

The Benefits of *Nigella sativa* for Skin Diseases and Heal Skin Injuries: An Overview of Phytochemicals and Pharmacological Properties

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ARTICLE INFO

Received: 📅 December 01, 2023

Published: 📅 December 13, 2023

Citation: Abdalsalam Kmail. The Benefits of *Nigella sativa* for Skin Diseases and Heal Skin Injuries: An Overview of Phytochemicals and Pharmacological Properties. Biomed J Sci & Tech Res 54(1)-2023. BJSTR. MS.ID.008505.

ABSTRACT

Nigella sativa (*N. sativa*) is a medicinal plant with a long history of use in various traditional systems of medicine, such as Arab and Islamic medicine, Unani, Ayurveda, and Chinese medicine. *N. sativa* has many active compounds, such as alkaloids, saponins, and thymoquinone, that give it a wide range of health benefits. It can act as a diuretic, bronchodilator, antihypertensive, antidiabetic, and analgesic. Moreover, *N. sativa* has antimicrobial, anti-inflammatory, and antineoplastic properties, which make it a promising natural treatment for skin conditions. This article summarizes the current evidence on the effects of *N. sativa* for the management of acne vulgaris, melanoma, vitiligo, atopic dermatitis, plaque psoriasis, and wound healing. This review examines the most recent studies on the role of *N. sativa* in preventing and treating skin diseases and injuries, with a focus on its phytochemicals and pharmacological properties. We conducted a comprehensive literature review using various electronic databases, including Google Scholar, PubMed, Science Direct, and MedlinePlus, to collect data on the therapeutic properties of *N. sativa* and thymoquinone in skin disorders. Our findings provide substantial evidence supporting the efficacy of *N. sativa*/thymoquinone in facilitating the healing of a variety of skin diseases. However, it is essential to establish the most effective treatment dosages and the optimal administration route. Further research is also required to explore potential side effects and to evaluate the performance of these natural products in clinical trials.

Keywords: *Nigella sativa*; Skin Diseases; Wound Healing; Phytochemicals; Traditional Medicine

Introduction

Skin is the human biggest organ, made up of layers, tissues, and structures that protect it from infections, regulate its temperature, and maintain its internal balance. The skin consists of the epidermis, dermis, subcutaneous tissues, and other components that support its structure and function. However, many people suffer from skin diseases that can damage the skin and cause lesions and wounds. These can affect the skin's ability to function properly and result in serious or fatal consequences. Therefore, skin diseases are an important issue in medicine [1]. Skin diseases can occur due to various factors, such as fungal growth, bacterial infection, allergic reaction, microbial invasion, or pigment alteration [2]. The most common skin disorders

include acne, alopecia areata, atopic dermatitis, psoriasis, raynaud's phenomenon, rosacea, skin cancer and vitiligo as well as, viral and environmental skin disorders [3] (Figure 1). From ancient, plants were employed for therapeutic purposes. As early as 3,000 BC, the Chinese and Egyptians employed therapeutic herbs. Herbs were employed in medicinal practices by cultural groups such as African and Native American. But origin of traditional medical was in Siddha, Ayurveda, Unani, and TCM that included herbal remedies. Plant-based medications and other botanicals have become increasingly popular in the Western world in recent years [4]. Plant extracts and their active compounds have the ability to modulate inflammation at the cellular level as well as growth factors, and cytokines which involved in skin diseases [5,6].



Figure 1: The most common skin diseases.

Natural chemicals can aid in the production of new blood vessels, connective tissue development, and skin cell repair [7,8]. Among medicinal plants, 40 plants are currently employed in the treatment of various types of skin diseases, such as acne, psoriasis, and allergy [9,10]. *Capparis spinosa*, *Solanum nigrum*, *Ferula hermonis*, *Eruca sativa*, *Hypericum triquetrifolium*, *Inula helenium*, *Linum pubescens*, *Urtica dioica*, roots of *Saponaria officinalis*, and seeds of *N. sativa* are the most common plants used in the management of skin diseases [8,11]. Clinical trials on skin disorders have shown that *N. sativa* essential oil and crude extract are effective. (Atopic dermatitis, Atopic eczema, Wart, Eczema, Acne vulgaris, Acute cutaneous leishmaniasis, Arsenical keratosis, Psoriasis, Vitiligo, Infant skin infections, Acute radiation dermatitis,) It can be applied as an alternative treatment that helps patients with skin-related problems. [12]. Despite the challenges encountered in finding and guarantees the purity of active compounds, there are a number of clinical trials on herbal products accessible. These studies give important information about the possible advantages and efficacy of employing plant extracts and phytochemicals to treat skin diseases. A brief discussion of *N. sativa*, chemical composition and their promising ability to control skin diseases including healing injuries by regulating inflammation, antioxidant, and antibacterial potency is presented in this review. These natural remedies have shown potential in reducing and curing skin diseases *in vitro*, *in vivo* and in clinical studies.

