

Review article

A Review On *Nigella sativa* (Kalonji) Seeds: A Universal HealerAnjum Areefa^{1*}, Aslam Mohd², Chaudhary Shahid Shah³¹MD. Scholar, Dept of Ilmu Advia, Jamia Hamdard, India, ²Professor, Head, Dept of Ilmu Advia, Jamia Hamdard, India,³Assistant Professor, Dept of Ilmu Saidla, Jamia Hamdard, India

ABSTRACT

Nigella sativa commonly known as Black seed, Black cumin or Kalonji (Family Ranunculaceae) is a widely used for its miraculous healing power. Use of *N. sativa* seeds and oil has splendid historical past in diverse traditional systems of medicine and food. In Tibb-e-Nabwi (Prophetic Medicine), it is considered as one of the greatest forms of healing medicine. Phytochemically; it contains fixed oil, protein, alkaloids saponin and essential oil. Therapeutic properties of this plant are due to the presence of thymoquinone which is one of major active component and has different beneficial properties. In Unani System of Medicine the diseases are treated with nontoxic herbal drugs. As per Unani classical literature *N. sativa* perform various pharmacological actions like carminative, anti-inflammatory, analgesic, diuretic, emmenagogue, galactagogue, expectorant etc. Ample of phytochemical, pharmacological and clinical researches has been executed on *N. sativa*, which may include antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, bronchodilator, hepato-protective, renal protective, gastro-protective, antioxidant properties, etc. This review is an effort to summarize the literature on scientific researches of pharmacognostical characteristics, chemical composition and pharmacological activities of the kalonji seeds

Keywords *Nigella sativa* (*N. sativa*), Healing Medicine, Thymoquinone (TQ), Prophetic Medicine.

INTRODUCTION

Medicinal plants have been used for treating diseases for several decades in various indigenous and traditional systems of medicine. Among the various potential medicinal plants, *N. sativa* is a dicotyledonous miraculous herb of ranunculaceae with a strong historical and religious background (Ahmad *et al.*, 2013). The seeds of *N. sativa* are the sources of the active ingredient which have been utilized for thousand years as a spice and food preservative, as well as a defending and therapeutic remedy for several disorders (Sultana *et al.*, 2015). Historical use of *N. sativa* has been mentioned in various religious and ethnic books (Tembhure *et al.*, 2014). In Islam, it is considered as one of the greatest form of healing medicine existed as a remedy for all diseases except death in one of the saying of Prophet Muhammad It is also commended for use on consistent basis in Tibb-e-Nabwi (Prophetic Medicine) (Ahmad *et al.*, 2013; Tembure *et al.*, 2014; Paarakh, 2010). *N. sativa* seeds are identified as the curative black cumin in the holy bible; it is also described as the melanthion (little black seed) by Hippocrates and Dioscorides. In the Greco Arab/ Unani-Tibb system of medicine which construct from the work Hippocrates and others Unani physician, his contemporary Galen and Ibn- Sina has regarded *N. sativa* as a valuable remedy in hepatic and digestive

disorder. The famous book of medicine by Ibn-Sina “The cannon of medicine (980-1037) revealed historical importance of *N. sativa* as seeds that stimulates the body’s energy and help recovery from fatigue and dispiritedness” (Tembhure *et al.*, 2014; Paarakh, 2010). In ayurvedic medicine, the seeds are employed for action like astringent, bitter, stimulant, diuretic, emmenagogue, anti-helminthic and used in jaundice, intermittent fever, dyspepsia, paralysis, piles and skin diseases etc (Paarakh, 2010). The aim of current review is to emphasize the traditional uses, pharmacological investigations that has been carried out on the plant so that the therapeutic potential of the said herb can be further explored for the betterment of humanity. Further study should be performed to investigate its aptitude.

Taxonomic classification

Kingdom	Plantae
Subkingdom	Tracheobionta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales
Family	Ranunculaceae
Genus	<i>Nigella</i> L.
Species	<i>N. sativa</i>

Synonym of *N. sativa* in various languages

(Tembhure *et al.*, 2014; Dymock *et al.*, 2005; Anonymous, 1992; Satyavati *et al.*, 1987)

English: Black cumin, Love-in-a-mist, Fennel flower, Nutmeg

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flower, Damascena, Devil in the Bush; Arabic: Habatut Barakah; Shuneez; Habbat-us-sauda; Kamune-asvad; Persian: Siyadanah; Hindi: Kalonji, Kalajira; Sanskrit: Krishana – Jiraka, Upakunchika, Kaalaajaajee, Sushavee, Ajaji, Kalvanjika, Kalika; Bengali: Mungrela; Malayalam: Karun shiragani; Tamil: Karun shiragam; Telugu: Nillajila; Kannar: Karijirigi

Habitat

N. sativa is a small elegant herb, mostly attained and cultivated in India, Southern Europe, Pakistan, Syria, Turkey, Saudi Arabia and is a native of Southern Europe, North Africa and South West Asia. In India, it is found in Punjab, Himachal Pradesh, Gangetic plains, Bihar, Bengal, Assam, Maharashtra (Sultana *et al.*, 2015; Paarakh, 2010).

PHARMACOGNISTAL DESCRIPTION

Macroscopic feature of plant

It is an annual flowering plant ascending upto 30-60cm with linear-lanceolated leaves and has tap root; the flowers are white, yellow, pink or pale purple color, 5-10 petals on solitary long peduncle; sepals are ovate, acute and clawed. A fruit capsule comprise of 3-7 united follicles, each enclosing black seeds of size 0.2cm x 0.1cm are dicotyledonous, flattened, oblong, tubercular having rough testa containing white oily kernel; slightly aromatic in odor, taste bitter and takes about 10-15 days to germinate. Flowering and fruiting occur from January to April and is cultivated in dry soil in month of November till April (Forounzafar *et al.*, 2014; Phulwaria *et al.*, 2014; Ahmad *et al.*, 2013; Paarakh, 2010; Dymock *et al.*, 2005; Anonymous., 1992; Kirtikar *et al.*, 1987).

