

Nigella sativa (Kalonji): A Black Seed of Miracle

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ABSTRACT

It is recommended by the World health organization (WHO) that most of the world's population depends on herbal medicine for their health care. *Nigella sativa* is commonly known as a Black seed, Black cumin or 'Habbatul Barakah' i.e. an annual herb possessing a wide range of medicinal uses apart from its commercial significance as a spice yielding plant. It has long been used in the folk medicine system of the Arabian Gulf region, Far East Asia, and Europe. Seeds and oils of *N. Sativa* are the primary medicinal source from ancient times. It is one of the most common herbal plants used worldwide and possesses various chemical constituents such as thymoquinone, thymohydroquinone, dithymoquinone, thymol, nigellidine, carvacrol, nigellidine, nigllimine, nigellidine, and alpha-hederin. There are more than 100 constituents isolated from the plant. These chemical compounds have many pharmacological activities such as antibacterial, antiviral, anti-inflammatory, wound healing effect and also for acne vulgaris, skin cancer, pigmentation and many other cosmeceutical properties. Much scientific research on *N. sativa* has been conducted over the last five decades to investigate chemical and pharmacological properties. In this review, the phytochemicals, pharmacological properties, Ayurvedic properties and folk uses of *Nigella sativa* are briefly explained.

Keywords: *Nigella sativa*, Kalonji, Antinephrotic, Immunomodulatory, Black cumin

INTRODUCTION

Nigella sativa L. is a small perennial plant long up to 20 to 90 cm and comes under the Ranunculaceae family [1]. It is

mostly found in southern Europe, North Africa and Southeast Asia and cultivated in various countries in the world like the Middle Eastern, Mediterranean region, South Europe, India, Pakistan, Syria, Turkey, Saudi Arabia [2,3]. The seeds of the plant are considered as a spice and also known as black seed. The seeds have two kinds of oil, fixed and essential and also contains other components such as proteins, alkaloids, and saponins [4,5,6]. Thymoquinone is the major compound isolated from the black seed. The compound is isolated from both essential oil and fixed oil. The plant is utilized as a medicine in different cultures for many years [7,8]. In India, it is locally named as 'Kalonji' which has been utilized from ancient times [9]. Kalonji seeds are utilized for the treatment of diseases like diarrhea and asthma [10,11]. According to historical literature, *N. sativa* is considered a holy herb of the Middle East. Its seeds are most revered and heal almost everything except death. According to the Unani Tibb system of medicine, the herb is a valuable remedy for several diseases. The famous book of medicine "The cannon of medicine" by Ibn-Sina mentioned that black seeds stimulate the body's energy and helps in recovery from fatigue [12]. *Nigella sativa* is an amazing spice with great literature and religious background. According to the Ayurvedic system of medicine, *Nigella sativa* is a highly utilized medicinal plant. The seeds of *N. sativa* are suggested with buttermilk to obstinate hiccups and also utilized in loss of appetite, vomiting and dropsy. Many Ayurvedic formulations are

used to treat different diseases like obesity and dyspnoea. Seeds are also used in mercury poisoning, sore and leprosy [13]. Many chemical compounds are isolated from the *N. sativa* plant-like thymoquinone (30-48%), thymohydroquinone, dithymoquinone, p-cymene (7-15%), carvacrol (6-12%), 4 cymene, carvacrol, 4 terpineol, t-anethol, sesquiterpene longifolene and a-pinene. These compounds possesses many pharmacological properties. Thymoquinone is the most active phytochemical compound from all of above [14]. Many types of researches have been done on the *N. sativa* plant for their pharmacological activities like antimicrobial, anticancerous, antioxidant, antidiabetic, antinephrotoxic, antiparasitic, antimalarial, antinociceptive effects, anti-ulcer, anti-histaminic, cardiovascular and many others [15]. The vernacular names and taxonomical classification of *Nigella sativa* is shown in table no 1 and table no. 2 respectively.

