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Nigella sativa seed, its oil and thymoquinone: Topical, Dermo- Therapeutic Applications

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Nigella sativa seed (Ranunculaceae), commonly known as black cumin or black seed, has a long history of folklore usage in various traditional systems of medicine like Unani, Ayurveda, Chinese and Arabic. *Nigella sativa* seed has been commonly used as treatment for a variety of health conditions pertaining to the respiratory system, digestive tract, kidney and liver functions, cardiovascular system, skin and immune system support, as well as for general well-being. In Islamic literature, it is considered as one of the greatest forms of healing medicine[1,2].

1. ACTIVE INGREDIENTS

Nigella sativa contains many active components, such as alkaloids (nigellicines and nigelledine), saponins (alpha-hederin), flavonoids, proteins, fatty acids, and many others that have positive effects in the treatment of different diseases[1,3,4]. Thymoquinone (TQ), is an abundant constituent of *Nigella sativa* seeds' volatile oil, and most of the herb's biological properties are attributed to it.[1, 3,5]

The pharmacological properties of *Nigella sativa* and its active component TQ had been investigated by *in vitro, in vivo* and clinical studies. These studies have indicated a wide range of pharmacological effects such as immunomodulatory, anti-inflammatory, analgesic, hypoglycemic, antihypertensive, antiasthmatic, antimicrobial, antipyretic, antioxidant and anticancer [1, 6].

2. DERMATOLOGICAL AND COSMECEUTICAL APPLICATIONS

Nigella sativa has been used for centuries for the treatment of many skin conditions including skin infections, inflammatory skin conditions, wounds and skin pigmentation effect[6].
Studies attributes its therapeutic use to its anti-microbial, anti-inflammatory, anti-oxidant, wound healing properties.

2.1 ANTIMICROBIAL EFFECTS

Skin infections and some skin conditions can be caused by viruses, bacteria, fungi, or parasites. The most common bacterial skin pathogens are *Staphylococcus aureus* and group A β-hemolytic streptococci. Herpes simplex is the most common viral skin disease. Of the dermatophytic fungi, *Trichophyton rubrum* is the most prevalent cause of skin and nail infections.

Most skin infections cause erythema, edema, and other signs of inflammation. Focal accumulations of pus (furuncles) or fluid (vesicles, bullae) may

[1] Tavakkoli A, et al., Review on Clinical Trials of Black Seed (Nigella sativa) and Its Active Constituent, Thymoquinone. J Pharmacopuncture. 2017 ;20(3):179-19.
[2] Ahmad A, et al. A review on therapeutic potential of Nigella sativa: a miracle herb. Asian Pac J Trop Biomed. 2013;3(5):337-52.
[3] Rajabian A. and Hosseinzadeh H. Chapter 24 - Dermatological Effects of Nigella sativa and Its Constituent, Thymoquinone: A Review. Nuts and Seeds in Health and Disease Prevention, (Second Edition). 2020, P. 329-355.
[4] Aljabre S.H.M et al. Dermatological effects of Nigella sativa. Journal of Dermatology & Dermatologic Surgery 19 (2015) 92-98.
[5] Harzallah HJ, et al., Chemical composition, antimicrobial potential against cariogenic bacteria and cytotoxic activity of Tunisian Nigella sativa essential oil and thymoquinone. Food Chemistry.2011; vol. 129, no. 4, pp. 1469–1474.
[6] Ahmad ME, et al., A Review on the Cosmeceutical and External Applications of Nigella sativa. J Trop Med. 2017.

form. Alternatively, lesions may be scaling with no obvious inflammation [7].

Black seed's antimicrobial effects include those on gram-negative and gram-positive bacteria, viruses, parasites, and fungi pathogens[1]. The inhibitory activity of NS and its active ingredient TQ against these species might explains its successful use in folk medicine for the treatment of skin infections.

2.1.1 Anti-bacterial:

Studies have been shown that NS seed ether extract and TQ both exhibited inhibitory effect against gram-positive and gram-negative bacteria.