Microscopic feature of seed

Transverse section of seed demonstrate single layer of epidermis comprising of elliptical, thick-walled cells covered externally by papillose cuticle. 2-3 layers of parenchymatous cells, a reddish-brown pigmented layer composed of tangentially elongated cells, followed by rectangular, radially elongated cells. Endosperm consists of moderately thick-walled polygonal cells, numerous oil filled globules and embryo entrenched in it (Paarakh, 2010; Ahmad *et al.*, 2013; Anonymous, YNM).



Fig. A & B. Flowers and Seeds of *Nigella sativa*

UNANI DESCRIPTION

Properties

Temperament (Mizaj): Hot², Dry² (Khan, 2014; Ghani, YNM; Kabiruddin, YNM; Anonymous, 1992) Hot³, Dry³ (Ghani, YNM; Hakeem, YNM).

Taste (Maza): Slightly bitter (Khan, 2014; Kabiruddin, YNM;

Anonymous, 1992; Hakeem, YNM), Acrid in taste (Ghani, YNM)

Odour (*Boo*): Pleasant odour like a lemon (Dymock *et al.*, 2005), strong smell (Hakeem, YNM; Khan, 2014).

Adverse Effect (*Muzir*): It affect liver (Khan, 2014; Ghani, YNM), cause diphteria (Kabiruddin, YNM; Hakeem, YNM), harms kidney (Hakeem, YNM; Ghani, YNM), lungs and patient with headache (Ghani, YNM).

Main Function (*Nafa-e-Khas*): Diuretic and Emmenagogue (*Mudir-e-Baul wa Haiz*) and Jaundice (*Yarqaan*) (Kabiruddin, YNM; Hakeem, YNM), Abortifacient (Mukhrij-e-Janeen), Haemorrhoids (*Bawaseer*) (Hakeem, YNM).

Corrective (*Musleh*): *Cucumis sativus* (*Tukhme Khyaar*) (Khan.,2014; Ghani, YNM), *Sterculia urens* (*Kateera*) (Ghani, YNM; Kabiruddin, YNM; Anonymous, 1992; Hakeem, YNM), Drugs of cold temperament (*Sard Ashiyaa*) (Kabiruddin, YNM; Hakeem, YNM), *Bumusa arundinacea* (*Banslochan*) (Ghani, YNM; Anonymous, 1992), Vinegar (*Sirka*) (Ghani, YNM; Anonymous, 1992; Hakeem, YNM), *Cichorium intybus* (*Kasni*) (Ghani, YNM)

Substitute (*Badl*): *Olea europeae* (*Samaghe zaitoon*) (Khan, 2014; Ghani, YNM), *Lepidium sativum* (*Tukhme Rashaad*) (Khan, 2014; Ghani, YNM), *Pimpinella anisum* (*Anisoon*) (Kabiruddin, YNM; Khan, 2014; Ghani, YNM; Hakeem, YNM), *Anethum sowa* (*Sowa Seed*) (Khan, 2014; Hakeem, YNM), *Hyoscyamus niger* (*Ajwain Khurasani Seed*) (Ghani, YNM; Anonymous, 1992; Khan, 2014)

Important Unani formulations:

Habb-e-Hilteet, Jawarish Shoneez, Majoon Kalkalanaj (Kabiruddin, YNM; Anonymous, 1992; Anonymous, YNM); Majoon Fanjosh, Majoon Kundur (Anonymous, YNM)

Special Use of *N. sativa* by Ancient Unani Physician:

Externally:

- ♦ Jaundice (*Yarqaan*) - Use as nasal drop (*qutoor*) by mixing kalonji with mother milk (Kabiruddin, YNM; Ghani, YNM; Khan, 2014; Kirtikar *et al.*, 1987; Anonymous, YNM)
- ♦ Migraine (*Shaqeeqa*) and Chronic headache - used as nasal drop (*sauoot*) by mixing paste of kalonji in vinegar (Kabiruddin, YNM; Hakeem, YNM; Anonymous, 1992; Anonymous, YNM)
- ♦ Poison (*Samoom-e-Barida*) - Used as paste (*Zamad*); Tumours (*Sulaa*), Ptylosis (*Intishare Shaar*) - Used as liniment. (Khan, 2014)

Ayurvedic description (Satyavati *et al.*, 1987)

- ♦ Properties

Taste (*Rasa*): Bitter (*Kattu*), Pungent (*Tikta*); Properties (*Guna*): Lightness (*Laghu*), Dryness (*Rooksha*), Sharp (*Teekshna*); Potency (*Veerya*): Hot (*Ushna*).

- ♦ Action/ use-

Appetizer (*Rochana*), *Carminative* (*Deepana*), *Digestive* (*Paachana*), *Pacifier* (*Vaatakaphahara*), *Eliminate foul smell* (*Daurgandhya-naashana*), *Brass* (*Pittala*), *Nootropic drug* (*Medhya*), *Purify uterus* (*Garbhaashayashodhaka*), *Beneficial for eye* (*Chakshushya*), *Phantom tumour* (*Gulmahara*), *Decrease emesis* (*Chardihara*), *Helps in diarrhoea* (*Atisaarahara*)

(vitiated condition of vata and kapha).

Afaal (Pharmacological Action) and Mawaqae istimal (Indications)

