremely distressing to patients as it noticeably alters their appearance and can attract unwelcome attention. Due to the chronicity of the condition, there should be a variety of alternative and adjuvant treatment options available to these patients. This review sets out to determine the place of *N. Sativa* oil in the current treatment landscape for vitiligo.

Nigella sativa

N. sativa, commonly known as black seed or black cumin, is native to Eastern Europe and Western Asia, and renowned for its wide-ranging medicinal properties. The therapeutic use of N. sativa and its extracts date back to the first century, when the herb was employed to treat a broad spectrum of ailments, including the flu, toothaches, and headaches [6]. Although the medicinal properties of *N. sativa* are not fully understood, they are partly attributed to the seed's complex chemical composition [7]. The ingredients can be broadly classified into fixed oils, proteins, alkaloids, saponins, and essential oils, with essential oils showing the most significant therapeutic potential. Lesser-known compounds, such as nigellone and p-cymene, which fall into the essential oil category, have notable therapeutic applications due to their bronchodilator and analgesic effects, respectively [8]. However, the most significant impact comes from the primary active ingredient, thymoquinone.

Biochemically, thymoquinone is a monoterpene consisting of a benzene ring, two hydroxyl groups, and one isopropyl and methyl side chain [9]. Its molecular structure and abundant side chains contribute to its potent antioxidant properties, enhancing the body's innate ability to mitigate cell damage. Intrinsic and extrinsic stressors, such as toxins, environmental exposure, and metabolic byproducts, lead to the formation of reactive oxygen species (ROS) and free radicals. Normally, these are eliminated by the glutathione reductase pathway. However, in cases of severe metabolic dysregulation or localized stress, excessive radical production can overwhelm the body's regulatory capacity, leading to accelerated cellular aging, immunosuppression, and an increased risk of DNA mutations. The high thymoquinone content of *N. sativa* helps preserve radical-protective enzymes within the body, including catalase, glutathione-S-transferase, and glutathione reductase, thereby enhancing the body's ability to manage oxidative stress [10]. This protective effect, combined with the added nutraceutical benefits from the other components of *N. Sativa*, make it of significant therapeutic interest.

Today, this herb is utilized in both traditional and allopathic medicine for its cardioprotective, gastroprotective, and neuroprotective effects, and it also serves as a prophylactic against future diseases due to its anti-cancer and anti-metabolic properties [7]. Its metabolic benefits are broad, with studies showing that supplementing with 1 gram of N. sativa oil significantly reduces several cardiometabolic risk factors, including HbA1c, total cholesterol, LDL, triglycerides, blood pressure, and C-reactive protein, while also increasing HDL-C levels [11]. The nutraceutical has also demonstrated efficacy in treating various skin conditions, including atopic dermatitis, due to its immunomodulating properties, which downregulate inflammatory cytokines such as IL-4, IL-5, and IFN-gamma [12]. This finding suggests a potentially broad therapeutic scope for *N. sativa* in treating skin diseases like psoriasis, chronic urticaria, and contact dermatitis, which similarly involve the dysregulation of these key cytokines.

Vitiligo

Vitiligo is a chronic, autoimmune depigmentation disorder with a multifactorial pathogenesis that is still not fully elucidated. This cutaneous condition is characterized by the development of white macules on the skin that are well-demarcated due to the destruction of epidermal melanocytes, cells that are responsible for the color of our skin and hair. The body's dysregulated attack on melanocytes by autoantibodies creates areas of depigmentation, which can range in localization and symmetry [13]. These physiologic changes to one's body can undoubtedly affect the psyche, as vitiligo is associated with a range of mental health disorders such as anxiety and depression. While there are both genetic and environmental risk factors for the development of vitiligo, linkage analysis has revealed loci on chromosomes 17p13 and 22p12 that are paramount in disease trajectory [14]. Specifically, transcription factor XBP1, which is regulated by 22q12, is involved in the expression of the HLA class II gene and cellular response to stress.

The management of vitiligo is largely dependent on disease severity and activity. Patients with advanced disease are recommended a combination of systemic steroid therapies and phototherapy such as UVB, which successfully prevents the relapse of vitiligo [15]. UV therapy in addition to sun exposure is also imperative to the repigmentation process. Importantly, phototherapy is not recommended for small children, who mainly benefit from mini-pulses of systemic steroid monotherapy. For patients with more stable disease that is localized to sensitive areas such as the face, topical JAK inhibitor ruxolitinib is recommended. Ruxolitinib is a JAK 1 and 2 inhibitor that suppresses IFN-gamma signaling, which essentially deactivates chemokine receptor ligands (CXCL9, CXCL10, CXCL11) that are highly expressed in depigmented skin lesions [16]. Additionally, ruxolitinib serves as a chimeric anti-CD20 antibody, which serves to dysregulate the inflammatory cascade particular to vitiligo.