Nigella sativa, TQ and also thymohydroquinone (THQ) exhibited inhibition activity against the most common wound infecting microorganisms, including methicillin resistant *Staphylococcus aureus* (MRSA), *S. aureus, P. aeruginosa*, and *E. Coli* [3,8]. Studies attribute the antibacterial effect NS, mainly to the presence of TQ and melanin[9].

TQ and THQ demonstrated synergistic effect in combination with antibiotics (ampicillin, cephalexin, chloramphenicol, tetracycline, gentamicin, and ciprofloxacin) especially against of *S. aureus*[10].

Synergistic activity with antibiotic and activity against multi-drug-resistant bacteria are highly important, mainly due to the fact that the resistance of microbial strains to existing antimicrobial drugs has been increased.

In vivo study exhibited immense therapeutic potential of *Nigella sativa* extracts in *S. aureus* or *E. coli*-infected BALB/c mice [3,11].

Nigella sativa extract showed almost similar results to topical mupirocin in the treatment of neonates with *staphylococcal pustular* skin infections with no side effects[12]

2.1.2 Anti-fungal

Dermatophytosis is a fungal infection related to the keratinized tissue of hair, nails, and skin. Three main pathogenic dermatophyte genera including Microsporum, Trichophyton, and Epidermophyton. Wounds are prone to candidiasis, a yeast infection by *C. albicans* that was often observed in immunocompromised and diabetic patients [3].

Nigella sativa oil and TQ showed *in-vitro* antifungal activity against most pathogenic fungi, including some dermatophytes clinically isolates such as *Trichophyton rubrum, Trichophyton interdigitale, Trichophyton mentagrophytes, Epidermophyton floccosum* and *Microsporum canis*[13]. The study suggest that anti-dermatophyte activity of *Nigella sativa* was mainly due to the presence of TQ [3, 14]. TQ showed more potent activity against fungal strains than Amphotericin B, a standard antifungal drug[6].

2.1.3 Anti-parasitic

In a preclinical study, TQ and *Nigella sativa* extracts induced potent *in vitro* anti-leishmanial activity[15]. Anticutaneous leishmanial activity of

[7] Aly R and Baron S. Microbial Infections of Skin and Nails. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 98.

8 El-Fatatry HM. Isolation and structure assignment of an antimicrobial principle from the volatile oil of Nigella sativa L. seeds. Die Pharmazie. 1975;30:109-111.

[9] Islam MH, Ahmad IZ and Salman MT. Antibacterial activity of Nigella sativa seed in various germination phases on clinical bacterial strains isolated from human patients. E3 Journal of Biotechnology and Pharmaceutical Research. 2013; vol. 4, pp. 8–13.

[10] Halawani E. Antibacterial activity of thymoquinone and thymohydroquinone of Nigella sativa L. And their interaction with some antibiotics. Advances in Bio Research. 2009;3:148-152.

[11] Hosseinzadeh H, Fazly Bazzaz B, Haghi MM. Antibacterial activity of total extracts and essential oil of Nigella sativa L. seeds in mice. Pharmacologyonline. 2007;2:429-435.

[12] Rafati S, Niakan M, Naseri M. Anti-microbial effect of Nigella sativa seed extract against staphylococcal skin Infection. Medical Journal of the Islamic Republic of Iran. 2014;28:42.

[13] Gupta S, et al., Potential herbs and its phytoconstituents against fungal infection: a systematic review. World Journal of Pharmaceutical Research. 2012; vol. 1, pp. 1– 20.

[14] Aljabre SH, et al. Antidermatophyte activity of ether extract of Nigella sativa and its active principle, thymoquinone. Journal of Ethnopharmacology. 2005;101:116-119.

[15] Mahmoudvand H, Tavakoli R, Sharififar F. Leishmanicidal and cytotoxic activities of Nigella sativa and its active

Nigella sativa seeds ethanolic extract was also shown *in vivo* in BALB/c mice infected with cutaneous leishmaniasis. Lesion diameter and symptoms of inflammation including redness, swelling and secondary infections were significantly lesser in the test group as compared to the controls[16].