Pharmacological Action (Afaal)	Uses (Mawaqae istimal)	Classical References	Ethnobotanical References
Expectorant (Munafis-e-Balgham)	Asthma (<i>Zeequn Nafas</i>) Pleural Effusion (<i>Zatul Janab</i>) Cold (<i>Nazla</i>) and Cough (<i>Sual</i>) Chest pain (<i>Dard e Sadar</i>)	Kabiruddin, YNM; Ghani, YNM Khan, 2014 Hakeem, YNM	Kirtikar <i>et al.</i> , 1987 Anonymous, YNM
Phlegmatic diseases (Balgami Amraz)	Externally: Corynza (<i>Zukaam</i>)- snuffing of roast seed or as nasal drop by mixing its powder with olive oil Internally: Cold (<i>Nazla</i>) and Cough (<i>Saul</i>)	Kabiruddin, YNM Ghani, YNM Khan, 2014	Dymock <i>et al.</i> , 2005 Anonymous, 1992
Anti-flatulence (<i>Muhallil e Riyah</i>)	Flatulence (<i>Nafkhe Shikam</i>) Colic (<i>Qoolinj Reehi</i>) Stomachache (<i>Dard-e-Shikam</i>)	Kabiruddin, YNM Khan, 2014 Hakeem, YNM Ghani, YNM	Kirtikar <i>et al.</i> , 1987 Anonymous, YNM Anonymous, 1992
Stomach tonic (<i>Muqawwi-e-Meda</i>)	Weakening of Stomach (<i>Zauf-e-meda</i>)	Kabiruddin, YNM	Anonymous, YNM Dymock <i>et al.</i> , 2005
Laxative (<i>Mulaiyin</i>) and Purgative (<i>Mushil</i>)	Chronic constipation (<i>Qabz Daimi</i>)	Kabiruddin, YNM	Kirtikar <i>et al.</i> , 1987
Liver tonic (<i>Muqawwi-e-Jigar</i>)	Weakening of liver (<i>Zauf-e-Jigar</i>), Jaundice (<i>Yarqaan</i>), Hepatitis (<i>Warm-e-Jigar</i>)	Khan, 2014	
Antihelminthic (<i>Qatil-e-Kirmu-shikam</i>)	Helminthiasis (<i>Kirm-e-Shikam</i>)	Kabiruddin, YNM Khan, 2014 Hakeem, YNM	Kirtikar <i>et al.</i> , 1987 Dymock <i>et al.</i> , 2005 Anonymous, YNM
Emmenagogue (<i>Mudir-e-Haiz</i>)	Amenorrhoea (<i>Ehtebaas-e-Haiz</i>)	Kabiruddin, YNM Ghani, YNM Hakeem, YNM Khan, 2014	Anonymous, 1992 Dymock <i>et al.</i> , 2005 Kirtikar <i>et al.</i> , 1987 Anonymous, YNM
Diuretic (<i>Mudir-e-Baul</i>)	Dysuria (<i>Ushrul Baul</i>) Kidney and Bladder stone (<i>Hisate Kuliya wa Masana</i>)-Paste of kalonji when used with honey help in excretion of stones from kidney and bladder Renal colic (<i>Waj'a ul Gurda</i>)	Ghani, YNM Hakeem, YNM	Dymock <i>et al.</i> , 2005 Kirtikar <i>et al.</i> , 1987
Galactagogue (<i>Mudir-e-Labn</i>)	Increase Lactation (<i>Idra-e-Sheer</i>)-Intake of kalonji for longer time helpful in increasing maternal milk	Ghani, YNM Khan, 2014	Anonymous, 1992 Dymock <i>et al.</i> , 2005 Kirtikar <i>et al.</i> , 1987
Analgesic (<i>Musakkin-e-Alam</i>)	Renal colic (<i>Waj'a ul-Gurda</i>) Backache (<i>Dard e kamar</i>) Dysmenorrhoea (<i>Ushr ul Tams</i>) Pain in uterus (<i>Waj'a ul Reham</i>) Headache (<i>Sudaa</i>)	Kabiruddin, YNM Khan, 2014	Anonymous, YNM
Detergent (<i>Jali</i>) (Externally)	Scald (<i>Bahek</i>), Vitiligo (<i>Bars</i>), Tinea (<i>Da'ad</i>), Alopecia (<i>Da-us-salab</i>), Acne (<i>Basoorlabn</i>)-used as liniment by using kalonji alone or by mixing with vinegar along with appropriate drug.	Kabiruddin, YNM Khan, 2014	Anonymous, 1992 Dymock <i>et al.</i> , 2005 Anonymous, YNM
Styptic (<i>Habis e Dam</i>) (Externally)	Externally: Haemorrhage (<i>Jiryaa-e-Dam</i>), Hemorrhoids (<i>Bawaseer</i>)	Kabiruddin, YNM Hakeem, YNM	
Coctive (<i>Munzif</i>) and Desiccative (<i>Mujaffif</i>)	Wound healing (<i>Mudammil-e-qurooh</i>), Ascites (<i>Istisqaa</i>)	Ghani, YNM Hakeem, YNM Khan, 2014	Anonymous, 1992
Nervine tonic (<i>Muqawwi-e-Asaab</i>)	Externally: Paralysis (<i>Falij</i>) - massage with kalonji oil, Bell's palsy (<i>Laqwa</i>) -massage with kalonji oil, Tetnus (<i>Kuzaz</i>)	Kabiruddin, YNM; Khan, 2014	Kirtikar <i>et al.</i> , 1987 Anonymous, YNM
Abortifacient (<i>Musqit-e-Janeen</i>)- in high dose	Abortion (<i>Istiqrar-e-Hamal</i>)		Anonymous, 1992 Dymock <i>et al.</i> , 2005
Anti-inflammatory (<i>Muhallil-e-awram</i>)	Arthritis (<i>Waj'a ul-mufasil</i>)	Kabiruddin, YNM Hakeem, YNM	Anonymous, 1992 Anonymous, YNM
Emetic (<i>Muqui</i>)	Nausea (<i>Gisyaan</i>) & Vomiting (<i>Qai</i>)	Khan, 2014	

Rubefacient (<i>Mushakhin</i>)	Baldness (<i>Sa'afa</i>) - mix kalonji with oil, wax and is apply on bald portion of head. Ringworm (<i>Qooba</i>) - used as liniment by mixing it with vinegar.	Khan, 2014 Kabiruddin, YNM	
Antipyretic (<i>Da'afae Humma</i>)	Tertian Fever		Kirtikar <i>et al.</i> , 1987
Anti-microbial (<i>Qatil-e-Jaraseem</i>)	Externally : Scald (<i>Bahak</i>), Scabies (<i>Jarb</i>) - used as liniment by making a paste with seed and vinegar and mix it with rose oil. Ringworm (<i>Qooba</i>) - used as liniment by mixing it with vinegar.	Khan, 2014 Kabiruddin, YNM	

