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THERAPEUTICS, PHYTOCHEMISTRY AND PHARMACOLOGY OF AN IMPORTANT UNANI DRUG KALONJI (*NIGELLA SATIVA* LINN): A REVIEW

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ABSTRACT

The seed of *Nigella sativa*, Linn is known as *Kalonji*. The plant *Nigella sativa* is a short-lived, aromatic, annual herb. It is an amazing herb with a rich historical and religious background. The height of the plant is approximately 20-60 cm. The seeds are angular, of generally small size. They are black or dark gray with a rough grooved surface and an oily white interior. The seeds are the source of active ingredients of this plant. The seeds have an immense medicinal value and are known to have numerous medicinal properties. They are also used for flavouring and seasoning bread, pickles, and bakery products. It is among widely used seeds and has been employed either as a medicinal grain or as a food ingredient in several countries. The plant has shown diverse biological and pharmacological activities. It has been used in Unani Medicine (*Tibb-e-Unani*) and other Traditional Systems of Medicine from time immemorial. Keeping in view the medicinal importance of the drug in Unani Medicine, an attempt has been made to review the available literature on traditional uses and pharmacological properties of the plant.

***KEYWORDS*:** *Nigella sativa, Kalonji.*

INTRODUCTION

Kalonji is a famous plant drug used in a number of pathological conditions. It is scientifically known as *Nigella sativa* Linn (F - Ranunculaceae). Among the promising medicinal plants, *Nigella sativa* Linn, is an amazing herb with a rich historical and religious background (Goreja, 2003). Although the entire plant has medicinal value but its seed and seeds oil has more important and interesting medicinal values. Its different parts are used after little processing as a single and compound drug. It is a bushy, self-branching plant with white or pale to dark blue flowers. It reproduces with itself and forms a fruit capsule which consists of many white trigonal seeds. Once the fruit capsule has matured, it opens up and the seeds contained within are exposed to the air, becoming black in colour (Schleicher & Saleh, 1998). Historically, it has been recorded that the seeds of the plant were prescribed by ancient Egyptian and Greek physicians to treat headache, nasal congestion, toothache, nasal congestion, toothache, and intestinal worms, as well as a diuretic to promote menstruation and increase milk production (Goreja, 2003; El-Dakhakhny, 1965). The seeds of the plant are the source of active ingredients of this plant. It is the black seed referred to by the prophet Mohammad (SAWS) as having healing powers (Goreja, 2003). Prophet Mohammad (SAWS), himself used to take these seeds with the syrup of honey for therapeutic purpose (Ghaznavi, 1991). An authentic saying of the prophet Mohammad (SAWS) about black seed is also quoted in Al-Bukhari: Abu Huraira (RA) narrated that Rasulullah (SAWS) said "Use the black seed, which is a healing for all diseases except As-Sam" and As-Sam is death (Al-Bukhari, 1976). This black seed is also identified as the curative black cumin in the Holy Bible and is described as the Melanthion of Hippocrates and Discroides and as the Gith of Pliny (Junemann, 1998). The seeds are angular, of generally small size (1-5 mg). Possessing health promoting benefits, black cumin seed is among widely used seeds and has been employed either as a medicinal grain or as a food ingredient in several countries (Rouhi *et al*., 2012). The seeds have an immense medicinal value and are known to have numerous medicinal properties, mainly in Unani and Ayurveda systems of medicine (Abdulelah & Zainal-Abidin, 2007). *Kalonji* has been used by millions of people in Southeast Asia, the Middle East and Africa to improve general health and fight various diseases (Malhotra, 2006; Ramadan, 2007). It is used in food and medicine in many countries including Egypt, India, Iran, Pakistan, Saudi Arabia and Syria. It is widely used in conventional medicine for curing a variety of respiratory and gastrointestinal ailments in the entire Islamic world

(Riaz *et al*., 1996). The seeds are also used for flavouring and seasoning bread, pickles, and bakery products (Ramadan & Morsel, 2002). The fatty oil obtained from the expression of the seeds is reported to be used for edible purposes (Anonymous, 1966). Two type of oil is derived from the seed: one is black coloured volatile oil while the other is white and viscous like Caster oil (Najmul Ghani, 2011).

Nigella sativa is an annual aromatic plant native to Southwest Asia and the Mediterranean region. Its cultivation has been traced back more than 3,000 years to the kingdom of the Assyrians and ancient Egyptians (Khan, 2009). Presently, it is cultivated in various parts of the world, including Asia, the Middle East and North Africa (Rabbani *et al*. 2011). It is widely cultivated throughout South Europe, Syria, Egypt, Saudi Arabia, Turkey, Iran, Pakistan and India (Riaz *et al.*, 1996). It is also cultivated in Lebanon and Israel. In India, the plant is distributed all over country but mostly found and cultivated in Punjab, Himachal Pradesh, Gangetic Plains, Bihar, Bengal, Assam and Maharashtra (Paarakh, 2010).

The plant *Nigella sativa* is a short-lived annual, herbaceous plant. The height of the plant is approximately 20-60 cm. It possesses grayish green linear leaves that are wispy and thread like (Muschler, 1912; Khan, 1999; Ahmad & Ghafoor, 2007). They are 2- 3 pinnatisect, 2.5- 5.0 cm long, cut into linear or linear-lancelate segments. Flowering and fruiting occurs from March to May (Anonymous, 1992). The flowers are delicate, pale blue or white, with a variable number of sepals and 5-10 petals that are about 2.5 cm wide (Muschler, 1912; Khan, 1999; Ahmad & Ghafoor, 2007). They are terminal, peduncled, sometimes within an involucres or bracts. There are 5 sepals that are regular, deciduous, petaloid, imbricate (Chatterjee & Pakrashi, 2005). They are ovate acute and clawed. It also contains 8 nectarial petals, geniculate, with a saccate gland in the knee, one on the face and one on the apex of each lobe (Kirtikar & Basu, 1991). Numerous stamens are also found (Chatterjee and Pakrashi, 2005). Carpels are 5-7 in number, inflated, watery at the sides, united at the top; beak as long as the ovary (Kirtikar & Basu, 1991). The fruit is large and inflated, with 3-7 integrated follicles, each one with numerous seeds. The seeds are normally small (1-5 mm long), black or dark gray with a rough grooved surface and an oily white interior (Khan, 1999; D'Antuono *el al*., 2002; Benkaci-Ali *et al*., 2007). They are roughly triangular and possess a strongly pungent smell. They contain about 21% protein, 35% carbohydrate and 35-38% plant fats and oils (Ahmad & Ghafoor, 2007). The seeds are small dicotyledonous, trigonus, angular, rugulose-tubercular, 2-3.5 × 1-2 mm; odour slightly aromatic and taste bitter (Duthie, 1960; Rajsekhar & Kuldeep, 2011). Transverse section of seed shows single layered epidermis consisting of elliptical, thick cells, covered externally by a papillose cuticle and filled with dark brawn contents. Epidermis is followed by 2-4 layers of thick walled tangentially elongated parenchymatous cells, followed by reddish brown pigmented layer composed of thick walled, rectangular elongated cells. Inner to the pigment layer, is present a layer composed of thick walled rectangular elongated or nearly columnar, elongated. Endosperm consists of thin walled, rectangular or polygonal cells mostly filled with oil globules. The powder microscopy of seed powder shows brownish black, parenchymatous cells and oil globules (Khan *et al*., 1979; Mitra, 1985).