In a randomized 12 weeks clinical trial, patients treated daily with topical honey-based hydroalcoholic *Nigella sativa* along with intralesional injection of glucantime once per week compared with patients applied just honey as a component of the treatment showed more efficacy in increasing the clinical cure and decreasing the residual scar size and the required dose of glucantime[17].

2.2. WOUND HEALING

Wound healing is one of the common topical use of *Nigella sativa* in traditional medicines[3]. Scientific research attributed the beneficial effects of *Nigella sativa* and TQ on wound healing to their anti-inflammatory, antioxidant, and antibacterial properties.

Nigella sativa oil exhibited efficacy in treating burn wounds and repairing chemically induced burns of rabbit skin[18]. The wound healing effects were further revealed in cutaneous wounds in rabbit model as produced granulation tissue formation, and angiogenesis, fibroblast proliferation, and collagen synthesis involving in wound healing process[19].

In a burn wound model in rats, *Nigella sativa* was found to shorten the healing process both histopathologically and statistically as compared to antiseptic standard drug silver sulfadiazine and the control group[20] . It was also being found that *Nigella sativa* oil has good activity on increasing collagen formation and increasing rate of epithelialization[21].

Wound healing potential of *Nigella sativa* aqueous extract was investigated using human gingival fibroblast monolayer *in vitro* model. The extract was found to scavenge free radicals and increase proliferation of the fibroblasts and wound closure activity accompanied with elevated level of bFGF[22].

2.3. ANTI-INFLAMMATORY PROPERTIES OF *NIGELLA SATIVA* AND THYMOQUINONE, USED TO TREAT SKIN CONDITIONS

Nigella sativa seeds have been used in traditional medicine in Southeast Asian and the Middle East countries for treatment of wart, skin rashes, rheumatism, and related inflammatory diseases. *Nigella sativa* seed is widely used to treat skin disorders such as psoriasis, eczema and acne.[3]

Inflammatory reaction has a major role in chronic inflammatory skin diseases such as psoriasis, atopic dermatitis and acne. An inflammatory reaction cascade initiating the production of pro-inflammatory mediators such as cytokins, chemokine and/or eicosanoids. Inflammation

principle, thymoquinone. Pharmaceutical Biology. 2015;53:1052-1057.

[16] Bafghi AF, et al. The in vivo antileishmanial activity of alcoholic extract from Nigella sativa seeds. African Journal of Microbiology Research. 2011;5:1504-1510.

[17] Nilforoushzadeh MA, et al. Efficacy of adding topical honey-based hydroalcoholic extract Nigella sativa 60% compared to honey alone in patients with cutaneous leishmaniasis receiving intralesional glucantime. Journal of Skin Leishmaniasis. 2010;1:26-31.

[18] Abu-Zinadah OA. Using Nigella sativa oil to treat and heal chemical induced wound of rabbit skin. JK Science. 2009;21:335-346.

[19] Shahani M, et al. Effect of Nigella sativa extract oil on granulation tissue in cutaneous wound: an experimental study in a rabbit mode. Medical Forum. 2013;24:72-77.

[20] Yaman, IAS. et al., Efects of *Nigella sativa* and silver sulfadiazine on burn wound healing in rats. 2010; Veterinarni Medicina, vol. 55, no. 12, pp. 619–624.

[21] P. Sarkhail, et al., Burn healing potential of Nigella sativa seed oil in rats. 2011; International Journal of Pharmaceutical Sciences and Research, vol. 2, no. 1, pp. 34–40.

[22] Ab Rahman MR, Abdul Razak F, Mohd Bakri M. Evaluation of wound closure activity of Nigella sativa, Melastoma malabathricum, Pluchea indica, and Piper sarmentosum extracts on scratched monolayer of human gingival fibroblasts. Evid Based Complement Alternat Med. 2014;2014:190342.

could be characterized by symptoms such as redness, swelling, itching, heat, and pain.