Herbal medications such as *N. sativa* may be of considerable benefit as we explore different treatment modalities for vitiligo [5]. Thymoquinone and its anti-inflammatory, antioxidant, and antitumor effects, protect cells against oxidative stress generated by free radicals. It also helps to stimulate the release of melanin and skin repigmentation through acetylcholine stimulation. This topical therapy has also been shown to reduce the size of skin lesions and accelerate the rate of repigmentation when compared to alternative methods such as fish oil [17]. Clinicians should be cognizant of the medical advantages such treatment presents, especially since they elicit little to no significant side effects. Thymoquinone has also been shown to inhibit NF-kB activity in mouse melanoma cells, supporting theories of its prevention of metastatic melanoma. The inhibition of such inflammatory pathways in addition to various reactive oxygen species poses significant medical advantages to both patients and healthcare workers, as this product is easily accessible.

Nigella Seed Oil and Vitiligo

The immunomodulating properties and availability of *N. sativa* oil make it an attractive treatment option for vitiligo. Few papers discuss the interplay between *N. sativa* oil and vitiligo. However, the studies that have been performed indicate that *N. sativa* oil could positively affect the outcomes of patients with vitiligo. Before studies involving human subjects, the effects of *N. sativa* oil were observed on the melanophores of the wall lizard. Following the application of *N. sativa* oil to the skin of the lizard, skin darkening was noted. This is hypothesized to be a result of thymoquinone stimulation of the cholinergic receptors in melanophores [18]. The promising pigment changes discovered in this study encouraged further research into the mechanisms of *N. sativa* oil and its potential translation into use in depigmentation disorders. According to a study by Sarac et al. topical application of a cream containing *N. Sativa* oil twice daily for six months in 33 patients with vitiligo demonstrated statistically significant regimentation of the skin in the hands, face, and genital region [17]. Significant improvement in patient pigmentation in just six months is an exciting finding benefiting patients who may have suffered from pigment changes in these areas for years.

Additionally, Ghorbanibirgani et al. conducted a double-blind randomized control trial to compare the topical use of *N. sativa* oil to fish oil. 52 patients previously diagnosed with vitiligo were included and assigned to apply either *N. Sativa* oil or fish oil topically. Patients applied the treatment twice daily for six months. It was found that topical application of *N. Sativa* oil was more effective in reducing the size and appearance of depigmented lesions when compared to topical fish oil. The greatest improvements in these patients were noted in the upper extremities, trunk, head, and neck [5]. These promising studies indicate that *N. sativa* oil has the potential to be used as an

alternative or adjuvant therapy in patients with vitiligo. The topical application of the oil is promising, especially for patients who are struggling with noticeable depigmentation of facial skin and hands.

N. sativa, like other herbal supplements, poses numerous benefits ranging from its accessibility to versatility. This, in addition to its minimal side effects, makes it an appealing and effective remedy for those looking for a more natural approach to vitiligo management. This holds true for individuals conflicted with other inflammatory skin conditions such as acne and psoriasis, for which *N. sativa* also proves effective [19]. These advantages can be due to *N. sativa's* enhanced penetration through the skin barrier. Amin et al. concluded that the higher contents of linoleic acid and unsaturated fatty acids in *N. sativa* oil aided in its percutaneous absorption [20]. These findings are clinically worthy and should be discussed between the patient and provider when curating the most effective cutaneous treatment plan for vitiligo.

Further Direction and Research Recommendations

Although past clinical studies have shown significant repigmentation results in vitiligo patients after treatment with *N. Sativa* in comparison to fish oil after four months, long-term clinical trials (>6 months) with larger subsets of participants are needed to fully assess the effectiveness of repigmentation in patients with vitiligo [5]. Although the results were significant, participant nutrition was not controlled during this double-blind trial. It has previously been shown that diet may influence the production of melanin in vitiligo patients. Therefore, future clinical trials controlling participant nutrition in addition to the proper examination of serum vitamin B12, folate, and zinc (Zn) throughout the study should be pursued [21]. Additionally, it has been discussed that *N. Sativa* may alter the metabolism of co-administered pharmaceutical agents [4]. Combination studies determining the bioavailability and intestinal permeability of a variety of co-administered drugs may be needed to assess long-term vitiligo treatment with *N. Sativa.*

Conclusion

In conclusion, vitiligo remains a complex and challenging dermatological condition with limited treatment options, underscoring the need for novel therapeutic approaches. Our comprehensive review has highlighted the potential of *N. sativa* oil as a promising adjunct therapy in the management of vitiligo. The bioactive compounds in *N. sativa*, particularly thymoquinone, appear to exert multiple beneficial effects, including anti-inflammatory, antioxidant, and immune-modulatory actions, which may contribute to the stabilization of melanocyte function and the promotion of skin repigmentation.

Clinical and experimental evidence suggests that black seed oil may offer a viable alternative or complementary treatment to current therapies, particularly for patients seeking natural or adjunctive options. However, the clinical implications of these findings are still emerging, and further research is needed to establish the optimal formulation, dosage, and long-term safety of *N. sativa* oil in vitiligo treatment. Comparative studies that assess its effectiveness against standard therapies are crucial in determining its place in integrative dermatological care and clinical practice.

The integration of *N. sativa* oil into vitiligo management protocols could represent a significant advancement in the field, especially for patients who have not responded well to conventional treatments. Nonetheless, the need for comprehensive, long-term clinical trials cannot be overstated, as these will provide the necessary evidence to support its widespread use and help clinicians develop guidelines for its effective application. As research progresses, *N. sativa* oil may emerge as a key component of a more
holistic and personalized approach to vitiligo care, offering new hope to patients with this often frustrating condition.

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