Flowering and fruiting occur from January to April. It is generally cultivated on dry soil between November to April and seeds take about 10-15 days to germinate. It can also be propagated from the callus culture *in vitro* from leaf, stem and root explants from aseptically grown seedlings (Rajsekhar & Kuldeep, 2011). The fruit when attain maturity, are trimmed from the plant dried and then crushed to separate the seeds. The seeds collected are further dried, garbled and packed in airtight containers. They are then stored in cold and dry place totally free from moisture (Anonymous, 1992).

Vernaculars

The plant is known by different vernacular names in different language, areas and traditions: *Shewadaru, Siyahdaru* (Afganistan); *Habbatussuda* (Arabic); *Kalijira, Kalzira, Mungrela* (Bengal); *Kalonji* (Bombay); *Samonne* (Burma); *Kare jirage, Karijirigi, Karimsiragam* (Canarese); *Kulanjan* (Deccan); *Hubsindee* (Egypt); Black cumin, Nutmeg Flower, Small Fennel (English); *Shuniz, Siyah dana, Shunoz* (Farsi); *Cumin noir, Faux cumin, Gith, Nielle de Crete, Nielle romaine, Nigelle Cultivee, Nigelle romaine* (French); *Schwarzkuemmel, Gemeiner Schwarzkuemmel, Roemischer Schwarzkuemmel* (German); *Kalonji-jirum* (Gujrati); *Qesah* (Hebrew); *Kamoon, Kalonji, Magrela, kala dana, kala jaji, Mangrela, krishan jirak* (Hindi); *Cinnamonea, Cuminella, Erbaspezie* (Italian); *Karejirage* (Kanad); *Karijirigi* (Kannar); *Tukmigandana* (Kashmir); *Ku sheng* (Malaya); *karunchirakam, karunshiragam* (Malayalam); *Kalaunji jire* (Marathi); *Shuniz, Siahdanah, Siyahbiranj* (Persian); *Tchernushka* (Russian); *Kunchi, Bashpika, Kalajaji, Karava, Krishnajiraka, Kunchika, Kunjika, Musavi, Prathvika, prithvi, Prithu, Prithuka, Sthulajiraka, Sushavi, Upakunchiraka, Upakuncika, Karavi, Krsnajiraka* (Sanskrit); *Kalodi* (Sindhi); *Karun jiragam, Karun Shiragam, Karum ciragam* (Tamil); *Nellajeelakaira, Nullajilakara* (Telgu); *Qura chorak Aodi* (Turkey); *Sheenu, Sinu* (Unani); *Kalonji* (Urdu) (Anonymous, 1966; Anonymous, 1992; Bhandari, 2014; Ibn Baitar, 1999; Kabiruddin, YNM; Kirtikar & Basu, 1991; Lubhaya, 1984; Najmul Ghani, 2011; Prajapati, 2003; Usmani, 2008).

***Mizaj* (Temperament)**

Some Unani physicians described the temperament of *Kalonj* as Hot and Dry in second degree (Najmul Ghani, 2011; Kabiruddin, YNM). While the others categorized it

as Hot and Dry in third degree (Ibn Baitar, 1999; Ibn Sina, 1992).

***Afa'al* (Action)**
In classical Unani literature, various actions of the plant *kalonji* (*Nigella sativa*) have been described in details such as *Mukhrij-e-sang-e-gurda wa masana*, *Musakkin-e-alam*, *Dafe dard dandan*, *Tiryaq-e- zahar sard*, *Dafe humma*. Oil- *Muqawwi bah wa muqawwi aasab* (Abdul Hakim, 1999); *Munaffis-e-balgham*, *Muhallil wa Kasir-e-riyah*, *Muqawwi-e-meda*, *Mulayyan*, *Qatil kiram-e-shikam*, *Musakkin-e-awja* (Lubhaya, 1984; Kabiruddin, YNM); *Mudir-e-bol*, *Mudir-e-haiz*, *Mudirr-e-sheer*, *Mukhrij-e-janeen*, *Mohallil-e-awram*, *Mukhrij deedan-e-shikam*, *Jali*, *Jazib*, *Munzij* (Najmul Ghani, 2011); *Muqawwi-e-dimag*, *Muqawwi-e-asab* (Ansari, 2009); *Mufatteh-e-sudad*, *Muqawwi-e-jigar*, *Habis khoon nifas* (Khan, 1313H).

***Istemal* (Uses)**
Kalonji has been described to be useful in various diseases such as *Bawasir*, *Yarqaan*, *Sardi*, *Zukam*, *Sua'al*, *Dard-e-seena*, *Matli*, *Istisqa*, *Qaulanj reehi*, *Facial fairness*, *Sang-e-gurda wa masana*, *Laqwa*, *Nazul-ul-ma*, *Dard-e-sar*, *Wajaul mafasil*, *Daad*, *Kharish* (Abdul Hakim, 1999); *Ihtabas-e-tams*, *Dama*, *Qillat-e-laban* (Ibn Baitar, 1999); *Zoaf-e-dimag*, *Nisyan* (Ansari, 2009); *Nafakh-e-shikam*, *Dard-e-shikam* (Syed, 1993); *Dard-e-kamar*, *Amraz-e-balghami* (Lubhaya, 1984); *Deedan-e-ama'a*, *Waja-ul qutn*, *Ziqun nafas*, *Bars*, *Baheque*, *Sa'afa*, *Daus salab*, *Basur-e-labniya* (Usmani, 2008); *Falij*, *Khidar*, *Ra'sha*, *Kuzak*, *Sura'a* (Khan, 313H).

Kalonji acts as abortifacient; when used as decoction abort live or died foetus. Its oral administration, in form of powder in a dose of 5 ratti to 1.25 masha, relieves the dysmenorrhea (Najmul Ghani, 2011) and regulates the menses in amenorrhea (Ali, 1993). It is used along with ghee to glow the facial skin. *Nigella* seeds in a dose of 7-10 gm with water have beneficial effect in dog bite. Instillation of mixture of 7 seeds powder of *Kalonji* along with women's milk, in nostrils is very effective for the patient suffering from jaundice. The chronic headache and shaqiqua are relieved by instillation of *Nigella* powder with vinegar into nostrils (Lubhaya, 1984). Instillation of its powder with olive oil cures the allergic rhinitis. Paste of *Nigella* seeds with wax or oil is useful for alopecia (Najmul Ghani, 2011). Instillation of its powder with oil of Iris ensata (Irsa) cures the *Ibtedai Nazulul ma'a* (cataract) (Ibn Baitar, 1999; Ibn Sina, 1992). It is most power full brain tonic; used in dementia and memory loss (Ansari, 2009). The powder of *kalonji* in a dose of 2 gm with honey cures the neuralgic disorders (Ali, 1993). It is used with watery curd or honey in patients suffering from hiccup (Ibn Sina, 1992; Lubhaya, 1984). Its local use as a *tila* (painting) with vinegar cures the *Bars*, *Bahaque*, *Da'ad*, *Sa'afa*, *Da-us salab* and *Basure labniya* (Usmani, 2008). The paste of kalonji along with vinegar is applied on abdomen to kill the intestinal worm (*Kaddu dana*) and on wart to remove it (Najmul Ghani, 2011). It is locally applied along with vinegar on *Awram-e-balghami* to resolve and *Qoruh* to heal. It is administered per oral in Hummiyat-e-balghamiya wa saudavia (Ibn Sina, 1992). The *Kalonji* grinded in water and mixed with honey is used as a syrup to excrete the renal and bladder stone along with urine. The ash of *Kalonji* is used to shed of the *masse* of piles as an oral and local application. Seeds are scattered between folds of woolen clothes to preserve them against insect attack. Geelani stated that it cures the sour belching, which is due to *Balgham* and *Sauda*. It acts as galactogouge when used for a long time in lactating mothers. Chewing of *Kalonji* cures the bad odour of mouth (Najmul Ghani, 2011). It relieves joint pain, headache, leucoderma, and scabies on its local application (Abdul Hakim, 1999). *Kalonji* oil is used orally along with olive oil to cure impotency and infertility. Its local application increases the libido. Its massage relieved the weakness and pain of thigh muscles. Oral and local administration oil is useful in *Falij*, *Khidra*, *Rasha* and *Kozaz* (Najmul Ghani, 2011).