Nigella sativa was found to inhibit eicosanoid generation (thromboxane B2 and leukotrienes B4) during inflammatory processes and membrane lipid peroxidation[23]. Nigellone, the carbonyl polymer of TQ, was found to inhibit histamine release from rat peritoneal mast cells *in vitro*[24].

2.3.1. Psoriasis

Psoriasis is characterized by uncontrolled proliferation, poor epidermal differentiation and inflammation.

The ethanolic extract of *Nigella sativa* seed showed good antipsoriatic activity *in-vitro* in HaCaT human keratinocyte cell line compared to asiaticoside as positive control. The extract also exhibited *in-vivo* antipsoriatic activity in the mouse tail model for psoriasis that was equivalent to the standard tazarotene (0.1%) gel and indicated as significant epidermal differentiation[25].

2.3.2. Acne vulgaris

Acne vulgaris is the most common chronic inflammatory disease of the skin. The Antimicrobial and anti-inflammatory properties of *Nigella sativa* oil have been suggested to be responsible for the positive effects of the extracts for acne.

The antibacterial potential of *Nigella sativa* seed extract exhibited *in-vitro* activity against *Propionibacterium acnes*, the bacterial pathogen involved in acne vulgaris[26]. In clinical study on acne subjects, *Nigella sativa* oil lotion 10% significantly reduced mean lesion count of papules and pustules after 2 months of therapy [26].

A double-blind, active-controlled, randomized study that lasted 8 weeks and in which 70 patients participated evaluated the topical use of *Nigella sativa* oil, for the treatment of mild to moderate acne vulgaris. *Nigella sativa* oil lotion 20% was more effective and safe than benzoyl peroxide lotion 5%, the common treatment for mild to moderate stage of acne vulgaris [27].

2.3.3 Eczema

Hand eczema is a pruritic dermatitis severely influencing the patient's quality of life. A double-blinded clinical trial was carried out in 60 patients with hand eczema for 4 weeks to assess effect of *Nigella sativa* on severity of hand eczema and patients' life quality[28]. *Nigella sativa* was found to be as effective as betamethasone in enhancing quality of life and alleviating the severity of eczema and that both were more effective than Eucerin.

In a double-blind, placebo-controlled study, patients with allergic diseases, including allergic rhinitis, bronchial asthma, and atopic eczema were treated with 500 mg *Nigella sativa* oil capsules. The NS oil-treated group showed statistically significant improvement and decreased the IgE and eosinophil count compared with the placebo group[29].

[23] Houghton PJ, Zarka R, de las Heras B, Hoult JR. Fixed oil of Nigella sativa and derived thymoquinone inhibit eicosanoid generation in leukocytes and membrane lipid peroxidation. Planta Medica. 1995;61:33-36.
[24] Chakravarty N. Inhibition of histamine release from mast cells by nigellone. Annals of Allergy. 1993;70:237-242.
[25] Dwarampudi LP, et al. Antipsoriatic activity and cytotoxicity of ethanolic extract of Nigella sativa seeds. Pharmacognosy Magazine. 2012;8:268.
[26] Bhalani U, Shah K. Preparation and evaluation of topical gel of Nigella sativa (kalonji). International Journal of Research and Development in Pharmacy & Life Sciences. 2015;4:1669-1672.
[27] Hadi NA, Ashor AW. Nigella sativa oil lotion 20% vs. benzoyl peroxide lotion 5% in the treatment of mild to moderate acne vulgaris. Iraqi Postgraduate Medical Journal. 2010;9:371-76.
[28] Ebadi A, Younespour S, et al. Comparison of therapeutic effect of topical Nigella with betamethasone and eucerin in hand eczema. J Eur Acad Dermatol Venereol. 2013;27(12):1498-504.
[29] Kalus U, et al. Effect of Nigella sativa (black seed) on subjective feeling in patients with allergic diseases. Phytotherapy Research. 2003;17:1209-1214.