Table 1: Vernacular names of *Nigella sativa*

English	Fennel Flower, Nutmeg Flower, Raman coriander, Blaxkseed, black caraway, black sesame
Hindi/Urdu	Kalaunji/Mangrail
Russian	Chernushka, Herbrew, Ketzakh
Turkish	Corek out
Arabic	Habbat ak-barkah
Indonesian	Jintan hitam
Bosnian	Curekor
French	Nigelle de Crete, toute epice
Germany	Schwarzkummel
Portuguese	Cominho-negro
Spanish	Ajenuz, aranuel
Swedish	svartkummin
Assamese	Kaljeera, kolajeera
Bengali	Kalo jeeray
Kannada	Krishna Jeeriage
Tamil	Karum, jeerakam

Table 2: Taxonomical classification of *Nigella sativa*

Taxonomical Rank	Taxon
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales
Family	Ranunculaceae
Genus	<i>Nigella</i>
Species	<i>Nigella sativa</i>
Common Name	Black Cumin

Botanical Description of *Nigella sativa*

Nigella sativa (figure 1) is little prostrate annual herb. The herb is long

about 44 cm to 60 cm. Leaves are divided into two linear segments long up to 3cm. They are opposite in pair on either side of the stem. The lower leaves are small and petiolate whereas the upper leaves are long. The plant has divided foliage. Flowers are pale blue on solitary long peduncles. It grows terminally on its branches. Seeds are trigonous and black in color. *N. sativa* reproduces with itself and forms a fruit capsule that consists of many white trigonal seeds when the fruit capsule matured. Fruit opens up automatically and the seeds within are exposed to the air becoming black and it is also known as black seeds. Seeds are triangular in shape, black in color and possess a pungent smell. It contains a considerable quantity of oil [16,17]



Figure 1. *Nigella sativa* (Kalonji)

Geographical Distribution: The plant is widely distributed in different areas of the world. It is mainly found in India and Pakistan. The species is grown in Syria, Lebanon, Israel, South Europe and Bangladesh. *N. sativa* is cultivated in the times of winter same as wheat. In India, it is specially grown in Punjab, Himachal Pradesh, Gangetic plains, Bihar, Assam and Maharashtra [18,19].

Phytochemical of *N. sativa*

There is very little research work done on the phytochemicals of *N. sativa*. The seeds of the plant are reported to contain few chemical compounds like

nigellone, nigellicine, nigellimine, nigellimine-N-oxide, avenasterol-5-ene, avenasterol-7-ene, campesterol, cholesterol, citrostadienol, cycloeucaenol, 24-ethyllophenol, obtusifoliol, sitosterol, stigmastanol, stigmasterol, stigmasterol-7-ene, beta-amyrin, butyrospermol, cycloartenol, 24-ethyllophenol, gramisterol, lophenol, 243-methyllophenol, obtusifoliol, sitosterol, stigmasterol-7-ene, beta-amyrin, butyrospermol, cycloartenol, 24-methylene-cycloarthanol, taraxerol, tirucallol, 3-O- $[\beta$ -D-xylopyranosyl (1-3)- α -L-rhamnopyranosyl (1-4)- β -D-glucopyranosyl (1-6) β -D-glucopyranosyl] hederagenin, volatile oil (0.5-1.6%), fatty oil (35.6- 41.6%), oleic acid, esters, esters of unsaturated fatty acids with C15 and higher terpenoids, esters of dehydrosteraric and linoleic acid, aliphatic alcohol, nigellidine, carvone, d-limonene, cymene, α,β -unsaturated hydroxyl ketone, steroids, hederagenin glycoside, melanthin,

melanthigenin, bitter principle, tannins, resin, protein, reducing sugar, glycosidal saponin, 3-O- $[\beta$ -D-glucopyranoside, cycloart-23-methyl-7,20, 22-triene-3 β , 25-diol, nigellidine-4-O-sulfite, nigellamines A3, A4, A5, C, nigellidine A1,A2,B1 and B2 [20,21,22,23,24,25]

The seed oil of the plant *N. sativa* contains cholesterol, campesterol, stigmasterol, β -sitosterol, α -spinasterol, (+)-citronellol, (+)-limonene, p-cymene, citronellyl acetate, carvone, nigellone, arachidic, linolenic, linoleic, myristic, oleic, palmitic, palmitoleic and stearic acids, Fixed oil isolated from the *N. sativa* species are linoleic acid (55.6%), oleic acid (23.4%) and palmitic acid (12.5%) and volatile oils are trans-anethole (38.3%), p-cymene (14.8%), limonene (4.3%) and carvone (4.0%), 2-(2-methoxypropyl)-5-methyl-1,4-benzenediol, thymol and carvacrol. Vanilliac acid are isolated from the root part of the plant [26,27,28,29,30,31].