***Muzir* (Adverse effect)**
Kalonji leads to diphtheria and unconsciousness when used in a large dose. It has adverse effect of kidney, organs of urinary system, lungs, liver and causes headache (Najmul Ghani, 2011).

***Musleh* (Corrective)**
Kateera / *Bansalochan* / *Kasni* / *Tukhm-e-Khayar* are used as corrective. It may also be corrected by mixing with vinegar or water of *Kasni* / *Khurfa* (Najmul Ghani, 2011).

Pharmacological Actions
(As described in Ethnobotanical and traditional literature)
The drug *Nigella sativa* is described in detail in ethnobotanical and scientific literature and various actions have been reported to possess by it. Some pharmacological actions and therapeutic uses are as follows:
Seeds are diuretic, carminative, emmenagogue, stimulant (Anonymous, 1966), digestive, aromatic, anthelmintic, (Nadkarni, 1954), thermogenic, anti-inflammatory, deodorant, appetizer, sudorific, febrifuge, expectorant, anodyne, constipating, galactogogue (Prajapati *et al*., 2003). It also acts as diaphoretic, anti-bilious, stomachic. Its oil is locally applied as anaesthetic (Nadkarni, 1954). The seeds are lactiferous, stimulant uterine contraction (Chatterjee & Pakrashi, 2005); abortifacient (Kirtikar and Basu, 1991); sternutatory (Lindley, 1984). They also possess some other activities such as analgesic, antihistaminic, anti-allergic, anti-oxidant, anti-cancer, immune stimulation, anti-asthmatic, antihypertensive, hypoglycemic, anti-bacterial, antifungal, anti-viral and anti-parasitic (Randhawa, 2008). Kalonji seeds and / or their extracts have antidiabetic (Fararh *et al*., 2002), antihistaminic, antihypertensive, anti-inflammatory

(Hajhashemi *et al*., 2004), antimicrobial, antitumour (Khan *et al*., 2003) and insect repellent effects (Fisher, 2002). The clinical and animal studies shows that the extracts of black seed have many therapeutic effects such as bronchodilator and immunomodilative (El-Kadi & Kandil, 1987), antibacterial (Hanafy & Hatem, 1991; Prajapati *et al*., 2003), hypotensive, (Zaoui *et al*., 2000), hepatoprotective and antidiabetic (Panahi *et al*., 2011).

Therapeutic uses

The seeds of *Nigella sativa* have long been used in folk medicine in the Middle and Far East as a traditional medicine for a wide range of illness, including bronchial asthma, headache, dysentery, infections, obesity, back pain, hypertension and gastrointestinal problems (Schleicher & Saleh, 1998; Al-Rowais, 2002). Its use in skin condition as eczema has also been recognized worldwide (Goreja, 2003). Externally, the seeds can be ground to a powder, mixed with a little flour as a binder, and applied directly to abscesses, nasal ulcers, orchitis and rheumatism (Salem, 2005). Kalonji has been used for a variety of conditions related to respiratory health, stomach and intestinal complaints, kidney and liver function, circulatory and immune system support and rheumatism and associated inflammatory diseases (Malhotra, 2006; Ramadan, 2007). The seeds are also utilized for enhancing milk production in nursing mothers, promoting digestion and fighting parasitic infections (Rabbani *et al*., 2011). The seeds are given with butter milk to cure obstinate hiccup and employed as a corrective of purgatives and other medicines. They are useful in indigestion, loss of appetite, fever, diarrhea, dropsy, and puerperal diseases. They have a decided action as a galactagogue; a decoction of the seeds is given to recently delivered females in combination with a few other medicines; it also stimulates uterine contractions. They are useful in dysmenorrhoea and amenorrhoea and in large doses cause abortion. Seeds form a very useful remedy in worms. With sweet oil the decoction forms a useful application in skin diseases. The seeds fried, bruised, tied in muslin bag and smelt relieve cold and catarrh of the nose by constant inhalation. Seeds are also used in scorpion sting. A confection known as Jawarish-e-Kamooni is used in diarrhea, indigestion, dyspepsia and sour belching; it removes foul breath and watering from mouth (Nadkarni, 1954). The application of seeds is good in lung complaints, cough and jaundice, both internally and externally. Its use is also good in hydrophobia, ascites, tertian fever, paralysis and for eye-sores. It is a good adjunct as a purgative and for piles (Kirtikar and Basu, 1991). The seeds are useful in skin diseases, cephalalgia, jaundice, inflammatory fever, paralysis, halitosis, anorexia, dyspepsia, flatulence, diarrhea, dysentery, cough, amenorrhoea, dysmenorrhoea, helminthiasis especially tape worms, intermittent fever, and agalactia (Prajapati *et al*., 2003). The seeds are used in treatment of mild cases of puerperal fever (Anonymous, 1966). They reduced to powder also mixed with sesamum oil much used as an external application in eruptions of skin, for scorpion sting (Chopra *et al*., 1956). They are also recommended in menstrual troubles. Essential oil from seeds is used in common cold and coughs (Chatterjee and Pakrashi, 2005). Inhalation of its volatile oil is useful to treat chronic colds. It is useful in paralysis, facial palsy, migraine, amnesia and palpitations. The oil of *Kalonji* is effective in treating skin conditions like eczema and boils. The oil of the seeds is also effective for treating earaches (Khan, 1999; D'Antuono *et al*., 2002; Iqbal *et al*., 2011). The crude oil and thymoquinone (TQ) extracted from kalonji seeds and oil are effective against many diseases like cancer, cardiovascular complications, diabetes, asthma, kidney disease etc. it is effective against cancer in blood system, lung, kidney, liver, prostate, breast, cervix, skin with much safety (Khan *et al*., 2011).

Phyto-chemistry

Very little phytochemical work has been carried out on *Nigella sativa*. The plant contains more than 100 valuable elements. It is an important source of protein, essential fatty acids and various vitamins such as A, B, B_2, C and niacin. It also contains minerals like calcium, iron, magnesium, potassium, selenium and zinc (Rabbani *et al*., 2011). The seeds contain about 21% protein, 35% carbohydrate and 35-38% plant fats and oils (Ahmad & Ghafoor, 2007; Rabbani et al, 2011). Beside the volatile and fatty oils, black cumin seeds contain a bitter principle (nigellin), tannins, resin, reducing sugar (mostly glucose), saponins and arabic acids and other alcohol-soluble organic acids. The free amino acids present in dormant seeds are cystine, lysine, aspartic acid, glutamic acid, alanine, tryptophan, voline and leucine: asparagine is not present. An amorphous saponin ($C_{20}H_{32}0_7$, m.p. 310°) which on hydrolysis yields a yellow phenol ($C_{14}H_{22}O_2$, m.p. 275°) and glucose, and a toxic saponin, melanthin, which gives on hydrolysis melanthigenin ($C_{30}H_{48}O_4$, m.p. above 325°, probably identical with hederagenin) are also identified. A lipase is also seen in the seeds (Anonymous, 1966).