The Use of Natural Products to Regulate Skin Diseases

Natural substances may be used as a great natural solution to artificial medicines or other unpleasant methods for tendinopathy treat-

ment [13]. The goal of curing skin disorders process is to restore the integrity of the tissue. However, in some cases, skin may lag healing and fail to reach healthy through the normal process of repair. This can result in a chronic inflammatory case that leads to the development of chronic wounds. These wounds have specific characteristics, such as a high bacterial exposure, unregulated growth factors, inflammatory mediators, and proteolytic enzymes which favor tissue destruction over repair. Imbalanced proteolytic activity is a fundamental result of this chronic inflammatory response at the wound site [14]. Traditional medicine has been employed for centuries to cure various skin diseases. A study conducted in northern Maputaland, South Africa, found that 47 plant species from 35 families were used to treat 11 different skin diseases, such as abscesses, acne, burns, boils, incisions, ringworm, rashes, shingles, sores, wounds, and warts [15]. The survey also discovered that the area's general population relied on medicinal plants for their primary health treatment. Another review article evaluated and contrasted traditional medical practices and ethnobotanical knowledge of medicinal plants in Albania, Cyprus, Greece, and Turkey for the treatment of skin problems [16]. The purpose of the study was to determine traditional knowledge and use of medicinal plants for the treatment of skin problems among traditional healers in Thailand's Songkhla district [17].

Ozonated oil offers encouraging results as a good candidate for the treatment of skin problems due to its antioxidant activity and reduced side effects than the standard of care [18]. Citrus Limetta hexane extracts were found to exert cytotoxic effects on skin fragments in a dose-dependent manner against lesions generated by hydrogen

peroxide [19]. Traditional therapies include rubbing the body with curative oils such as pure cold pressed olive oil, coconut oil, and avocado oil to minimize irritation and reduce the risk of skin infection [20]. In rats, the gel containing *Agaricus sylvaticus* extract was efficient for skin healing [21]. Clinical studies have revealed that growth factors produced by adipose-derived stem cells can effect cosmetic changes and provide stimulation for cellular renewal processes [22].

N. Sativa

N. sativa plant (Figure 2) is belonging to the family Ranunculaceae, which includes about 2,000 species of flowering plants. It is also known as black cumin, nigella, kalonji, or charnushka. It is native to eastern Europe and western Asia, but it has been naturalized in many other regions of the world [23,24]. It has been used for centuries as a

spice and herbal medicine in various cultures. *N. sativa* has a rich ethnobotanical history, as it has been mentioned in many religious and historical texts. For example, it is said that the Prophet Muhammad (PBUH) stated that black seed is a cure for every disease except death [24,25]. It is also reported that black seed was found in the tomb of the ancient Egyptian pharaoh Tutankhamun. Moreover, it has been used by various civilizations, such as the Greeks, Romans, Persians, Arabs, Indians, and Turks, for various purposes, such as food, medicine, perfume, dye, and insect repellent [24,25]. Some of the traditional uses of *N. sativa* include treating asthma, cough, bronchitis, fever, diarrhea, dyspepsia, hypertension, diabetes, rheumatism, skin disorders, wound healing, and infertility. It is also used as a carminative, stimulant, diuretic, emmenagogue, galactagogue, and purgative. The seeds, oil, and extracts of *N. sativa* are the main parts used for these purposes [23,25].



Figure 2: *N. sativa* flower, oil and seeds.

N. sativa has also been studied for its phytochemistry and pharmacology, as it contains various bioactive compounds, such as thymoquinone, thymohydroquinone, dithymoquinone and thymol [26] (Figure 3). These compounds have shown various biological activities, such as antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer, immunomodulatory, neuroprotective, and hepatoprotective [25,27]. However, more clinical trials are needed to confirm the safety and efficacy of *N. sativa* for human health. Phytochemicals

of *N. sativa* extracts and seed oils include essential oils, fatty acids, sterols, and vitamins found to have injury healing, antimicrobial, anthelmintic, antitumor, anti-inflammatory, antioxidant, antidiabetic, antihistaminic, vasodilator, bronchodilator effects, as well as, it modulates allergic response, lower sugar and cholesterol, stimulates bone marrow, increases interferon production, pregnancy prevention, and decreases anxiety are all benefits of *N. sativa* L. [25,27-31] (Table 1).