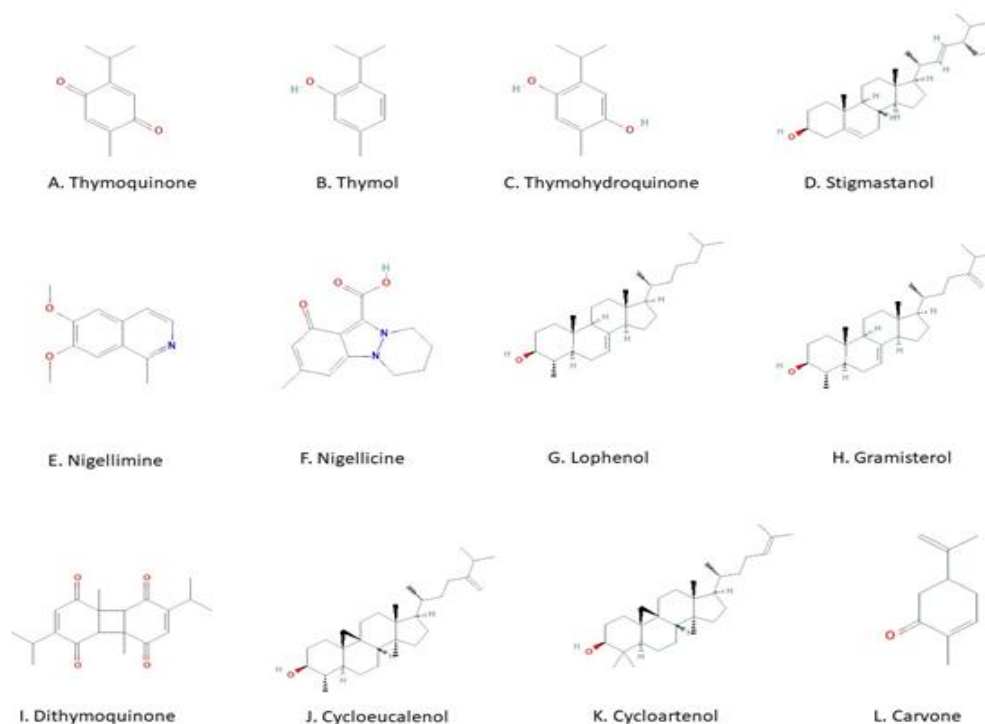


Figure 2. Chemical structure of some phytochemicals of *Nigella sativa* (Kalonji)

Folk View

According to Zohary and Hopf, archaeological evidence about the earliest cultivation of *N. sativa* is still scanty, but

they found seeds of this herb in several sites from ancient Egypt including Tutankhamen's tomb [32]. The role of this herb in Egypt is still unknown. According to

the literature, *N. sativa* is a traditional condiment of the old-time and seeds of the herb were extensively used to flavor food. According to the Unani Tibetan system of medicine, *N. sativa* has been considered a valuable remedy in many diseases. The seeds of *Nigella sativa* stimulate the body's energy and help in recovery from fatigue and dispiritedness. It was also utilized indigestion problems. The seeds have been traditionally utilized for the treatment of asthma, bronchitis, rheumatism, and related inflammation diseases mostly in the Middle East and Southeast Asian countries. It was also used to increase milk production in nursing mothers, to promote digestions and to fight parasitic infections. The seed oil has been utilized to treat skin problems such as eczema and boils. The Arabic quoted this herb as 'Habbatul barakah' means the seed of blessing. *Nigella sativa* has been utilized by Asians, Africans for medicinal purposes like respiratory health, stomach, intestine, kidney, liver function, circulatory, immune system and for general overall well-being. It is one of the greatest forms of healing medicine in Islam. Prophet Muhammad quoted that the black seed can cure every ailment except death as mentioned in the hadith [33].