The seed have been reported to yield ester of unsaturated fatty acids with C_{15} (ester of dehydrostearic and linoleic acid) and higher terpenoids, carvone, d-limonene, cymene, nigellone, thymol, citronellyl acetate, (+) citronellol, aliphatic alcohols, and α, β-unsaturated hydroxyl ketones, alkaloids, steroids and gederagenin glycoside, α-hederin (a triterpene saponin), thymoquinone, dithymoquinone, thymohydroquinone (Chatterjee & Pakrashi, 2005). The seeds contain a yellowish volatile oil 1.5 % and a fixed oil 37.5 %, albumen, sugar, mucilage, organic acids, metarbin, toxic glucoside, melanthin resembling helleborin, ash 5 %, moisture and arabic acid. Volatile oil is the active constituent. It consists of (1) Carvone 45-60%, an unsaturated ketone, (2) terpene or d-limonene called cervene and (3) Cymene (Nadkarni, 1954). A new isoquinoline alkaloid nigelllimine N-oxide; an alkaloid nigellicine were isolated from seeds. A saponin isolated from seeds and characterized as 3-O-[*β*-D-

xylopyranosyl(1→3)-α-L-rhamnopyranosyl(1→2)-α-Larabinopyranosyl]-28-O-[α-L-ahamnopyranosyl] (1→4)-*β*-D-glucopyranosyl(1→6)-*β*-D-glucopyranosyl]-hederagenin (Rastogi & Mehrotra, 1993, Vol. IV).

The seeds are reported to contain nigellidine (Rahman, 1995), carvone, d-limonene, cymene, α, β-unsaturated hydroxyl ketone, steroids, hederagenin glycoside, melanthin, melanthigenin, bitter principle, tannin, resin, protein, reducing sugar, glycosidal saponin, 3-O-[β-D-xylopyranosyl(1→2)-α-L-rhamnopyranosyl(1→2)-β-D-glucopyranosyl]-11-methoxy-16, 23-dihydroxy-28-methylolean-12-enoate, stigma-5,22-dien-3-β-D-glucopyranoside, cycloart-23-methyl-7,20,22-triene-3β,25-diol, nigelliidine-4-O-sulfite (Ali *el* al., 2008), nigellamines A3, A4, A5, C (Morikawa *el* al., 2004), nigellamines A1, A2, B1 and B2 (Morikawa *el* al., 2004). The seed contains esters of dehydrostearic and linoleic acid with sesqui and higher terpenoids and aliphatic alcohol, an unidentified α, β-unsaturated hydroxyketone (Sharma *et al*., 2005; Rastogi & Mehrotra, 1993, Vol. III). Nigellone isolated from essential oil (Rastogi & Mehrotra, 1993, Vol.I). Cholesterol, campesterol, stigmasterol, *β*-sitosterol and α-spinasterol isolated from seed oil (Rastogi & Mehrotra, 1993, Vol. II). Various molecules such as avenasterol-5-ene, avenasterol-7-ene, campesterol, cholesterol, citrostadienol, cycloeucalenol, 24-ethyllophenol, gramisterol, lophenol, 24-methyllophenol, obtusifoliol, sitosterol, stigmastanol, stigmasterol, stigmasterol-7-ene, *β*-amyrin, butyrospermol, cycloartenol, 24-methylene-cycloartanol, taraxerol, tirucallol and arachidic, linoleic, linolenic, myristic, oleic, palmitic, palmitoleic and stearic acids are isolated from seed oil (Rastogi & Mehrotra, 1993, Vol. IV).

Fixed oil contains linoleic acid (55.6%), oleic acid (23.4%) and palmitic acid (12.5%). Volatile oil contains trans-anethole (38.3%), p-cymene (14.8%), limonene (4.3%), and carvone (4.0%) (Nickavar *et al*., 2003), 2-(2-methoxypropyl)-5-methyl-1, 4-benzenediol, thymol and carvacrol (Enomoto *et al*., 2001).

The essential oil of the seeds contain (+) Limonene, p-cymene, citronellyl acetate, carvone and (+) citronellol (Rastogi & Mehrotra, 1993, Vol. III). The component glycerides of the seed oil are trilinolein, oleodilinolein, dieleolinolein, palmitol-oleo-linolein and stearo-oleolinlein (Prajapati *et al*., 2003). Leaves: leaves contain ascorbic acid (257.70 mg/100 g.) and dehydroascorbic acid (29.5 mg / 100 g) (Anonymous, 1966). Root and shoot are reported to contain vanillic acid (Bourgou *et al*., 2008).

Analysis of black cumin seed gave the important values such as: total ash, 3.8- 5.3; ash insol in HCL, 0.0-0.5; volatile oil, 0.5 - 1.6; ether extract (fatty acid), 35.6 - 41.6; and alcoholic acidity (as oleic acid), 3.4 - 6.3 %. The seeds give on stea-distillation a yellowish brown volatile oil with an unpleasant odour. It has the following characteristics: $d^{15°}$, 0.875 - 0.886 ; n^{20}_{D} , 1.4836-1.4844 ; $[\alpha]_{D}$, + 1.43° to +2.86 °; acid val., up to 1.9; ester val., 1-31.6; ester val. after acetylation, 15-73; sol. in2 - 4.5 or more volume of 90% alcohol (Anonymous, 1966).

Pharmacological Studies

A number of studies have been carried out on *Nigella sativa* Linn in recent years showing that it possesses diverse pharmacological effects. Some of the important pharmacological effects are as follows:

Abortifacient

A clinical study reveals that hot water extract of *Nigella sativa* as well as whole seeds in large oral doses cause abortion in human pregnant females (Malhi & Trivedi, 1972; Oommachan & Khan, 1981).

Analgesic and Anti inflammatory

Ethanolic extract of *Nigella sativa* seeds given intraperitoneally caused significant analgesic effect on nociceptive response initiated by 0.6% acetic acid; although this analgesic effect was less than that produced by diclofenac sodium (Bashir & Qureshi, 2010). Thymoquinone is reported to inhibit the generation of thromboxane A2 and leukotriene B4, thus suggesting an inhibitory effect on both the cyclo-oxygenase and lipo-oxygenase pathway (El-Dakhakhny *et al*., 2002).

The analgesic activity of black seed was assessed by using acetic acid induced writhing, formalin and light tail flick tests. Anti-inflammatory activity was evaluated using carrageenan-induced paw oedema in rats and croton oil induced ear edema in mice. Black cumin seed essential oil was found to produce a significant analgesic effect in acetic acid-induced writhing, formalin and light tail flick test. Intraperitoneal injection of the same doses significantly inhibited carrageenan-induced paw oedema (Hajhashemi *et al*., 2004).