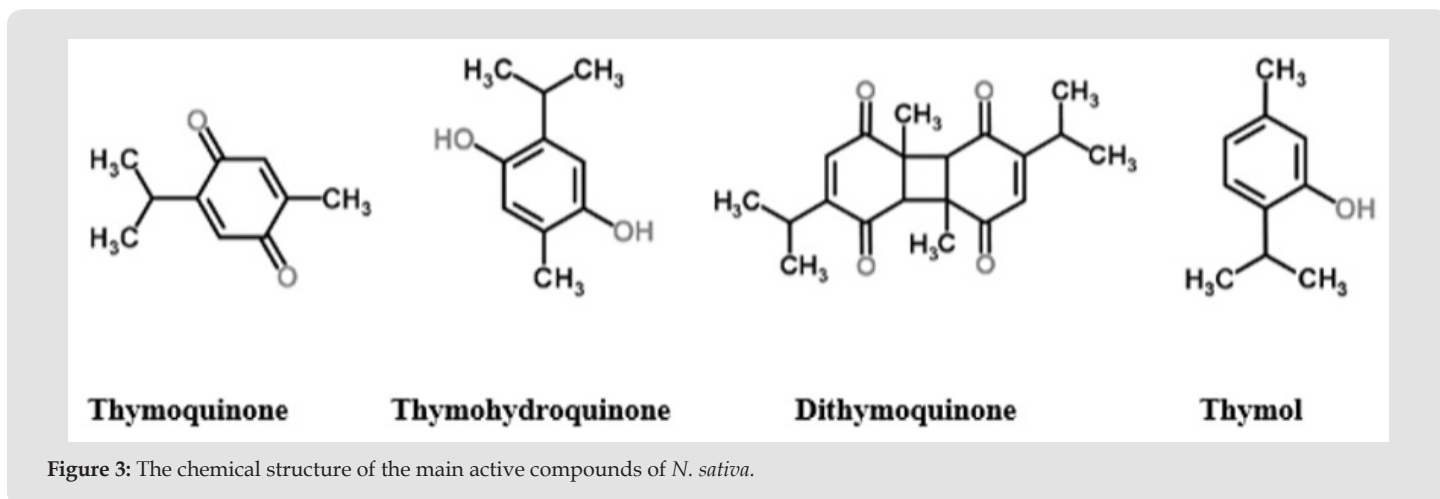


Figure 3: The chemical structure of the main active compounds of *N. sativa*.

Table 1: The main health benefits of *N. sativa*.

Benefit	Description	Source
Antioxidant	Neutralize free radicals and prevent oxidative damage to cells. This may protect against various chronic diseases.	[25, 31]
Cholesterol-lowering	Lower total and LDL levels, as well as blood triglycerides. This may reduce the risk of heart disease.	[25, 31]
Cancer-fighting	Induce cell death, inhibit tumor growth, and modulate the immune system.	[25, 31]
Immune-boosting	Enhance the immune system and increase the production of antibodies and immune cells. This may help fight infections and diseases.	[31]
Anti-inflammatory	Reduce inflammation and swelling in the body. This may help with conditions such as arthritis, asthma, and allergies.	[25, 27,31]
Cognitive-enhancing	Improve brain function and memory by protecting the brain from oxidative stress and increasing the levels of neurotransmitters.	[25, 27]
Skin and hair health	Improve the appearance and health of the skin and hair by moisturizing, nourishing, and healing them. It can also treat skin conditions such as eczema, acne, and psoriasis.	[25, 27]
Diabetes management	Lower blood sugar levels and improve insulin sensitivity. This may help prevent or treat type 2 diabetes and its complications.	[25, 31]
Pregnancy prevention	Inhibit the implantation of fertilized eggs in the uterus.	[31]

The Phytochemical Profile of *N. Sativa*

The main constituents of *N. sativa* seeds (Figure 4) are fixed oil, proteins, carbohydrates, crude fiber, minerals, and essential oil. Detailed compounds of these constituents are listed in (Table 2). Other new compounds include the triterpene saponin (3-O-[-D-xylopyranosyl-(1 2)--L-rhamnopyranosyl-(1 2)--D-glucopyranosyl])The steroidal glucoside (stigma-5,22-dien-3--D-glucopyranoside), the cycloartenol (3-O-[-D-xylopyranosyl-(1 3)--L-rhamnopyranosyl-(1 4)--D-glucopyranosyl]nigellidine-4-O-sulfite, as well as -11-methoxy-16-hydroxy-17-acetoxy hederagenin were detected in the chemical composition of *N. sativa* [32,33]. Magnoflorine, kaempferol 3-O-rutinoside, and -hederin are among the new ingredients recently discovered [34]. Added to the above, many micronutrients and fatty acids (linoleic, oleic, and palmitic acids) also found within the plant contents [35]. Seven monoterpene hydrocarbons in *N. sativa* made up 52.61% of the overall composition of essential oil; p-cy-

mene (28.76%), -thujene (12.88%), trans-verbenol (5.99%), -pinene (3.71%), -pinene (3.69%), sabinene (1.7%), and limonene (1.69%). The oxygenated monoterpene group in *N. sativa* essential oils was dominated by 2-isopropyl-5-methyl-1,4-benzoquinone (35.7%), also known as thymoquinone. There are five components in *N. sativa* hydrocol; 1,8-cineole (0.4%), linalool (0.5%), trans-verbenol (2.83%), terpinen-4-ol (7.21%), and thymoquinone (89.05%) [36]. LC-MS/MS analysis of the *N. sativa* cake revealed 36 distinct chemicals [37].