"Narrated Khalid bin Said: We went out and Ghalib bin Abjar was accompanying us. He fell ill on the way and when we arrived at Medina he was still sick. Ibn Abi 'Atiq came to visit him and said to us, "Treat him with black cumin. Take five or seven seeds and crush them (mix the powder with oil) and drop the resulting mixture into both nostrils, for 'Aisha has narrated to me that she heard the Prophet saying, 'This black cumin is healing for all diseases except As-Sam.' 'Aisha said, 'What is As-Sam?' He said, 'Death.' " (Bukhari)

Nigella sativa is popular in bread and cakes to detoxifying the body from worms and parasites. The oil contains nigellone that is used for the treatment of asthma, bronchitis and coughs [34,35,36]. The seed oils of the *N. sativa* have a long history of folk usage in Arabian and Indian

civilizations. They are sometimes scattered in the folds of woolen fabrics to preserve them from insect damages [37,38,39,40,41].

Ayurvedic View

Kalonji is a traditional plant used for many years. In the Ayurveda medicine system seeds of *N. sativa* are effective against many diseases like cough, bronchitis, asthma, chronic headache, migraine, dizziness, chest congestion, dysmenorrhea, obesity, diabetes, paralysis, hemiplegia, back pain, infection, inflammation, rheumatism, hypertension, and gastrointestinal problems such as dyspepsia, flatulence, dysentery, and diarrhea [42]. The plant utilization is also described for the stimulation, diuretic, emmenagogue, lactagogue, anthelmintic and carminative. It is also applied to abscesses, nasal ulcers, orchitis, eczema and swollen joints [43]. The oil of the kalonji seeds is considered to be a local anesthetic [44]. The Seeds and seed oil the *N. sativa* are edible and also utilized in traditional dishes. It is used as a flavoring agent in pickles. Rasa Panchak of the *N. sativa* (kalonji) [45,46] is mentioned in table no. 3 below:

Table 3: Rasa panchak of *N. sativa* (Kalonji)

Sanskrit/ English	Sanskrit/ English
Rasa/ Taste	Katu, Tikta / Pungent, bitter
Virya / Potency	Ushana / Hot
Vipaka / Metabolic property	Katu/ Pungent
Guna / Physical property	Laghu, Ruksha, Tikshna / Light, Dry, sharp

According to Ayurveda, kalonji increases the pitta dosha (Fire+Water elements), pacifies the Vata dosha (air element) and reduces the Kapha dosha (earth+ water elements). The plant is suitable for Kapha body type and Vata body type and mostly preferred to Vata-Kapha disorders. It is not suitable for Pitta body type and pregnant women. It is helpful in the reduction of the formulation of Ama Dosha (Fire element).

Kalonji Benefits & Uses

1. **Holiosis (Bad Breath):** Ayurveda recommends kalonji use in bad breath. It

has antihalitosis action. The antihalitosis properties are attributed to its antibacterial and antimicrobial actions in the mouth. For bad breath, take a half teaspoon of kalonji seeds and chew it 2 times a day. It is given for a month for permanent relief from halitosis.

- 2. Anorexia, Indigestion & Flatulence:** Due to appetite, stimulant, digestive and carminative properties, kalonji helps in anorexia, indigestion and flatulence. It improves the secretion of digestive juice and improves liver function, it improves appetite in cases of anorexia. It prevents the formation of intestinal gas and aids in releasing the wind. So, it helps in flatulence, abdominal distension and abdominal pain occurring due to gas formation. In these diseases, you can chew a half teaspoon of kalonji seeds just before eating foods.
- 3. Asthma:** Kalonji reduces the inflammation of airways and regulates mucus secretion. Some Ayurvedic studies showed kalonji decoction reduces the severity and frequency of wheezing in asthma [47,48].
- 4. Dysmenorrhea:** In Ayurveda and folk medicine, Kalonji seeds are utilized for improving menstrual flow and alleviating menstrual pain.
- 5. Galactogenic Action:** Similar to cumin seeds, kalonji seeds also have galactagogic action. It improves the breastmilk supply and inhibits breastmilk abnormalities. It passes through the breastmilk and helps the baby to improve digestion. But in some cases, it can also cause constipation in babies.