A study was carried out to evaluate anti-inflammatory and antioxidant properties of *Nigella sativa* oil in patients with rheumatoid arthritis. The study reveals that it could improve inflammation and reduce oxidative stress in patients with rheumatoid arthritis. It is suggested that *Nigella sativa* may be a beneficial adjunct therapy in this population of patients (Hadi *et al*., 2014).

The anti-inflammatory effect of thymoquinone on arthritis in rat model was investigated. Sign of inflammation on the claw and radiological signs were searched for and TNF-α and IL-1β were measured. The results showed that thymoquinone suppressed adjuvant-induces arthritis in rats (Tekeoglu *et al*., 2006; Tekeoglu *et al*., 2007).

The analgesic and anti-inflammatory effects of polyphenols from seed were evaluated in mice and rats using the acetic acid-induced writhing, formalin, light tail flick, carragenan-induced paw edema and croton oil-induced ear edema models. The findings suggest that

Nigella sativa seed polyphenol have potent analgesic and anti-inflammatory effects (Ghannadi et al., 2005).

Nigella sativa seed essential oil was found to produce a significant analgesic effect in acetic acid-induced writhing, formalin and light tail flick tests. The mechanism other than opioid receptor is involved in the analgesic effect since naloxone could not reserve this effect. Both systemic and local administration of Nigella seed essential oil showed anti-inflammatory activity (Hajhashemi *et al.*, 2004).

The *in vitro* aqueous extract of *Nigella sativa* seeds was studied on nitric oxide production by murine macrophages. The results indicate that the extract exhibits an inhibitory effect on nitric oxide production by murine macrophages. This study validates the traditional use of seeds for the management of rheumatism (Mahmood *et al*., 2003).

The antiinflammatory and analgesic effects of aqueous extract of *Nigella sativa* was investigated in animal models. The antiinflammatory effect was demonstrated by its inhibitory effect on carrageenan induced paw edema. It also produced significant increase in the hot plate reaction time in mice indicating analgesic effect (Al-Ghamdi, 2001).

Anthelmintic

The anthelmintic activity of *Nigella sativa* was evaluated against intestinal nematodes of sheep via egg hatch assay and faecal egg counts reduction test *in vitro* and *in* vivo, respectively. The study showed that *Nigella sativa* seed extracts possess anthelmintic activity, thus justifying their use in traditional and veterinary practices (Al-Shaibani *et al*., 2008).

Anti-asthmatic

A study was carried out to investigate the potential effect of thymoquinone, seed constituent of *Nigella sativa*, on airway-induced hypersensitivity. The results showed that thymoquinone possesses marked anti-allergic and anti-asthmatic activity and may have beneficial effects in the prevention or treatment of many allergic diseases (Abd-el-Aziz *et al*., 2011).

Anti cancer

Thymoquinone shows promising *in vitro* and *in vivo* antineoplastic growth inhibition against various tumour cell lines and inhibitory activity on cancer cell growth and its capability for inducing apoptosis (Gali-Muhtasib *et al*., 2004).

Thymoquinone also exhibited antineoplastic activities in prostate cancer cells have now been evidenced that the compound effectively blocks G1-phase prostate cancer cells from entering the S phase and thus may prove to be useful in treating prostate cancer, particularly in hormone refractory cases (Kaseb *et al*., 2007).

Anticonvulsant

Intracerebroventricular injection of thymoquinone at doses of 200 and 400 µm prolonged the time until onset and reduce the duration of tonic-clonic seizures in pentylenetetrazol induced epileptic seizures. The results indicate that thymoquinone may have anticonvulsant activity, probably through an opioid receptor-mediated increase in GABAergic tone (Hosseinzadeh *et al.*, 2005).

The investigation of anticonvulsant and antioxidant activities of *Nigella sativa* oil on pentylenetetrazol (PTZ) kindling seizures in mice were carried out. The result shows that *Nigella sativa* oil possesses anti-epileptogenic properties as it reduces the sensitivity of kindled mice to the convulsion and lethal effects of PTZ induces oxidative injury in the brain (Ilhan *et al*., 2005).

Antiepileptic

A study was carried out to evaluate the anticonvulsant and antioxidant activities if *Nigella sativa* oil on pentyleneterazol kindling seizures in mice. It significantly decreased the oxidative injury in the mouse brain tissue. *Nigella sativa* oil showed anti-epileptogenic properties as it reduced the sensitivity of kindled mice to the convulsive and lethal effects of pentyleneterazol (Ilhan *et al*., 2005).

Antifungal

Few studies have been conducted for the antifungal effect of *Nigella sativa*. The ether extract of *Nigella sativa* seed and its derivative, thymoquinone, were found to inhibit some opportunistic fungi: *Aspergillus niger*, *Fusarium solani* and *Scopulariopsis brevicaulis* and many species of three important genera of dermatophytes: *Trichophyton*, *Epidemophyton* and *Microsporum*, isolated from the clinical cases (Aljabre *et al*., 2005; Randhawa *et al*., 2005; Aljabre, 2005).

A study was carried out to test the effect of an aqueous extract of *Nigella sativa* seeds on candidiasis in mice. These results indicate that the aqueous extract of seeds exhibits inhibitory effect against candidiasis (Khan *et al*., 2003).

Antifungal activities of the *Nigella sativa* seeds oil were tested against twenty fungi including pathogenic and industrial strains. The result reveals that all the oil have significant activities against the fungi, but the volatile oil showed stronger and wider range of antifungal activities (Islam *et al*., 1989).

Antimicrobial

Antimicrobial activity of extracts of *Nigella sativa* seeds was evaluated against three Gram positive i.e. *Bacillis subtalis*, *Entereococcus faecalis*, *Staphylococcus aureus* and two Gram negative microorganisms i.e. *Pseudomonas aeruginosa*, *Salmonella typhi*. Methanolic, hot water and cold water extracts of this plant was taken for antimicrobial assay through disc agar diffusion technique using commercial filter paper disc applied on

inoculated Muellar Hilton agar plates. Based on the results obtained in this study, it may be concluded that plant extracts have a stronger and broader spectrum of antimicrobial activity against a number of food borne bacteria and the extracts may be used to discover bioactive natural products that may serve as a basic source for the development of new antimicrobial compounds to overcome the problem of increasing resistance to known traditional antibiotics (Khalid *et al*., 2011).

Similarly, considering the development of resistance against the presently available antibiotics for *Helicobacter pylori*, a clinical trial was conducted to investigate the activity of *Nigella sativa* seed for the eradication of *H. pylori* in non-ulcer dyspeptic patients and found to possess anti *H. pylori* activity comparable to the standard triple therapy (Randhawa, 2008).

The data obtained from an antimicrobial study of black seed oil shows that it is a high antimicrobial activity against gram-positive bacteria and yeasts, but has no sporicidal activity. Thus, the use of oil as flavouring agent in food and as antiseptic agent in topical pharmaceutical preparations can be recommended (Toama *et al*., 1974).

The antimicrobial activity has been evaluated by using disc diffusion method. The results of the antimicrobial activity of *Nigella sativa* oil were compared with the standard and accordingly, the efficacy of volatile oil was far better than the standard (Gerige *et al*., 2009).

The *Nigella sativa* seed essential oil obtained by hydrodistillation, dry steam distillation, steam distillation of crude oils obtained by solvent extraction and supercritical fluid extraction were tested for their antibacterial activities. All oil samples were significantly more active against Gram-positive than against Gram negative bacteria (Kokoska *et al*., 2008).