The investigations found that *N. sativa* seedcake contains a variety of phytochemicals, including a high quantity of protein, carbs, fiber, alkaloids and flavonoids, and phenolics with strong antioxidant activity [35]. The hydroethanolic *N. sativa* extract caused collagen fibers to be well ordered and epidermal diameter to grow significantly [38]. The analysis of detected phytochemicals from the GC-MS spectrum revealed that they had high reacting affinity for wound healing-associated target proteins including PKC-II, TNF, IL-1, PDGFRA, VEGF-A, and TGFBR1 kinase [39].

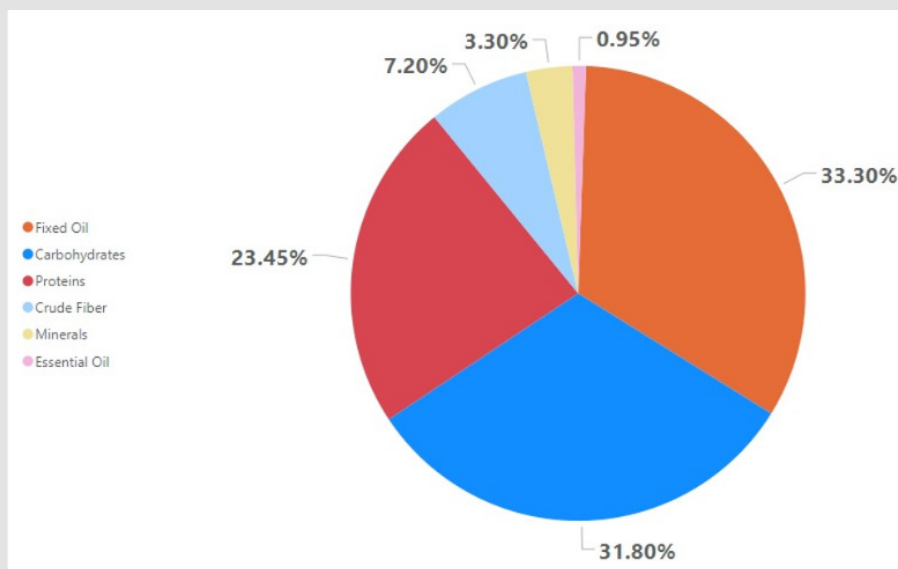


Figure 4: Percentage of the *N. sativa* seeds components.

Table 2: *N. sativa* seed main phytochemicals.

Saponins, Alkaloids, Vitamin, Lipids [32,53, 54]	Fixed Oil (Fatty Acids, Sterols, Tocopherols) [53-59]	Amino Acids [32,53,103,104]	Minerals [32,53,103,104]	Essential Oils [95,96,105-107]	Carbohydrates [108]
α-hederin	Linoleic	Glutamic acid	Copper	Thymoquinone	Glucose
Hederagenin	Oleic	Phenylalanine	Zinc	Thymohydroquinone	Rhamnose
nigelicine	Palmitic	Lysine	Phosphorus	Dithymoquinone (nigellone)	Xylose
nigellidine	Stearic	Threonine	Iron	p-cymene	Arabinose
nigellamines A1, A2, A4, A5, B1, B2, C	Eicosadienoic	Arginine	Niacin	Thymol	
riboflavin	Linolenic acids	Aspartic acid	Calcium	Limonene	
vitamin A, C	β-sitosterol	Histidine	Thiamin	Carvone	
pyridoxine	Stigmasterol	Leucine	Pyridoxine	Carvacrol	
Thiamin, Niacin, Folic acid	Campesterol	Isoleucine	Folic acid		
methylnonadeca-15, 17-dienoate	Avenasterol	Glycine			
pentyl hexadec-12-enoate	Lanosterol	Methionine			
pentyl pentadic-11-enoate	Tocopherol α, β, γ	Valine			