Ayurvedic Formulation of Kalonji

Anupam: Mostly given in Kapha disorder.

Modern View

There are many issues which is faced by the Global herbal drug industry in today's scenario mostly the practice of making these drugs adulterated. This is the major reason why people lost faith in these

herbal drugs nowadays [49,50,51,52,53,54]. In today's time, intentional adulteration is practiced in many different ways like by substituting standard commercial variety, by substituting superficially similar but inferior drugs, by substituting artificially manufactured drugs, the substitution of exhausted drugs and by substituting toxic materials. Adulteration can be either intentional or unintentional. These adulteration processes ultimately degrade the quality of the original drugs. The herbal plant vendors use these adulteration techniques so smartly that these remain undetectable until and unless examination on a microscopic level and chemical level are implied [55,56,57]. The major disadvantages associated with adulteration are deterioration and degradation of drugs. Adulteration also increases the cost of drugs and produces adverse effects instead of showing actual biological affect [58]. The traditional herbal drugs and their formulations are associated with negligible toxicity and are free from any kind of adulteration. Traditional Ayurvedic herbal formulations of Kalonji plants are associated with a wide range of medicinal properties too which cures a variety of ailments without causing any severe harm to the human body. Health risks are usually associated with the modern adulterated drugs. For instance, the modern anti-obesity drugs have side effects associated with them whereas the anti-obesity activity of *Nigella sativa* is well demonstrated by many studies where the least toxicity and adverse effects were observed [59]. The kalonji oil has immune-modulatory activities and has a good effect on diverse conditions from deficiencies of the immune system. So, pharmaceutical industries produced kalonji seeds oils and distributed them worldwide. There are many unsaturated fatty acids isolated from the kalonji seeds which are very useful for the well-functioning immune system. Many scientific studies have been reported that the black seed oil of *Nigella sativa* possesses immune-modularly properties because it contains at least 60%

of the daily need for unsaturated fatty acids. Some of the unsaturated fatty acids cannot be formed by the human body so it has to be taken externally. Pure black seed oil is a very important product in naturopathy. It is utilized by the herbal industry as a nutritional supplement. A teaspoon of black seed oil mixed with yogurt is given to the children from the age of 4 years for a healthy dietary supplement.

Reported Therapeutic Studies of *Nigella sativa*

Various studies have been conducted on this plant to know its pharmaceutical and therapeutic uses. Large-scale clinical studies are still needed to prove the clinical efficacy of this herb, especially in skin diseases, immunomodulatory disorders and cancers.

1. Anti-bacterial Activity: Many studies have been reported the antibacterial activity of *N. sativa*. Thymoquinone is the major chemical constituent isolated from this plant. It was found to have antibacterial activity against most bacteria especially in Gram-positive cocci type such as *staphylococcus aureus* and *staphylococcus epidermidis* [60,61,62,63].

2. Antiviral activity: A few recent studies have been done on the antiviral effect of *Nigella sativa*. A study was held in 2013 which showed significant results about the effect of *N. sativa* oil against hepatitis C virus (HCV). A clinical study was done on 30 patients with HCV who were not eligible for IFN/ribavirin therapy. 450mg of *N. sativa* oil in capsular dosage form were administered orally 3 times daily. After 3 months, a reduction in overall viral counts and improved oxidative stress was noted, clinical condition and glycaemic control in a diabetic patient [64].

3. Antifungal Activities: From the reported studies it is clear that *Nigella sativa* possesses antiviral activity against most pathogenic fungi [65]. Thymoquinone was examined for antifungal activity against most fungal strains [66]. A comparative study

was reported that the antifungal activity of *Nigella sativa* was more potent than Amphotericin B drug (an antifungal drug). One more study reported the antifungal activity of *N. sativa*. The methanolic and ethanolic extract of the seeds of *N. sativa* was examined on different pathogenic fungal strains. These strains were *Aspergillus*, *Candida*, *Cryptococcus* and *Issatchenkia* species. The decoction was prepared by the cold maceration technique and assessed by "The National Committee of Clinical Laboratory Science" (NCCLS) method. It was found that methanolic extract of the plant showed major inhibition of fungal growth against *Candida parapsilosis* and *Issatchenkia Orientalis* and ethanolic extract showed significant inhibition against *Issatchenkia orientali* respectively [67].