The ethanol extract of seeds has inhibited the growth of Methicillin resistant *Staphylococcus aureus* at a concentration of 4 mg/disc with an MIC range of 0.2- 0.5 mg/ml (Hannan *et al*., 2008). The methanol extract of seed was found to exhibit anti-plaque action by inhibiting *Streptococcus mutants*, thus preventing dental caries (Namba *et al.*, 1985). Alcoholic extract showed antibacterial activity against *Micrococcus pyogenes* var. aureus, *Shigella dysenteriae, S. sonnei, S. boydii, Vibrio Cholerae* and *E. coli* (Ferdous *et al*., 1992). In another study, it was found to be exhibit antibacterial activity against *Bacillus pumilus, B. subilis, Streptococcus mutants, Staphylococcus aureus, S. lutea* and *P. aeruginosa* (El-Kamali *et al*., 1998).

Antinociceptive

Antinociceptive effect of watery suspension of *Nigella sativa* seeds was evaluated by formalin test in which the stimulus is standardized and measures potency and duration of response. *Nigella sativa* significantly inhibited the behavioral changes caused by acute nociceptive stimuli (hot plate, early phase and late phase of formalin test). The results suggest that watery suspension of *Nigella sativa* seeds induced antinociceptive is due to an inhibitory effect of this seeds on the nociceptive systems and / or inflammatory mediators. This may implicate an opioid activity of *Nigella sative* seeds constituents particularly thymoquinone (Al-Shebani and Al-Tahan, 2009).

An experimental study was carried out to examine the antinociceptive effects of *Nigella sativa* oil and thymoquinone in mice. The administration of Nigella sativa oil (50-400 mg/kg) by oral route suppressed the nociceptive response in the hot-plate test, tail-pinch test, and acetic acid-induced writhing test and in the early phase of the formalin test in a dose dependent manner (Abdel-Fattah *et al.*, 2000).

Antioxidant

The possible antioxidant activity of essential oil of *Nigella sativa* was evaluated by diphenylpicrylhydracyl assay. A rapid evaluation for antioxidants, using two TLC screening methods, showed that thymoquinone and the components carvacrol, amethole and 4-terpineol demonstrated respectable radical scavenging property (Burits & Bucar, 2000).

The free radical scavenging effects of thymol, thymoquinone and dithymoquinone were studied on reaction generating reactive oxygen species such as superoxide anion radical, hydroxyl radical and singlet oxygen using chemiluminescence and spectrophotometric methods (Kruk *et al*., 2000).

Antioxytocic

A study was carried out to evaluate the efficacy of the volatile oil of *Nigella sativa* seeds on the uterine smooth muscle of rats and guinea pigs *in vitro* using isolated uterine horns. The volatile oil inhibited the spontaneous movements of rat and guinea pig uterine smooth muscles and also the contractions induced by oxytocin suggesting its anti-oxytocic potential (Aqel & Shaheen, 1996).

Antispasmolytic activity

The volatile oil and ethanol extract of *Nigella sativa* inhibited spontaneous movements of rabbit jejunum (Aqel, 1993). The aqueous extract of seed caused mild to moderate dose dependent relaxation effects, increased the sensitivity of the ileum to acetylcholine and interacted with serotonin in a dose dependent manner (Chakma *et al*., 2001). It also showed spsmolytic activity mediated through calcium antagonist effect justifying the traditional use in diarrhoea (Gilani *et al*., 2001).

Antiurolithatic activity

Ethanol extract of *Nigella sativa* reduced the number of calcium oxalate deposits in ethylene glycol-induced kidney calculi in rats and also lowered the urine

concentration of calcium oxalate suggesting the use as antiurolithatic agent (Hadjzadeh *et al*., 2007). It has also been observed in a study that thymoquinone significantly decreased the number and size of calcium oxalate deposits in the renal tubules in ethylene glycol-induced kidney calculi in rats (Hadjzadeh *et al*., 2008).

Anxiolytic

The anxiolytic activity of aqueous and methanol extracts of *Nigella sativa* seeds for four weeks in rats was evaluated by open field and elevated plus maze models. The rats exhibited an increase in open field activity and produced anti-anxiety effect in elevated plus maze. Oral administration of *Nigella sativa* oil increased brain levels of 5-HT and tryptophan but the levels of brain 5-HIAA decreased significantly suggesting its anxiolytic use (Parveen *et al.*, 2009).

Cardiovascular

The effect of two months oral supplement of seeds of *Nigella sativa* to normal tars on cardiac haemodynamic *in vivo*, the ionotropic and chronotropic properties of the isolated hearts *in vitro*, and the cardiac responsiveness to progressive adrenergic stimulation by isoproterenol were investigated. The results showed the intrinsic cardiac contractile properties without evidence of an increased cardiac work load or energy consumption *in vivo* which makes these seeds an isotropic agent with hemodynamic profile (Al-Hariri *et al.*, 2009; El-Bahai *et al*., 2009; Yar *et al.*, 2008).

The effect of aqueous and macerated extract from *Nigella sativa* on heart rate and contractility of the isolated heart were examined. The result showed a potent inhibitory effect of both extract on both on heart rate and contractility of the guinea pig heart that was comparable and even higher than that of diltiazem which may be due to calcium channel inhibitory or an opening effect of the plant on potassium channel of the isolated heart (Boskabady *et al*., 2005; Shafei *et al*., 2005).

The hypotensive effect of the dichloromethane extract of seeds in the spontaneously hypertensive rat were evaluated. The mean arterial pressure decreased, respectively by 22 and 18 % in the *Nigella sativa* treated rat and nifedipine treated rat (0.5 mg/kg/day) (Zaoui *et al*., 2000).

The effect of oral treatment of Wistar albino rats with different doses of powdered seeds (100, 200, 400 & 600 mg/kg) for four weeks on the level of serum lipids were investigated. The result showed that it causes significant decreased in low density lipoprotein-cholesterol levels, triglycerides level and increase in high density lipoprotein-cholesterol level (Kocyigit *et al.*, 2009).

Central Nervous System

The possible beneficial effect of *Nigella sativa* in comparison to methylprednisolone on experimental spinal cord injury in rats was investigated. The morphology of neurons in methylprednisolone and *Nigella sativa* treated groups was well protected that suggest that *Nigella sativa* might be beneficial in spinal cord tissue damage (Kanter *et al*., 2006).

The effect of aqueous and methanol extract of defatted *Nigella sativa* seeds were evaluated on the central nervous system and on analgesic activity. The observations of the study suggest that both extracts possesses a potent CNS depressant and analgesic activity (Al-Naggar *et al.*, 2003). A study reveals that *Nigella sativa* seeds oil was found to potentiate pentobarbitone induced sleeping time (Khader *et al*., 2009).

In another study, it has been observed that aqueous and methanol extract of *Nigella sativa* seeds produced an alteration in general behavior, significant reduction of spontaneous motility, normal body temperature and analgesic activity against hot plate suggesting its CNS depressant activity (Khanna *et al.*, 1993).

Contraceptive

A study demonstrated that hexane extract of the seeds of *Nigella sativa* prevented pregnancy in Sprague-Dawley rats treated orally at 2 g/kg gaily dose on day's 1-10 post-coitum (Keshri et al., 1995). The ethanol extract of seeds exhibited antifertility effect in male rats that is probably due to inherent estrogenic activity (Agarwal et al., 1990).