2.4. SKIN PIGMENTATION

2.4.1. Vitiligo

Vitiligo is an autoimmune skin disease occurring due to the destruction of skin melanocytes that produce skin pigment. The therapeutic potential of *Nigella sativa* seed extract and TQ for the treatment of vitiligo skin conditions as well as the mechanism of skin darkening at the cellular level was evaluated. *Nigella sativa* and TQ, showed significant skin darkening on the isolated melanophores of the wall lizard. The melanin stimulatory effects were suggested to be mediated through cholinergic receptors of muscarinic nature within the isolated melanophores of wall lizard[30].

In a randomized, double blind clinical trial study, 52 patients topically used *Nigella sativa* oil twice a day for 6 months had a significant decrease in the vitiligo area scoring index with no significant side effects[31].

2.4.2 Sun protection

A *Nigella sativa* seed sunscreen cream was evaluated for its *in vitro* activity using Sun Protection Factor (SPF) method. The study suggested it as a good candidate for sunscreen or cosmeceutical purposes[32].

2.5 ANTI-AGING

Collagen and elastin are major supportive molecules for the structure of skin tissue, and their structural damage and degradation are directly associated with disruption of the skin barrier and the formation of skin wrinkles. A standardized sunscreen seed extract (TQ 5.12%), inhibited the activity of collagenase and elastases. The inhibitory effects may contribute to its overall anti-aging effects. sunscreen extract protected the structure of Bovine Serum Albumin (BSA) and type I collagen by inhibition of protein glycation and collagen cross-linking, respectively[33].

Since oxidative stress plays a crucial role in aging, *Nigella sativa* seed oil was studied in a mouse model of aging induced with D-galactose. *Nigella sativa* seed oil has exhibited an anti-aging effect that was shown through its antioxidant and anti-apoptosis properties. The study showed that administration of *Nigella sativa* oil reduced lipid peroxidation and reduced glutathione (GSH) content. The oil decreased Bax/Bcl2 levels and down-regulated the expressions of caspase-3 proteins in brain and liver tissues[34].

3. CONCLUSION

Nigella sativa seeds have been used for centuries in traditional medicine for the treatment of many skin conditions including skin infections, inflammatory skin conditions, wounds and skin pigmentation.

The pharmacological properties of *Nigella sativa* and its main active component thymoquinone had been investigated by *in vitro, in vivo* and clinical studies. These studies have indicated a wide range of pharmacological effects such as immunomodulatory, anti-inflammatory, analgesic, antiasthmatic, antimicrobial and antioxidant that might explain its successful use in folk medicine for the treatment of many skin conditions.

These beneficial effects of *Nigella sativa* and thymoquinone suggest there use for a wide range of cosmeceutical and dermatological skin conditions.

[30] Ali SA, Meitei KV. Nigella sativa seed extract and its bioactive compound thymoquinone: the new melanogens causing hyperpigmentation in the wall lizard melanophores. Journal of Pharmacy and Pharmacology. 2011;63:741-746.
[31] Ghorbanibirgani A, Khalili A1, Rokhafrooz D. Comparing Nigella sativa oil and fish oil in treatment of vitiligo. Iranian Red Crescent Medical Journal. 2014;16:-4515.
[32] Kale S, et al. Formulation and in-vitro determination of sun protection factor of Nigella sativa Linn. seed oil sunscreen cream. Int J PharmTech Res. 2010;2:2194-2197.
[33] Li H et al., Thymocid®, a Standardized Black Cumin (Nigella sativa) Seed Extract, Modulates Collagen Cross-Linking, Collagenase and Elastase Activities, and Melanogenesis in Murine B16F10 Melanoma Cells. Nutrients 2020;12:2146.
[34] Shahroudi MJ et al., Anti-Aging Effect of Nigella sativa Fixed Oil on D-Galactose-Induced Aging in Mice. Journal of Pharmacopuncture 2017;20[1]:029-035.