In another study, the essential oil and various extracts of *N. sativa* were evaluated against *Trichophyton mentagrophytes*, *Microsporum canis* and *microsporun gypseum* as dermatophyte fungal strains. The antifungal activity of *N. sativa* was studied by the disk diffusion method. The result showed potent antifungal effect on *T. mentagrophytes*, *M. canis* and *M. gypseum* [68].

In another study, it was concluded that *C. cyminum*, *Z. clinopodioides* and *N. sativa* oils possess antifungal properties. The result showed inhibition in the growth of *A. fumigatus* and *A. flavus* [69].

Some researchers reported various treatments of fungal infection by using natural products. *N. sativa* was also reported for enhancing antifungal effect [70,71]. To evaluate the anti-fungal activity a micro well dilution assay was performed against three human pathogenic fungal strains that are *Aspergillus flavus*, *Aspergillus niger*, *Candida albicans* and four bacteria i.e. *Escherichia coli*, *Staphylococcus sp.*, *Pseudomonas syringae* and *Bacillus subtilis*. It was found that the methanolic extract of *N. sativa* shows maximum inhibitory potential against all the test fungi and bacteria [72].

4. Antiparasitic Activity: A study was conducted to evaluate that methanolic extract of *N.sativa* possesses the antiparasitic activity. Extract was tested on Plasmodium-infected mice to evaluate the antiparasitic activity of *N. sativa*. The result showed an excellent suppression up to 94%, $P < 0.05$ compared with chloroquine. The antimalarial activity was found in the mice because of the antioxidant effect of the extract of *N. sativa* [73,74].

N. sativa oil possesses other activities against cestodes and nematodes actions [75,76]. A recent study evaluated that oil of *N. sativa* has an excellent effect in reducing the overall number of *Schistosoma mansoni* worms in the liver and minimizing the total number of ova that was found in both the liver and intestine [77,78,79].

From the reported studies it was evaluated that *N. sativa* oil and garlic extract were possessed antischistosomal and antioxidant activity. The extract was administered to infected mice. The result showed improvement in hematological, biochemical and antioxidant capacity of schistosomiasis mice compared to the infected untreated mice [80,81]. Another study was conducted on *N. sativa* oil and thymoquinone to evaluate their effectiveness against *Sch. mansoni* in infected mice. Results showed a reduction in chromosomal abnormalities, especially in chromosomes 2 and 6, and some in chromosomes 13 and 14 when compared with the control group [82].

One more study was conducted to know the value of *N. sativa* seeds against various parasites such as *Sch. mansoni*, *mirachidia*, *cercariae*, and adult worms. The beneficial results were found against all these parasites and even in their eggs. Seeds possess antioxidative properties against adult worms which inhibited the activities of some enzymes of glucose metabolism. After few days these enzymes were damaged and parasites was found to be weaker and killed later on [83,84].

4. Wound Healing Properties:

Thymoquinone is the chemical constituent that prevents oxidative injury and membrane lipid peroxidation in tissues. These effects recommended the wound healing application of *Nigella sativa* [85,86]. A study was conducted on the wound model rats to examine the wound healing effect of *N. sativa* plant. The result has shown that it increases the wound healing process by unknown mechanism compared to silver sulfadiazine [87]

Another study was reported that hexanic extract of *N. sativa* seeds has good activity on increasing collagen formation and increasing the rate of epithelialization. In the study, hexanic extract was applied topically to examine the healing efficiency of seeds oil on the second-degree burn wound models in rats. The animal models were divided into three groups of six for every group. Silver sulfadiazine was applied as an antiseptic standard drug. The result showed 81.20% reduction in the wound area which was more than the control group. The study showed complete regeneration of epidermis on the day 12 in the rat model [88].