PHYTOCHEMICAL STUDY OF *N. sativa*

Extensive phytochemical studies has been done to isolate and identify the chemical composition of *N. sativa*. Seeds include 36 to 28% fixed oil, proteins, alkaloid, saponin and 0.4 to 2.5% essential oil (Forouzanfar *et al.*, 2014; Tembhrne *et al.*, 2014). Pharmacological properties of black cummin is mainly due to presence of Thymoquinone (TQ). Important active volatile constituents of *N. sativa* are thymoquinone (30%-48%), thymohydroquinone, dithymoquinone, nigellone that is the only component of the carbonyl fraction of the oil (Ahmad *et al.*, 2013), α and β -pinene, d-limonene, d-citronellol, p-cymene and thymol (Forouzanfar *et al.*, 2014). Other component present in it are p-cymene (7%-15%), carvacrol (6%-12%), 4-terpineol (2%-7%), t-anethol (1%-4%), sesquiterpene longifolene (1%-8%) (Ahmad *et al.*, 2013; Tembhrne *et al.*, 2014).

Seeds contain two different types of alkaloids i.e. isoquinoline alkaloids e.g. nigellicimine and nigellicimine-N-oxide and pyrazol alkaloids or indazole ring bearing alkaloids which include nigellidine and nigellicine. Moreover, it also contain alpha-hederin, a water soluble pentacyclic triterpene and saponin, a potential anticancer agent (Sultana *et al.*, 2015; Ahmad *et al.*, 2013). Flavonoids present in seed are quercetin and kaempferol 3-glucosyl (1-2) galactosyl (1-2) glucoside and quercetin-3-(6-feruloyl glucosyl) (1-2) galactosyl (1-2) glucoside (Merfort *et al.*, 1997). Other than those triglycoside quercetin 3-glucoside, kaempferol 3-glucoside and rutin were also isolated from the seeds of *N. sativa* (Tembhrne *et al.*, 2014). The nutritional component of seeds contain protein (26.7%), fat (28.5%), carbohydrates (24.9%), crude fibre (8.4%) and total ash (4.8 %), vitamins and minerals like potassium, phosphorus, sodium, iron are main element and Copper, Magnesium, Manganese. Zinc and Calcium found at low levels (Al-Jassir, 1992; Sultana *et al.*, 2015). The seeds contain carotene which is

converted by the liver to vitamin A. Root and shoot are reported to contain vanillic acid (Ahmad *et al.*, 2013).

The fixed oil comprise of unsaturated fatty acids which includes: arachidonic, eicosadienoic (3%), linoleic (50-60%), linolenic, oleic (20%) (Sultana *et al.*, 2015) and saturated fatty acid comprise of palmitic (12.5%), stearic and myristic acid (Tembhrne *et al.*, 2014; Nickavara *et al.*, 2003). Beta-sitosterol, cycloartenol, sterol esters and sterol glucosides are also found (Forouzanfar *et al.*, 2104). α -sitosterol is a major sterol, which accounts for 44% and 54% of the total sterols in Tunisian and Iranian varieties of *N. sativa* oils, pursued by stigmasterol (6.57-20.92% of total sterols) (Sultana *et al.*, 2015).

Numerous chemical components reported are nigellone, avenasterol-5-ene, nigellone, nigellicine, nigellimine, nigellimine-N-oxide, avenasterol-7-ene, campesterol, cholesterol, citrostadienol, lophenol, obtusifoliol, stigmastanol, stigmasterol-7-ene, β -amyrin, butyro- spermol, cycloartenol, 24-methylene-cycloartanol, taraxerol, tirucallol, 3-O- $[\beta$ -D-xylopyranosyl(1 \rightarrow 3)- α -L-rhamnopyranosyl(1 \rightarrow 2)- α -L-arabinopyranosyl]-28-O- $[\alpha$ -L-rhamnopyranosyl(1 \rightarrow 4)- β -D-glucopyranosyl(1 \rightarrow 6)- β -D-gluco-pyranosyl] hederagenin, volatile oil (0.5-1.6%), fatty oil (35.6-41.6%), oleic acid, esters of unsaturated fatty acids with C-15 and higher terpenoids, esters of dehydrostearic and linoleic acid, aliphatic alcohol, melanthin, melanthigenin, bitter principle, tannin, resin, protein, reducing sugar, glycosidal saponin, 3-O- $[\beta$ -D-xylopyranosyl-(1 \rightarrow 2)- α -L-rhamno-pyranosyl-(1 \rightarrow 2)- β -D-glucopyranosyl]-11-methoxy-16, 23-dihydroxy-28-methyl-olean-12-enoate, stigma-5, 22-dien-3- β -D-gluco-pyranoside, cycloart-23-methyl-7, 20, 22- triene-3 β , 25-diol, nigellidine-4-O-sulfite, N. mines A3, A4, A5, C, N. mines A1, A2, B1, and B2 (Sultana *et al.*, 2015; Ahmad *et al.*, 2013; Paarakh *et al.*, 2010).