It has been observed in a study that powder of *Nigella sativa* seed (500 mg/ kg) has shown to possess anti-implantation activity in pregnant rats (Seshadri *et al*., 1981). In another study its ethanolic extract showed inhibition of ovulation when administered at 200 mg/kg in female rabbits (Vohora *et al*., 1973).

Diuretic activity

The diuretic activity of dichloromethane extract of *Nigella sativa* seeds was studied in rat. An oral dose of extract (0.6 ml/kg/day) significantly increased the diuresis by 16 % after 15 days of treatment. Urinary excretion of Cl-, Na+ and urea is also increased (Zaoui *et al*., 2000).

Galactagogue

An experimental study was designed to determine the galactagogue action of *Nigella sativa* seeds and its safety. Lactating mice were switched on to *Nigella sativa* containing diet from the day of labour for 15 days. *Nigella sativa* significantly increased serum prolactin level and the weight of litter compared with control group. Breast tissues of lactating mice kept on *Nigella sativa* containing diet showed larger acini, thicker epithelia and hyperactivity. No haematological, histological and biochemical side effects were caused by *Nigella sativa* (Al-Snafi *et al*., 2014).

Gastroprotective

The ethanol induced gastric mucosal lesions on male wistar rats were used to evaluate gastroprotective activity *Nagilla sativa* oil. The results revealed that *Nagilla sativa* oil and thymoquinone could protect gastric mucosa against the injurious effect of absolute alcohol and promote ulcer healing as evidenced from the ulcer index values. Thymoquinone protected against the ulcerating effect of alcohol and mitigated most of the biochemical adverse effects induced by alcohol in gastric mucosa, but to a lesser extent than *Nagilla sativa* oil (Kanter *et al*., 2005).

In another study, gastroprotective activity of *Nagilla sativa* was evaluated using gastric mucosal injury induced by ischaemia / reperfusion in rats. The study reveals that biochemical changes were accompanied by an increase in the formation of gastric lesions, which was reduced by the treatment of *Nagilla sativa* oils and its constituents (El-Abhar *et al*., 2003).

The effect of *Nigella sativa* aqueous suspension on experimentally induced gastric ulcers by various noxious chemicals and basal gastric secretion in rats were evaluated. It significantly prevented gastric ulcer formation induced by necrotizing agents, also ameliorated the ulcer severity and basal gastric acid secretion in rats. The antiulcer effect of *Nigella sativa* is possibly prostaglandin-mediated and/ or through its antioxidant and anti-secretory activities (Al Mofleh *et al.*, 2008).

The effect of oil and thymoquinone in an experimental model of ethanol induced ulcer in rats was evaluated. *Nigella sativa* and thymoquinone protected gastric mucosa against the injurious effect of absolute alcohol and promote ulcer healing (El-Dakhakhny *et* al., 2000; Kanter *et al*., 2005).

Results of a study reveals that the aqueous extract of the seed decreased the volume of acid in gastric juice in acetyl salicylic acid treated rats exhibiting its antiulcer activity (Akhtar *et al.*, 1996).

A study has been designed to investigate antiulcer activity of alcoholic extract of *Nigella sativa* by pyloric ligation and aspirin induced ulcer model in rats. The result shows that volume of gastric acid secretion, free acidity, total acidity and ulcer index were significantly reduced (Rajkapoor *et al*., 2002).

Hepatoprotective

A study was designed to evaluate the therapeutic effects of ethanolic extracts of *Nigella sativa* in the patient suffering from hepatitis C virus. The extract was prepared and formulated into gelatinous capsules. The findings suggest that the administration of test drug to HCV patients was safe, tolerable, decreased viral load, alleviate the altered liver function and improved clinical outcome (Abdel-Moneim *et al*., 2013).

In a study it has been concluded that *Nigella sativa* administration in hepatitis C virus patients is safe and tolerable and results in a significant improvement in viral load, oxidative stress and laboratory markers. Moreover, the clinical improvement and better glycemic control in patients with diabetes indicate a potential role for *Nigella sativa* in improving the clinical outcome of HCV patients (Barakat *et al*., 2013).

A study reported that the activity of *Nigella sativa* on lipid peroxidation, antioxidant enzyme systems and liver enzymes in calcium tetrachloride treated rats was evaluated. The result reveals that *Nigella sativa* decrease the elevated lipid per-oxidation and liver enzyme levels and also increase the reduced antioxidant enzyme levels in CCL_4 treated rats (Kanter *et al.*, 2003; Kanter *et al.*, 2005; Meral & Kanter, 2003; Turkdooan *et al.*, 2003).

Hypoglycemic

An experimental study was carried out to investigate the blood glucose lowering effect of *Nigella sativa* in alloxan induced diabetic rats. The finding suggests that it lowers blood glucose through enhancement of peripheral metabolism of glucose, an increase in insulin release and simultaneously a reduction in glucagon release or may be due to an intestinal reduction of absorption of glucose (Abbasi *et al*, 2014).

Nigella sativa seed was used as adjuvant therapy to evaluate antidiabetic activity on human volunteers. *Nigella sativa* at a dose of 2 gm/day for three months caused significant reduction in fasting blood glucose, 2hPG, and HbA without significant change in body weight. Fasting blood glucose was reduced but β-cell function was increased at 12 weeks of treatment (Abdullah, 2010).

The effect of the crud aqueous extract of *Nigella sativa* seeds on intestinal glucose absorption *in vitro* using a short circuit current technique and *in vivo* using an oral glucose tolerance test were investigated. It directly inhibits the electrogenic intestinal absorption of glucose *in vitro*. Together with the observed improvement of glucose tolerance and body weight in rats after chronic oral administration *in vivo*, these effects further validate the traditional use of these seeds against diabetes (Meddah *et al.*, 2009).

Oral administration of ethanol extract of the seeds (300/ mg/kg) to streptozotocin induced diabetic rats significantly reduced the elevated levels of blood glucose, lipids, plasma insulin and improved altered levels of lipid peroxidation products and antioxidant enzymes like catalase, superoxide dismutase, reduced glutathione and glutathione peroxidase in liver and kidney (Kaleem *et al*., 2006; Kanter *et al*., 2003).

The possible effect of *Nigella sativa* for four week against beta-cell damage from streptozotocin induced diabetes in rats was studied. *Nigella sativa* treatment

exerts a therapeutic protective effect in diabetes by decreasing oxidative stress and preserving pancreatic beta-cell integrity (Kanter *et al*, 2004).

The effect of *Nigella sativa* oil and its constituent thymoquinone on oxidative stress in the heart and brain in an experimental model of diabetes mellitus using streptozotocin were evaluated. The result suggested that *Nigella sativa* and thymoquinone correct streptozotocin - diabetes-induced alteration in cardiac creatine kinase muscle and brain types and brain monoamines due to their antioxidant properties (Hamdy & Taha, 2009).

The possible effect of the volatile oil of *Nigella sativa* seeds on insulin immunoreactivity and ultra structural changes of pancreatic beta-cells in streptozotocin-induced diabetic rats were evaluated. *Nigella sativa* treatment exerts a therapeutic protective effect in diabetes by decreasing morphological changes and preserving pancreatic beta-cell integrity thus suggestion it can be clinically useful for protecting beta-cell against oxidative stress (Kanter *et al*., 2009).