Abu-Al-Basal et al. investigated that ether extract of *N. sativa* seed possesses wound healing properties. Male BALB/c mice models were infected with 100 microL of *staphylococcal aureus* suspension at a dose of 10 colony-forming units in the mouse shaved mild dorsal skin. Results showed improvement in the healing process by decreasing the total and absolute white blood cell count, reducing tissue damage and decreasing bacterial expansion [89].

The *in vitro* study was conducted using a human gingival fibroblast monolayer. Aqueous extracts were evaluated for DPPH scavenging activity and the effect on HGF proliferation was determined. The result showed an increase in the rate of proliferation and closure activity was observed after using the oil [90].

5. Anti-inflammatory

5.1 Psoriasis: The ethanolic extract of *Nigella sativa* seeds was evaluated for

antipsoriatic activity. The screening of extract was done by using a mouse tail model for psoriasis. The result showed an increase in relative epidermal thickness when compared with the control group [91].

Ahmed et al., investigated the ethanolic extract of *N. sativa* to evaluate the antipsoriatic effect. Seed oil was applied in two dosage forms like ointment and oral form. Sixty patients with mild to moderate plaque and palmoplantar psoriasis were selected for this study. The result showed that an oral dose of *Nigella sativa* produced a good response in patients and possesses antipsoriatic effect [92].

5.2 Acne Vulgaris: It is one of the most widespread infections in human. Many scientific studies have been done and observed that the effect of *Nigella sativa* oil against acne vulgaris. Hadi and Ashok examined in their study that using 20% of *N. sativa* oil extract in the lotion formulation has better efficacy. 62 patients who has acne were selected for the study. Results showed *Nigella sativa* has less harmful than benzoyl peroxide lotion (the lotion used for mild to middle stage of acne vulgaris) [93]. Another study was conducted to examine *Nigella sativa* oil antibiotic effect in comparison with the standard drug amoxicillin. The gel was formulated from the oil using carbopol 940. This formulation was used as a therapy and a good result were obtained. However, *Nigella sativa* is a good herbal plant used for the treatment of skin that causes infection, irritation, rashes, dermatitis, acne and psoriasis.

6. Skin Pigmentation

6.1 Vitiligo: *Nigella sativa* oil is very effective for the treatment of various types of skin diseases such as vitiligo. The research was focused on the *Nigella sativa* oil efficiency against vitiligo. The research was held in patients suffering from vitiligo disorder. The scientist suggested putting fish oil and *Nigella sativa* oil as a therapy. The results showed a decrease in the lesion size and proved to be effective for vitiligo [94].

Another study observed that *Nigella sativa* has the power to spread melanin within the skin. The lyophilized seed extract of *Nigella sativa* was evaluated in the isolated melanophores of the wall lizard to know the mechanism of skin darkening at the cellular level. The study showed the mechanism of action that increased the intensity of melanin by increasing the sensitivity of cholinergic receptors inside the melanopsin. Melanopsin is the external part of lizard [95]. It was also observed that thymoquinone is beneficial for decreasing skin pigmentation and vitiligo.

7. Antioxidant activity: Many *in-vivo* and *in-vitro* studies have been conducted with *Nigella sativa* extracts to evaluate the antioxidant property. It was found that *Nigella sativa* and its derivatives possessed potential radical scavenging and inhibitory effects on oxidative stress [96,97,98,99]. Cherif et al., investigated the effect of dietary *Nigella sativa* seeds on meat fatty acids and evaluated oxidative activity. Twenty-eight Barbarine male lambs were selected for the study. The diet was given in two different feeding systems i.e. higher or low concentration. It was observed in the end that Thiobarbituric acid reactive substances (TBARS) were lower in the meat of lambs receiving NSS compared to the meat of lambs [100].