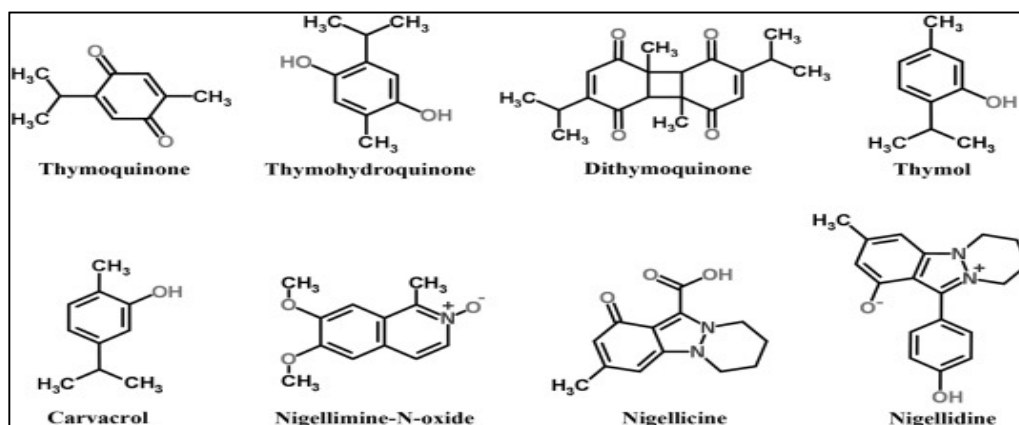


Fig. c Chemical Constituents Of *Nigella sativa*

ETHANOPHARMACOLOGICAL USES OF *N. sativa*

Traditionally seed of *N. sativa* are used in middle-eastern folk medicine for treating several diseases for more than 2000 years (Forouzanfar *et al.*, 2014). There is extensive historical description of folklore usage of *N. sativa* seeds and their oil in Indian and Arabian civilization as food and medicine (Ahmad *et al.*, 2013). The seeds were used as pungent appetizer, aromatic, thermogenic, diuretic, expectorant, purgative, anthelmintic, emmenagogue, antibacterial, anti-inflammatory, anodyne, febrifuge, galactagogue stimulant, sudoriferous, sedative and carminative (Sala, 1997). It is used for treatment of wide range of disease conditions related to respiratory system, digestive tract, kidney and liver function, cardiovascular system, skin care, fertility and immune system as well as for general health (Ahmad *et al.*, 2013; Aklaque, 2018; Phulwaria, 2018). Roasted seeds are given internally to stop the vomiting (Ahmad *et al.*, 2013; Sultana *et al.*, 2015).

In Indian and Arabian system of medicine, seeds are used for skin diseases, jaundice, gastrointestinal problems, anorexia,

conjunctivitis, diarrhea, dyspepsia, rheumatism, diabetes, hemorrhoids, helminthiasis, hypertension, halitosis, intrinsic hemorrhage, paralysis, amenorrhea, dysmenorrhea anorexia, asthma, cough, bronchitis, headache, fever, influenza and eczema (Forouzanfar *et al.*, 2014; Sala, 1997; Kirtikar, 1987). It is also traditionally used by Iranian therapists as a treatment for mastalgia (Aklaque, 2018).

In case of skin eruptions, seeds powder are mixed with sesame oil for local application (Kirtikar, 1987). Externally the oil is used as an antiseptic and local anesthetic. Due to its countless uses nigella has earned the Arabic approbation of 'Habbat ul Barakah', meaning the seed of blessing (Ahmad *et al.*, 2013; Phulwaria, 2018).

It is generally used to increase lactation in nursing mothers, to fight against parasitic infections, and to boost their immune system. Since they have very low level of toxicity seeds are also used in food like flavoring additive in the breads and pickles (Sultana *et al.*, 2015).

Pharmacological Activity	Conclusion of the study	References
Antibacterial activity	<ul style="list-style-type: none"> Antibacterial effect against G +ve and G -ve bacteria is shown by various crude extract of <i>N. sativa</i> seed, essential oil and due to presence of Thymoquinone (TQ), Thymohydroquinone and Melanin. Ethanol extract of <i>N. sativa</i> seed, oil, Thymoquinone and Carvacrol exhibit antibacterial and resistant modifying activity against Mithicilin Resistant <i>Staphylococcus aureus</i> and <i>Listeria monocytogens</i> respectively. Furthermore, <i>N. sativa</i> oil alone shows this activity against <i>Mycoplasma mycoides subsp mycoides</i> and <i>Schistosoma mansoni</i>. Methanolic, ethanolic and aqueous extract of <i>N. sativa</i> work against gallbladder and infantile septicemia pathogen. 	Bakathir <i>et al.</i> , 2011 Chaieb <i>et al.</i> , 2011 Mechraoui <i>et al.</i> , 2018 Reddy <i>et al.</i> , 2018 Hosseinzadeh <i>et al.</i> , 2007 Salem <i>et al.</i> , 2010 Mouwakeh <i>et al.</i> , 2019 Halawani, 2009 Morsi, 2000 Hannan <i>et al.</i> , 2008 Mouwaekh <i>et al.</i> , 2018 Onsa <i>et al.</i> , 2019 Abououf <i>et al.</i> , 2018 Shah <i>et al.</i> , 2018
Antifungal activity	<ul style="list-style-type: none"> Methanolic extracts, chloroform extracts and bioactive compound like Quinines, Dithymoquinone, Thymohydroquinone, and Thymoquinone of <i>N. sativa</i> and nano-particulated drugs-<i>Amphotericin-B</i>, <i>Ketoconazole</i> and <i>Thymoquinone</i> have the strongest antifungal effect against different strains of <i>Candida albicans</i> and dairy spoilage yeast specie and their biofilm respectively. Antidermatophyte activity of essential oil, various extract of <i>N. sativa</i> and Thymoquinone was tested against eight species of dermatophytes like <i>T. mentagrophytes</i>, <i>M. canis</i> and <i>M. gypseum</i> etc. Two antifungal defensins named Ns-D1 and Ns-D2 isolated from its seeds displayed antifungal activity towards phytopathogenic fungi. Fractioned methanolic extract and essential oil of <i>N. sativa</i> against <i>F. oxysporum</i>, <i>M. phaseolina</i> and <i>Aspergillus</i> species respectively show complete inhibition of the fungal biomass production. 	Khan <i>et al.</i> , 2003 Halamova <i>et al.</i> , 2010 Randhawa <i>et al.</i> , 2015 Aljabre <i>et al.</i> , 2005 Mahmoudvand, 2014 Rogozhin <i>et al.</i> , 2011 Aftab <i>et al.</i> , 2019 Khosravi, 2011
Anti-schistosomiasis activity	<ul style="list-style-type: none"> The effect of <i>Nigella sativa</i> Oil (NSO) and Anti-schistosomal activities of the Garlic Extract (AGE) against the liver damage induced by <i>Schistosoma mansoni</i> infection in mice shows its strong biocidal effects against all stages of the parasite and an inhibitory effect on egg laying of female worms. AGE and NSO prevent most of the hematological and biochemical changes and markedly improved the antioxidant capacity of schistosomiasis mice and disturbing the antioxidant enzymes of adult worms using <i>N. sativa</i> seeds play a role in the anti-schistosomal potency. 	Mohamed <i>et al.</i> , 2005 El Shenawy <i>et al.</i> , 2008
Antioxidant activity	<ul style="list-style-type: none"> TQ and methanolic extract of seed shows significant antioxidant activity along with anti-inflammatory, anticancer, antibacterial and antiarthritic activity in vivo and in vitro. Extract of <i>N. sativa</i> and <i>C. angustifolia</i> exhibit potential anti-oxidant activity. TQ also suppress the Fe-NTA-induced oxidative stress, and renal carcinogenesis in rats. 	Umar <i>et al.</i> , 2012 Bourgou <i>et al.</i> , 2012 Khan <i>et al.</i> , 2005 Mariod <i>et al.</i> , 2009 Reddy <i>et al.</i> , 2018 Al-Othmanetal., 2006 Gendy <i>et al.</i> , 2007