N. Sativa Studies on Various Skin Diseases

N. sativa has a wide range of applications for various diseases as well as infectious and chronic health problems. One of the common skin problems that *N. sativa* can help with is acne vulgaris, which is caused by bacteria that infect the pores of the skin. Some studies have shown that *N. sativa* oil can reduce the inflammation and the number of acne lesions, and can be as effective as some conventional treat-

ments. For example, one study compared a lotion with 20% *N. sativa* oil extract to a lotion with 5% benzoyl peroxide, which is a common ingredient in acne products [40]. The study found that both lotions had similar results in improving the acne condition, but the *N. sativa* lotion had fewer side effects and was less harmful to the skin [40]. Another study compared *N. sativa* oil to amoxicillin, which is an antibiotic drug, and found that they had the same effect in killing the bacteria

that cause acne [41]. The study also made a gel from *N. sativa* oil and tested it on acne patients, and found that it had good results in healing the skin [41]. Therefore, *N. sativa* is a natural and safe alternative for treating acne vulgaris, as well as other skin problems that involve inflammation, infection, irritation, rashes, dermatitis, and psoriasis. An experiment was conducted to determine the effect of *N. sativa* seeds on psoriasis. Psoriasis is a skin ailment characterized by red, scaly patches of skin. The trial revealed that employing ethanol extract of *N. sativa* seeds raised skin layer thickness in the case study group compared to the control group that received conventional treatment [42].

Another trial found that *N. sativa* oil was more effective as an antipsoriatic agent, particularly when taken as both a cream and a pill [43]. This confirmed that *N. sativa* possesses antipsoriatic properties and can alleviate psoriasis symptoms. One of the skin problems that *N. sativa* oil can help with is vitiligo, which is a condition that causes loss of skin color in patches. Vitiligo can affect the self-esteem and mental health of many patients. Some studies have explored the potential of *N. sativa* oil for treating vitiligo. A mixture of *N. sativa* oil and fish oil were tested on patients with vitiligo lesions. It has been found that both oils reduced the size of the lesions and improved the skin color [44]. Furthermore, when lizard skin used as a model, *N. sativa*

oil increased the amount of melanin, which is the pigment that gives color to the skin. This explained that *N. sativa* oil enhanced the sensitivity of the receptors that control the production of melanin. Thy-moquinone is the active ingredient *N. sativa* oil proposed to reduce external skin problems such as vitiligo and hypopigmentation [45].

Essential Oil

N. sativa essential oil (0.4-2.5%) has been shown to promote acute cutaneous wound healing, primarily by reducing the time of epitalization. *N. sativa* oil which includes essential oil have found to protect and reduce a wide range of skin diseases (Table 3). Essential oil used topically, may be explored as an alternative treatment approach to improve cutaneous wound healing. *N. sativa* L. essential oil may be useful in lowering oxidative stress, lipid peroxidation, and related problems, as well as in the treatment of diabetic wounds. As a consequence of its antioxidant, antibacterial, and anti-inflammatory properties, *N. sativa* L. essential oil can be employed as an alternate agent to existing therapies in future wound healing [46,47]. *N. sativa* oil has been presented as a valuable food component with a distinct aroma and flavor, which has been utilized in pickles, baked goods, confectionery, sauces, salads, and savory dishes [26].

Table 3: The potential benefits *N. sativa* oil for skin diseases.

Skin Disease	<i>N. Sativa</i> Form	Effect	Source
Acne vulgaris	Seeds, oil	Reduced acne severity and inflammation, improved skin hydration and barrier function	[108,109]
Eczema	Oil	Reduced eczema severity and itching, improved skin hydration and barrier function	[108,111, 112]
Vitiligo	Oil	Increased repigmentation of depigmented skin patches	[109,112]
Psoriasis	Oil	Reduced psoriasis severity and inflammation, improved skin hydration and barrier function	[36,111, 112]
Arsenical keratosis	Oil	Reduced keratosis severity and arsenic levels in blood and urine	[109]
Warts	Oil	Reduced wart size and number, increased clearance rate	[109,111]
Acute cutaneous leishmaniasis	Oil	Reduced lesion size and duration, increased healing rate	[109]

Thymoquinone and Arginine

Thymoquinone is the major bioactive ingredient, accounting for 30-48% of the essential oil, has high antioxidant and anti-inflammatory, immune-boosting, cell survival-improving, and energy metabolism-promoting properties, which may explain why they are so beneficial to our health. These include diabetes, obesity, hypotension, allergies, antimicrobial effects, and cancer [48,49]. Pretreatment with thymoquinone decreased Th-2-cell-mediated lung inflammation, eosinophilia, and goblet cell hyperplasia [11]. Furthermore, in rats, thymoquinone decreased COX-2 expression, PGD2 synthesis, as well as COX-1 expression and PGE2 generation. COX-2 contributes to the inducible inflammatory response by converting arachidonic acid into prostaglandins (a pro-inflammatory cytokine), whereas COX-1 contributes to the constitutive or "housekeeping" inflammatory response. COX-2 suppression is advantageous in situations of chronic

inflammatory issues since long-term elevated COX-2 activity is known to be an underlying cause of many chronic inflammatory conditions. The anti-inflammatory properties of black seeds and thymoquinone are primarily mediated by COX-2 and PGD2 inhibition [50-52]. Numerous research publications on the safety and efficacy of *N. sativa* and thymoquinone have been released. *N. sativa* thymoquinone reduce obesity-related low-grade inflammation by stimulating natural killer cell proliferation and differentiation, monocyte activity, T-cell-based immunity, and macrophage activity [11]. Thymoquinone, which can act as an antioxidant by breaking down free radicals and enhancing intracellular antioxidant capacity [53]. Arginine, one of the major amino acids found in *N. sativa*, has been proven to improve skin mucosal function, regeneration, and extracellular matrix production [54]. Compared to local superficial treatments, using *N. sativa* essential oil orally is less costly and simpler for consumers [55].