8. Anti-cancer Activity: Several studies have been conducted to examine the anticancer effect of *Nigella sativa*. The extract was tested in cancer cell-derived from mice. The result showed chemopreventive potential found in the thymoquinone [101,102,103]. Khalife et al., investigated that thymoquinone induced apoptosis through p53-independently with p21 and arrested cell-cycle S phase in human colon cancer cells. The active compound showed anticancer effects towards many cancer cell lines including MCF-7/Topo breast carcinoma cells and also decline regulator of NF-B and MMP-9 in Panc-1 cells and bcl-2 in gastric cancer

cells [104]. Ahmed et al., observed that a number of derivatives of thymoquinone like 6-menthoxybutyryl, 6-hencosahexanyl conjugate, 4-acylhydrazones and 6-alkyl are also potent to act against various cancer lines [105]. Periasamy et al., suggested that the Nanoemulsion of *Nigella* oil caused cell membrane blebbing, cytoplasmic vacuolation, marginalization of chromatin and fragmentation of the nucleus in MCF-7 cells [106,107,108,109,110].

9. Anti-Diabetic Effect: As per the study, the extract of *Nigella sativa* has potent anti-diabetic potential. Thymoquinone was injected in diabetic mice. The result showed a reduction in blood glucose level with augmentation of insulin level and C-peptide in models [111,112,113]. Another *in-vivo* study was conducted in the mice to evaluate the antidiabetic activity. The aqueous extract of *Nigella sativa* was administered daily in the models by gavage. It was found that extract significantly reduced the glycemia, TG, T-cholesterol, LDL-c and TBARS and possessed antihyperglycemic, antihyperlipidemic and antioxidant effect [114].

10. Effect on Nervous system: As per the study, the methanolic extract of *Nigella sativa* has antidepressant and analgesic property [115,116] and which was demonstrated by a study conducted on rat models. It was found that methanolic extract significantly increased the serotonin and reduced hydroxyindole acetic acid level in the rat brain [117].

11. Nephroprotective activity: As per the study, *Nigella sativa* in combination with ascorbic acid have a nephroprotective activity. The decoction was injected into the rabbits. It was found that decoction produced a nephroprotective effect by lowering serum creatinine, blood urea nitrogen and antioxidant activity [118,119].

12. Effects on pulmonary system: As per the study, the activity of nigellone and

thymoquinone was demonstrated by an *in-vivo* study carried out on 63 adult male rats. Models were divided into nine groups. The administration of *Nigella sativa* was found to be very effective and prevent Formaldehyde-induced apoptosis and epithelial damage [120].

13. Effects on Reproductive system: A study was conducted on Iranian infertile men with criteria of abnormal sperm count. The patient was prescribed *Nigella sativa* oil for 2 months. After 2 months it was concluded that daily intake of 5ml *Nigella sativa* oil improves abnormal semen quality in infertile men without causing any adverse effects [121,122].

The activity of *Nigella sativa* was demonstrated by *in-vivo* study carried out on a polycystic ovary rat model. Thymoquinone was found to be a potential remedy for balancing the hormonal level in the PCO rat [123].

Another study conducted in thirty male Wistar rats to investigate the adverse reproductive effects. The models were dosed with acetamiprid and *Nigella sativa* oil in combination with gavage for 45 days. The result showed stimulation in spermatogenesis and significantly increases the spermatids numbers and the weight of seminal vesicles [124].

Toxicity of the *Nigella sativa* and its derivatives

From the reported studies it was found that toxicity of fixed oil of *N. sativa* in mice after i.p. and p.o. administration that the LD₅₀ for thymoquinone was 89.7-119.7 mg/kg and 647.1-1094.8mg/kg respectively. It was found to be 45.6-69.4 mg/kg and 469.8-1118.8mg/kg in the rat after the i.p. and p.o. administered respectively [20].

CONCLUSION

Medicinal plants have been played a vital role in maintaining the health of the community since ancient times. *Nigella sativa* (kalonji) is one the most commonly used medicinal herbs in various systems of

medicine in the folk system, Ayurveda, Siddha and Yunani. This herb is associated with some significant therapeutic actions. It is utilized in the treatment of several diseases. As per the data of reported studies, thymoquinone is considered an active constituent with various biological properties like wound healing, anti-diabetic, anti-inflammatory, antidiabetic, antidepressant, nephroprotective, antibacterial, anti-viral, antifungals etc. Many clinical studies are suggesting that *Nigella sativa* possessed a wide range of benefits in skin disorders.

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