	<ul style="list-style-type: none"> • Dietary supplementation of its powder inhibits the oxidative stress alone thus very helpful in a patient of ulcerative colitis and hepatocarcinogens induced rats. • The <i>N. sativa</i> oil, its hydroalcoholic extract and TQ have protective effects on oxidative enzymes during ischemia-reperfusion injury (IRI) and play beneficial role in cerebrovascular insufficiency state and alter the oxidative activity in rat model. • Broiler chicks was treated with seed for 6 weeks prevented the liver from oxidative stress. • Pretreatment with TQ in colon carcinogenesis of Wistar rat have modulatory effect on erythrocyte lipid peroxidation and antioxidant status. <i>N. sativa</i> suppress the oxidative stress and enzyme activity induced by Nanoparticle (Cu and CdS). 	<p>Bodaghi <i>et al.</i>, 2019 Hosseinzadeh <i>et al.</i>, 2007 Fanoudi <i>et al.</i>, 2019 Sogut <i>et al.</i>, 2008 Harzallah <i>et al.</i>, 2012 Kumbhakara <i>et al.</i>, 2019</p>
Antidiabetic activity	<ul style="list-style-type: none"> • The therapeutic potentials of α-lipoic acid (α-LA), L-carnitine or <i>N. sativa</i> combinedly contribute significant reduce in the elevated blood glucose level in diabetic rats. • <i>N. sativa</i> seeds, its extract, oil and TQ show significant reduce in the elevated blood glucose level, it emphasizes on glucose-induced secretion of insulin, preserve pancreatic β-cell integrity and altered carbohydrate metabolic enzymes activity were restored to normal. It also show synergistic effect with human parathyroid hormone. Its extract is capable of producing insulin producing cell. • Clinically <i>N. sativa</i> oil shows effective adjuvant effect on the patient of insulin resistance syndrome and use of oil also decrease Fasting Blood Glucose and increase insulin levels in diabetic rats. Oral dose of 2 gm/day of its seed is a beneficial adjuvant to oral hypoglycemic agents in type 2 diabetic patients. • The in vivo antidiabetic activity of ethanolic extract <i>N. sativa</i> seed in diabetic Merionesshawi demonstrate insulin-sensitizing action by AMPK signaling pathway and by enhancing muscle Glut4 (Glucose transporter type4) content. • <i>N. sativa</i> and propolis methanol extract, <i>N. sativa</i> and <i>Cinnamomum cassia</i> and methanolic Extract of <i>N. sativa</i> and <i>Brassica alba</i> seeds exhibit its combinatorial antidiabetic capability. • The antihyperglycemic effect of <i>N. sativa</i> oil was more effective than <i>N. sativa</i> powder in reduction of glycemic status. It was observed that <i>N. sativa</i> seed reduced the higher blood glucose level and revealed overexpression to CAT, GST and Bcl2 (B-cell Lymphoma) genes and also to SOD, GPX and IGF-1 (Insulin like growth factor-1) by higher quantitative PCR in diabetic rats. • Furthermore use of <i>N. sativa</i> has been shown to increase the activity of rat parotid gland for insulin and glucagon that was markedly diminished with advance of age there by decreasing the incidence of diabetes. • Thymoquinone(TQ) nano-capsules (actually containing half of the doses of thymoquinone) produced better antihyperglycemic effect in type-2 diabetic rats as compared to thymoquinone alone. 	<p>Salama., 2015 Kanter <i>et al.</i>, 2009 Kapoor., 2009 Andaloussi <i>et al.</i>, 2008 Younus., 2018 Pari <i>et al.</i>, 2009 Altan <i>et al.</i>, 2007 Najmi <i>et al.</i>, 2008 Ranjbaran <i>et al.</i>, 2018 Abdelrazek <i>et al.</i>, 2018 Bamosa <i>et al.</i>, 2010 Andaloussi <i>et al.</i>, 2011 Rabey <i>et al.</i>, 2017 Kaur <i>et al.</i>, 2018 Arefin <i>et al.</i>, 2018 Askari <i>et al.</i>, 2019 Althnaian <i>et al.</i>, 2019 Kamal <i>et al.</i>, 2012 Rani <i>et al.</i>, 2018</p>
Anticancer activity	<ul style="list-style-type: none"> • TQ has a beneficial effect in conditioning T cells in vitro for adoptive T-cell therapy against cancer and infectious disease. <i>N. sativa</i> seed and extracts has cytotoxic effect in human breast cancer cells. • TQ and ethanolic extract of <i>N. sativa</i> has antitumor and anti-angiogenic effects. • TQ was cytotoxic towards human cervical squamous carcinoma cells which was determined by MTT assay and trypan blue dye exclusion test. • TQ exert antiproliferative effect in breast cancer cells and gastric cancer cell. TQ isolated from extract of <i>N. sativa</i> and <i>Thymus vulgaris</i> exerts a dose-dependent anti-proliferative effect on HeLa cancer cells. • <i>N. sativa</i> oil administration exerts potent inhibitory effects on rat tumor development and on cellular proliferation in multiple organ sites with no evidence of clinical side effects. • The aqueous extract of <i>N. sativa</i> significantly enhances splenocyte proliferation and NK (Natural Killer cell) cytotoxic activity against tumor cells. • TQ exerts antimetastatic activity on pancreatic cancer both in vitro and in vivo. <i>N. sativa</i> nano emulsion reduced the cell viability against human liver carcinoma cells. 	<p>Salem <i>et al.</i>, 2011 Mahmoud <i>et al.</i>, 2012 Shafi <i>et al.</i>, 2008 Peng <i>et al.</i>, 2013 Fathy <i>et al.</i>, 2018 Ng <i>et al.</i>, 2011 Woo <i>et al.</i>, 2011 Lei <i>et al.</i>, 2012 Butt <i>et al.</i>, 2019 Salim <i>et al.</i>, 2010 Majdalweih <i>et al.</i>, 2010 Wu <i>et al.</i>, 2011 Torres <i>et al.</i>, 2010 Tabassum <i>et al.</i>, 2019</p>
Immunomodulatory activity	<ul style="list-style-type: none"> • The potential immunomodulatory effects of aqueous extract, methanolic extract and volatile oil of <i>N. sativa</i> seed boost splenocyte proliferation, enhance WBC count, suppress primary macrophage and enhances NK cytotoxic activity against tumor cells and lethal infections. 	<p>Majdalaweih <i>et al.</i>, 2010 Ghonime <i>et al.</i>, 2011 Torres <i>et al.</i>, 2010 Abel-Salam., 2012 Mohamed <i>et al.</i>, 2009 Assayed., 2010</p>