N. Sativa and Wound Healing

A wound is defined as any physical, mechanical, chemical, or microbiological cause that lead to disorders in which bodily tissues, particularly skin epithelial cells, connective tissue, and muscle tissue, are damaged, causing nerve tissue and blood vessels to bleed [56,57]. The most common types of wounds are, acute wounds, closed wounds, open wounds, incised wounds, tear or laceration wounds, puncture wounds, abrasive or superficial wounds, penetration wounds, gun-

shot wounds, and chronic wounds [58]. Following wound creation, the healing process begins to heal the wounded or damaged tissues [56]. Wound healing (Figure 5) is a complicated process involving different cell groups, the extracellular matrix, and the activity of soluble mediators like growth factors and cytokines. Healing can be divided into four stages: coagulation and hemostasis; inflammation; proliferation; and wound remodeling with scar tissue development. The proper approach to wound treatment can have a significant impact on the clinical result [26].

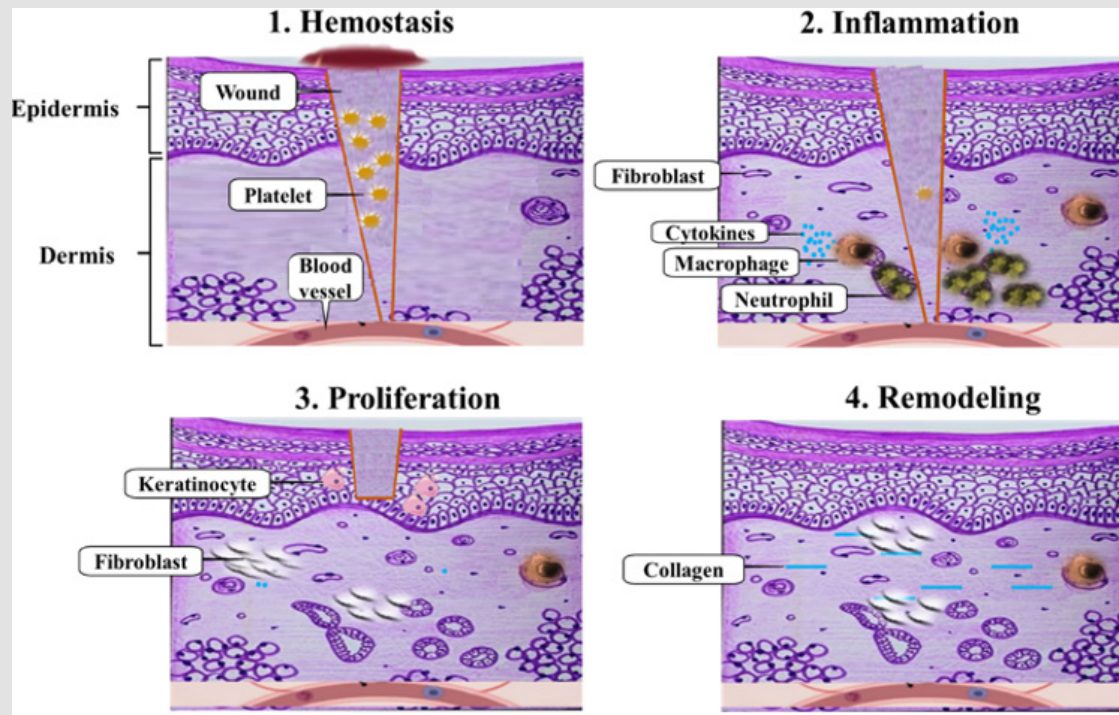


Figure 5: The physiological wound-healing stages. Hemostasis happens soon after bleeding and lowers blood flow by restricting blood arteries to halt bleeding after vascular damage. Inflammation: Hemostasis and acute inflammation are caused by the production of cytokines and growth factors, as well as the movement of leukocytes into the wound site. Increased migration and proliferation of keratinocytes, fibroblasts, endothelial cells, as well as leukocytes in the wound region. Remodeling: the interaction of stretching and pulling forces with scar tissue. They assist collagen in regaining its proper orientation [38,59].