	<ul style="list-style-type: none"> It has immunomodulatory activity in prophylactic treatment of opportunistic infections and as supportive treatment. When seed are co-administered with Oxytetracycline produce immunostimulant effect in pigeon. TQ is 90% preventive in experimental autoimmune encephalomyelitis and 50% curative in chronic relapsing due to its antioxidant effect. <i>N. sativa</i> oil is radioprotective agent against immunosuppressive and oxidative effects of ionizing radiation. Extract of <i>N. sativa</i> show potential immunomodulation effect on lung inflammation of ova-albumin sensitized guinea pigs and significantly improves symptoms and immune parameters in murine OVA-induced allergic diarrhea. 	<p>Boskabady <i>et al.</i>, 2011 Duncker <i>et al.</i>, 2012</p>
Anti-inflammatory and Analgesic activity	<ul style="list-style-type: none"> The aqueous extract of <i>N. sativa</i> was found to possess anti-inflammatory and analgesic activity. Extract of <i>N. sativa</i> and TQ significantly reduced pancreatic ductal adenocarcinoma (PDA) cell synthesis. TQ has an anti-inflammatory effect during the allergic response in the lung by inhibiting immune response. The shoots, roots and seeds methanol extracts of <i>N. sativa</i> has antioxidant, anti-inflammatory, anticancer and antibacterial activities. <i>N. sativa</i> oil reduces allergic rhinitis. It is also could be used for prevention and for asthma therapy. 	<p>Alemi <i>et al.</i>, 2012 Al-Ghamdi., 2001 Chehl <i>et al.</i>, 2009 El-Mezayen <i>et al.</i>, 2006 Pichette <i>et al.</i>, 2012 Nikakhlagh <i>et al.</i>, 2011 Ikhsan <i>et al.</i>, 2018</p>
Cardiovascular activity	<ul style="list-style-type: none"> TQ prevents decrease in platelet numbers and prothrombotic events and has cardio protective effect. Pretreatment with <i>N. sativa</i> oil reduces heart injury, normalizes cardiac histopathology, improve antioxidant enzyme status and cellular protein oxidation. <i>N. sativa</i> protect against hypertension-induced tissue damage and enhance cardiovascular function by its antioxidant and antihypertensive effects. 	<p>Nemmar <i>et al.</i>, 2011 Nagi <i>et al.</i>, 2011 Ebru <i>et al.</i>, 2008 Tasar <i>et al.</i>, 2012</p>
Gastro-protective activity	<ul style="list-style-type: none"> TQ has gastroprotective mechanisms via inhibiting proton pump, acid secretion and neutrophil infiltration, while enhancing mucin secretion, and nitric oxide production. It has anti-ulcer effect which is either prostaglandin-mediated or through its antioxidant and anti-secretory activities. <i>N. sativa</i> Oil and TQ possess gastroprotective effect against gastric lesions. TQ protects gastric mucosa against the ulcerating effect of alcohol and alleviate most of the biochemical harmful effects induced by alcohol in gastric mucosa. It can prevent and improve induced colitis and is also used for treating inflammatory bowel disease. <i>N. sativa</i> Oil significantly reduces the severity of intestinal damage in necrotizing enterocolitis. 	<p>Magdy <i>et al.</i>, 2012 Al Mofleh <i>et al.</i>, 2008 El-Abhar <i>et al.</i>, 2003 Khaled, 2009 Lei <i>et al.</i>, 2012 Tayman <i>et al.</i>, 2012</p>
Hepato-protective activity	<ul style="list-style-type: none"> <i>N. sativa</i> intraperitoneally relieves the adverse effects of ischemia reperfusion injury on liver. <i>N. sativa</i> protects hepatic tissue from harmful effects of toxic metals and reduce hepatic lipid peroxidation. TQ has modulatory influence on the antioxidant defense system and it also act as hepatoprotective by prevention of SOD suppression mediated by paraquat. <i>N. sativa</i> hydroalcoholic extract improves liver function during neonatal and juvenile growth. 	<p>Yildiz <i>et al.</i>, 2008 Kapoor., 2009 Zafeeret al., 2012 Lorestani <i>et al.</i>, 2018 Hosseinia <i>et al.</i>, 2018</p>
Nephroprotective activity	<ul style="list-style-type: none"> Vitamin C and <i>N. sativa</i> oil when given in combination have synergistic nephroprotective effect. TQ synergizes with its nephroprotective effect against cisplatin-induced and Gentamicin induced acute kidney injury by preventing degenerative changes in renal tissues of rats. <i>N. sativa</i> oil has protective effect in methotrexate-induced and Gentamicin induced nephrotoxicity. It also protects renal tissue against oxygen free radicals, precluding renal dysfunction and morphological abnormalities related to cyclosporin an administration. <i>N. sativa</i> also has protective effect against renal injury. It hinder the toxic effects of Gentamicin both in the biochemical and histopathological parameters. Therapeutic administration of <i>N. sativa</i> reduces the toxic effects of paracetamol on kidneys by preventing oxidative stress changes. <i>N. sativa</i> extract has antioxidant and anti-inflammatory effect and it also act as therapeutic agent to treat unilateral ureteral obstruction induced kidney damage. 	<p>Saleem <i>et al.</i>, 2012 Ulu <i>et al.</i>, 2012 Sayed-Ahmad <i>et al.</i>, 2007 Abul-Nasr <i>et al.</i>, 2001 Ali, 2004 Uz <i>et al.</i>, 2008 Yildiz <i>et al.</i>, 2010 Yaman <i>et al.</i>, 2010 Hadjzadeh <i>et al.</i>, 2012 Canayakin <i>et al.</i>, 2016 Hosseinian <i>et al.</i>, 2018</p>
Pulmonary-protective activity and anti-asthmatic effects	<ul style="list-style-type: none"> Nigellone possess anti-spasmodic effect and is useful in treatment of different respiratory diseases. 	<p>Wienkotter <i>et al.</i>, 2008 Boskabady <i>et al.</i>, 2008 Hossein <i>et al.</i>, 2008</p>

	<ul style="list-style-type: none"> ♦ Methanol and dichloromethane fraction of <i>N. sativa</i> have relaxant effect on pre contracted tracheal chains. ♦ <i>N. sativa</i> has protective effect on tracheal responsiveness and lung inflammation which was exposed sulfur mustard gas in guinea pigs. It is useful in lung injury and in clinical use. ♦ <i>N. sativa</i> oil reduces severity of lung damage due to hyperoxia. ♦ <i>N. sativa</i> has prophylactic effect on asthma disease and has anti-asthmatic effect on asthmatic airways although boiled extract has less effect than theophylline. 	Kanter, 2009 Tayman <i>et al.</i> , 2012 Boskabady <i>et al.</i> , 2007 Boskabady <i>et al.</i> , 2010
Anti-osteoporotic activity	<ul style="list-style-type: none"> ♦ <i>N. sativa</i> and TQ were shown to inhibit inflammatory cytokines such as interleukin-1 and 6 and the transcription factor, nuclear factor κB. Both NS and TQ have shown potential as anti-osteoporotic agent. 	Shuid <i>et al.</i> , 2012
Testicular-protective activity	<ul style="list-style-type: none"> ♦ TQ decrease the destructive effects of methotrexate on testicular tissue of patients. 	Gokce <i>et al.</i> , 2011
Neuro-pharmacological activities	<ul style="list-style-type: none"> ♦ The aqueous and methanol extracts of defatted <i>N. sativa</i> L. seeds were shown to hold a potent anti-depressant and analgesic activities. ♦ Long term administration of <i>N. sativa</i> enhance learning and memory. Its oil and TQ is used for treatment of anxiety. ♦ <i>N. sativa</i> oil appears to have a therapeutic potential in tramadol tolerance and dependence. ♦ Aqueous and hydroalcoholic extracts of <i>N. sativa</i> have neuroprotective effects in cerebral ischemia. ♦ <i>N. sativa</i> supplementation improves Pb-induced neurotoxicity and antioxidant potentials. ♦ TQ has protective activity against chemotherapy-induced neurotoxicity. 	AL-Naggar <i>et al.</i> , 2003 Perveen <i>et al.</i> , 2008 Perveen <i>et al.</i> , 2009 Gilhotra <i>et al.</i> , 2011 Abdel-Zaher <i>et al.</i> , 2011 Akhtar <i>et al.</i> , 2012 Butt <i>et al.</i> , 2018 Ustuna <i>et al.</i> , 2018
Anticonvulsant activity	<ul style="list-style-type: none"> ♦ Curcumin and <i>N. sativa</i> oil has anti- convulsant and antioxidative effect by reducing oxidative stress, excitability and the induction of seizures in epileptic animals and it also recovers from some of the adverse effects of antiepileptic drugs. ♦ Aqueous extract, fixed oil, volatile oil of <i>N. sativa</i> seeds and. TQ has antiepileptic effect when pass through maximal electroshock (MES)-induced convulsions and minimal neurological deficit (MND) test. 	Ezz <i>et al.</i> , 2011 Raza <i>et al.</i> , 2008
Contraceptive and anti-fertility activity	<ul style="list-style-type: none"> ♦ Hexane extract and ethanolic extract of <i>N. sativa</i> seeds exhibit antifertility activity due to its inherent estrogenic activity 	Keshri <i>et al.</i> , 1995 Agarwal <i>et al.</i> , 1990
Anti-oxytocic activity	<ul style="list-style-type: none"> ♦ <i>N. sativa</i> seeds and oil helps in inhibition of smooth muscle contraction of uterus induced by oxytocin stimulations and has anti- oxytocic effect. 	Aqel <i>et al.</i> , 1996
Toxicological studies	<ul style="list-style-type: none"> ♦ The low toxicity of <i>N. sativa</i> fixed oil has wide margin of safety for therapeutic doses. ♦ TQ is a safe compound, particularly when given orally to experimental animals. 	Zaoui <i>et al.</i> , 2002 Al-Ali <i>et al.</i> , 2008 Khader <i>et al.</i> , 2009

CONCLUSION

There is a prevalent use of herbal drug as traditional medicine and is gaining global popularity. One of them is *N. sativa* which have been used since antiquity as a natural therapy for various diseases and also their use were stated in Bible, *Tibb-e-Nabwi*, Cannon of Medicine and Ayurvedic literature. A lot of studies validate its significance in folk medicine as antihypertensive, anti-inflammatory, immune stimulant, analgesic, anti-microbial, anti-fungal, anti-oxidant, and as an anti-cancer. Further work can be desired to discover the pharmacokinetics, biochemical and therapeutic activities of active constituents and their collaboration with modern drugs. Cellular and molecular target of various constituent of *N. sativa* seed may be explored to get more effective and safer drug. Further thorough Clinical studies on *N. sativa* should be done so that humanity can be benefited.

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CONFLICT OF INTEREST

No conflict of interest is involved in writing of this article

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