N. Sativa Accelerate Healing

It refers to wound types that are done in a way that allows for anatomical and functional restoration throughout the usual healing time. Healing takes 20 to 30 days under ideal conditions [58]. An excellent wound healing response was observed using *N. sativa* oil, with wound healing completing following 14 days on day 21 in all tested Wistar albino female rats. In comparison to ozonated Sesame and Hypericum perforatum oils [59]. Moreover, *N. sativa* was convincing reason for faster wound healing in a rat model of burn wound damage, with no macroscopic or microscopic evidence of infection [58]. *N. sativa* oil dramatically improved the metabolic activity, proliferation, and viability of sheep tenocyte cells after 24 hours. Compared to oleic acid, LED, and their combination, dramatically boosted these activities over

48 hours [13]. The anti-inflammatory, antioxidant, and antibacterial properties of *N. sativa* L. seeds may explain their effectiveness in burn wound healing [60]. 95%EtOH of *N. sativa* *in vitro* promotes wound healing by inhibiting nitric oxide and superoxide anions, boosting fibroblast cell proliferation, and hastening wound closure [61]. Healing ability in a rat wound healing model occurred as a result of optimal histological healing with increased anti-oxidant induction and higher load bearing capacity [62].

Wound Healing and Diabetes

In contrast to acute wounds, diabetic wounds exhibit several molecular problems in the healing cascade, including deficiencies in fibroblast and keratinocyte activities, angiogenesis impairment, and

phagocytic activity impairment [63,64]. Variations in the secretion time and expression amount of growth factors including PDGF, TGF-1, EGF, VEGF, and bFGF have been hypothesized as one mechanism for diabetes-induced negative impact on wound healing [65,66]. Pro-angiogenic factors, such as VEGF, increase endothelial cell survival, migration, differentiation, self-assembly, and self-repair. When VEGF interacts to the VEGF receptor, various subsequent protein kinase pathways are triggered, resulting in the formation of new blood vessels [67]. Histological tests revealed that the *N. sativa* extract-treated rat groups had a very low number of inflammatory neutrophils and faster wound healing than the diabetes groups [38]. Hydroethanolic *N. sativa* extract healed wounds rapidly in diabetic rats. *N. sativa* seeds expedite wound healing in streptozotocin-induced diabetic mice in 15-18 days [38]. The anti-inflammatory markers were identified in *N. sativa* in the early days of the healing phase, and hence the healing effects of this may due, in part, to its anti-inflammatory activities [38]. Diabetic rats had much greater wound closure rates. After the third, tenth, and fourteenth days of wound therapy, macroscopical findings revealed that the granulation tissue was smoother and more alive, histological data revealed that wound healing was healthy and vascularization was decreased [47].

Patients with diabetes have a higher risk of infection, including complex skin and soft tissue infections [68]. According to a study done on injured rabbits, non-antibiotic amalgamates may have therapeutic and nutritional properties that promote wound healing [69]. An extending wound healing process, an excessive amount of reactive oxygen species destroying protein compositions of extracellular matrix elements, proteolytic enzymes and inflammation cytokines expansion, and oxidative stress are all incredibly prolonged in diabetic states [70].

Skin Angiogenesis

Angiogenesis (new blood vessels formation) is initiated during wound injury when diseases and inflammation diminish [71]. Angiogenic signals from macrophage-derived substances which induce endothelial cell proliferation, migration, and differentiation, leading in an increase in blood vessel creation [72]. Research found that lesions in rats healed lightning fast and effectively when *N. sativa* was applied. Certain processes that have been hypothesized to explain the influence on wound healing are likely to be enhanced angiogenesis and the formation of greater strain resistant tissues [73]. As a pro-angiogenic factor, PDGF promotes the development of new blood vessels, both PDGF and VEGF promote the beginning of angiogenesis [74]. During a certain time, frame, the healing process involves planned interactions between distinct cell types, biochemical mediators, and extracellular matrix components. Both ethanol and chloroform extracts boosted VEGF and PDGF expression in both normal human dermal fibroblasts (NHDFs) and human umbilical vein endothelial cells (HUVECs). This suggests that *N. sativa* seed extracts may improve cell survival and self-repair efficacy [73].

The Anti-inflammatory, Antioxidant and Antibacterial impact of *N. sativa* in Skin Diseases

Unsaturated fatty acids and essential oils, which make up the majority of the chemical composition of *N. sativa* oil, have been demonstrated in tests to have pharmacological effects corresponding to anti-inflammatory, antioxidant and antibacterial properties [18,35]. *N. sativa* considerably reduces nitric oxide production as well as blood levels of pro-inflammatory cytokines and other markers such as IL-4, IL-5, IL-6, IgE, IgG1, and OVA-specific IgG1 ovalbumin-treated rats. Rats given *N. sativa* had a lower T-cell response and less T-cell proliferation in the spleen, but no histopathological alterations in lung tissue. Untreated rats displayed alveolar wall thickening and an increase in the number of goblet cells. According to these findings, *N. sativa* suppresses Th-2-induced T-cell proliferation and differentiation, effectively preventing the inflammatory response [75,76]. A research demonstrated that topically applying *N. sativa* Hydroethanolic extract to full-thickness skin lesions in diabetic male rats reduced inflammation [38]. Free radical generation is an essential aspect of biological metabolism, but an imbalance leads to oxidative stress. Excessive lipid peroxidation destroys cellular membranes, which can lead to cell death and degenerative diseases [77-79].

N. sativa is with excellent antioxidant impact and radical scavenging capacities. It was discovered that the cream hydrosol had a greater antioxidant impact as well as wound healing capability [80]. Though substantial gains in pharmacological advantages, *N. sativa* seeds and their active chemicals are still a long way from clinical use [81]. Other researches emphasized the significance of *N. sativa* L. antioxidant potential appears to be inversely related to oxidative damage; nevertheless, the relationships between the antioxidant potential of *N. sativa* in oxidative stress settings require more study interventions [62]. Avoiding skin infection, antibiotic dressings, topical antibiotics, debridement, and antiseptic agents are utilized [82,83]. *N. sativa* essential oil showed decreasing the effects towards *Staphylococcus aureus*, *Listeria monocytogenes*, *Bacillus cereus*, *Bacillus subtilis*, *Salmonella* Hartford, *Escherichia coli*, *Pseudomonas aeruginosa*, *Vibrio parahaemolyticus*, and *Vibrio alginolyticus*, were ten times compared to crude oil, methanol, ethanol extracts [84-87]. Furthermore, *N. sativa* seed extracts suppress the microorganisms of dental caries *Streptococcus mutans* and *Lactobacillus acidophilus* [88]. *N. sativa* seed and its quinones dithymoquinone and thymohydroquinone have been shown to be effective dairy spoilage yeast preservatives.

Debaryomyces hansenii, *Saccharomyces cerevisiae*, *Yarrowia lipolytica*, *Kluyveromyces marxianus*, *Zygosaccharomyces microellipsoides*, and *Pichia anomala* are some of the organisms that have been isolated. [89]. Although *Cutibacterium acnes* is resistant to *N. sativa*'s antibacterial action [90], thymol, an *N. sativa* derivative, is a powerful antibacterial agent whether used alone or together with additional antibacterial agents [91]. As a result, it may be stated that antibac-

terial and antiseptic actions are one of the causes for reducing and management of skin diseases.

Conclusion

N. sativa has a wide range of benefits for skin diseases and injury healing, and its phytochemicals have shown promising results in clinical studies. More research, however, is required to fully evaluate and establish the efficacy or inadequacy of therapy with *N. sativa* [26]. Atopic dermatitis, vulgaris, arsenical keratosis, psoriasis, vitiligo, acute cutaneous leishmaniasis, warts, eczema, and acne have all been shown to benefit from *N. sativa*. *N. sativa* has several pharmacological and biological activities in addition to medical qualities and has been utilized as a nutraceutical and pharmaceutical alternative, similar to dietary supplements that claim to offer physiological benefits that could guard against chronic diseases [92-94]. The effectiveness of *N. sativa* essential oil and extract has been shown in the majority of clinical investigations. *N. sativa* seed oil contains several potent components, such as thymoquinone and nigellone, that have demonstrated effective anti-inflammatory effects. These compounds help reduce inflammation and soothe irritated skin, making it an ideal ingredient for individuals with conditions like acne, eczema, or rosacea [12,95-100].

Tissue engineering and regenerative therapeutics are the technologies of the future for building skin regulation systems. Improved quality control procedures for identifying, screening, and quantifying herbal ingredients, as well as well-designed pre-clinical and clinical trials, will open up new research avenues in skin diseases treatment [43]. One of the challenges of using *N. sativa* is the lack of standardization in the preparation of the plant extracts, which can lead to variations in the quality and quantity of the active ingredients [101-106]. Additionally, the safety of *N. sativa* has not been fully established, and there is a need for further studies to determine the optimal dosage and duration of treatment. Future studies should focus on the identification of the active components of *N. sativa* and their mechanisms of action, as well as the development of standardized methods for the preparation of *N. sativa* extracts. Moreover, clinical trials with larger sample sizes and longer follow-up periods are needed to evaluate the long-term safety and efficacy of *N. sativa* in the treatment of skin diseases [107-112].

Author Contributions

AK performed the study conception and design, data collection and analysis, wrote the review paper, read and approved the final manuscript and agreed to be accountable for all aspects of the work. AK is corresponding author and responsible for correctness reviewing data.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

I thank Professor Bashar Saad work at Arab American University-Palestine for his expertise and support. Also, I would like to thank Dr. Yamin Abu AlRub for his technical advice.

Funding

This research received no external funding.

Availability of Data and Materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Conflict of Interest

The author declares no conflict of interest.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.54.008505

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