Human Neutrophil Elastase

The oil extracted from the seed of *Nigella savita* were used to evaluate the potency on human neutrophil elastase activity. Inhibition of human neutrophil elastase activity by essential oil was found to be dose dependent. It has been observed from the study that the inhibitory effects of essential oil on human neutrophil elastase activity are due to the presence of bioactive molecules, mainly carvacrol. This compound is an inhibitor of human neutrophil elastase and could be considered as a natural antielastase agent and possible candidate for phytotherapy in the treatment of injuries that appear in some pathologic cases such as chronic obstructive pulmonary disease and emphysema (Kacem & Meraihi, 2006).

Hypolipidemic

Seeds of *Nigella savita* were evaluated for their effects on lipid profile in human beings. The powder of seeds of *Nigella savita*, were orally administrated to hypercholesterolemic patients at the dose of 1 gm before breakfast for two months. The study demonstrates that the seeds of *Nigella sativa* favourably modify the plasma lipid profile in hypercholesterolemic patients. It produces antiartherogenic effect by decreasing low density lipoprotein cholesterol level significantly. It also increases high density lipoprotein cholsterol level. It reduces triglycerides and the total cholesterol level by decreasing intracellular cholesterol. Thus it has a protective role in atherosclerosis (Bhatti, 2009).

A study demonstrated that petroleum ether extract of *Nigella sativa* exert lipid lowering and insulin sensitizing action in the rats. The treated rats had lowered triglycerides and higher HDL cholesterol (Le *et al*., 2004). The efficacy of thymoquinone, an active ingredient of *Nigella sativa* seeds, on Doxorubucin-induced hyperlipidemic nephropathy in rats was studied. The results showed that rat treated with thymoquinone for five days significantly lowered serum urea, triglycerides and total cholesterol (Badary *et al*., 2000). In another study, the *Nigella sativa* oil was administered for four weeks and showed significant decrease in serum cholesterol, triglycerides and significant elevation of serum high density lipoprotein level (El-DakhaKhani *et al*., 2000).

Immunomodulatory

The immunomodulating and cytotoxic properties of the volatile oil of *Nigella sativa* seed was investigated in rats. The results indicate that the oil is a potential immunosuppressive cytotoxic agent (Islam *et al*., 2004).

The radioprotective potential of *Nigella savita* crude oil was investigated against hemopoietic adverse effect of gamma irradiation. Oral administration of *Nigella sativa* seed oil before irradiation considerably normalized significant increase in malondialdehyde concentration with a significant decrease in plasma glutathione peroxidase, catalase and erythrocyte superoxide dismutase activities promising natural radioprotective agent against immunosuppressive and oxidative effects of ionizing radiation (Assayed, 2010).

Neural Tubal Defect

Maternal diabetes is responsible for many types of embryonic defects. Increased oxidative stress has been suggested to play a role in the pathogenesis of disturbed embryogenesis in diabetic pregnancies. A study was conducted to determine the effect of *Nigella sativa* extract on spinal cord neuroepithelium of diabetic rats' embryos. The finding of the study reveals that *Nigella sativa* has a protective effect against diabetic embryopathy and fetal loss (Panahi *et al.*, 2011).

Nephroprotective

A study has been designed to evaluate the nephroprotective activity of *Nigella sativa* against gentamicin induced nephrotoxicity in rats. Administration of *Nigella sativa* with gentamicin injection resulted significantly decreased indices of nephrotoxicity when compared with gentamicin group suggesting nephroprotective activity (Yaman & Balikci, 2010).

Nephroprotective activity of thymoquinone was evaluated against gentamicin induced nephrotoxicity. Thymoquinone supplementation resulted that it prevents gentamicin induced degenerative changes in kidney tissue (Ahmed & Nagi, 2007).

The nephroprotective activity of *Nigella sativa* oil was investigated against chronic cyclosporine A induced nephrotoxicity in rats. *Nigella sativa* oil significantly increased the functional and histological parameters and attenuated the oxidative stress induced by CsA (Uz et al., 2008).

A study has been designed to investigate the nephroprotective effect of *Nigella sativa* oil (0.5, 1.0 or 2.0 ml//kg) against gentamicin nephrotoxicity in rats. It produced a dose-dependent amelioration of the biochemical and histological indices of gentamicin nephrotoxicity that was statistically significant at the two higher doses used (Ali, 2004).

The effect of thymoquinone on nephropathy and oxidative stress induced by doxorubicin in rats was investigated. The result suggests that thymoquinone might be useful as protective agent for proteinuria and hyperlipidemia associated with nephrotic syndrome (Badary *et al.*, 2000).

The nephroprotective activity of *Nigella sativa* seeds was investigated and seeds were found to reduce significantly the cisplatin-induced nephrotoxicity, blood urea nitrogen, serum creatinine level as well as cisplatin-induced serum total lipid increase (El-Dalyl, 1998).

Result of a study reveals that oral treatment with extract of *Nigella sativa* was found to be a potent chemo-preventive agent causing the suppression of potassium bromated mediated renal oxidative stress; toxicity and tumor promotion response in rats (Khan *et al*., 2003).

In a study, it has been reported that *Nigella sativa* oil has protective effect on methotrexate-induced nephrotoxicity in albino rats (Abul-Nasr *et al*., 2001).

Pulmonary

A study has been designed to investigate the potential for *Nigella sativa* treatment to protect against lung injury after pulmonary aspiration of materials. The result indicated a significant reduction in the activity of inducible nitric oxide synthase and as rise in surfactant protein D in lung tissue of different pulmonary aspiration models after *Nigella sativa* therapy which suggests that it might be beneficial in lung injury (Kanter, 2009).

A study has been designed to investigate the antihistaminic effect of Nigellone. It was fond to inhibit effectively the histamine release from the mast cells suggesting its use in asthma (Chakravarthy, 1993).

It has been concluded in a study that the bronchodilator effect of *Nigella sativa* seeds has shown to be mediated possibly through calcium channel blackade (Gilani *et al.*, 2001).

The effect of volatile oil of *Nigella sativa* and thymoquinone were investigated and compared on the respiratory system of the urethane anaesthetized guinea pig. Intravenous administration of volatile oil induced dose dependent increase inn respiratory rate and intratracheal pressure whereas thymoquinone induced significant increase in the intratracheal pressure without any effect in the respiratory effects were mediated via release of histamine with direct involvement of histaminergic mechanism and indirect activation of muscarinic cholinergic mechanism (El-Tahir *et al.*, 1993).

Rheumatoid Arthritis

The aqueous methanolic extract of *Nigella sativa* was evaluated for rheumatoid arthritis in Wistar rats using inflammation induced oxidative stress and tissue damage model. The animals were immunized with collagen and disease developed after 13±1 days post induction. The finding of the study revealed the fact that the plant has promising potency against rheumatoid arthritis (Sajad *et al*., 2010).

Safety

Safety study of *Nigella sativa* was conducted and it has been observed that its seed powder did not produce any toxic effects at very high doses (Tissera *et al*., 1997) in rabbits. Its oil was also very safe when given orally to rats (Zaoui *et al*., 2002), and oral thymoquinone was also found to be quite safe (Badary *et al*., 1998).

Sickle Cells

The pharmacological action of oil extract of *Nigella sativa* in sickle cells was evaluated in human volunteers. The study concluded that 0.1 percent v/v concentration of oil extract of *Nigella sativa* resuted in approximately 80 percent reduction in the formation of sickle cells (Ibraheem *et al*., 2010).

Wound healing

A study was designed in order to compare the effect of *Nigella sativa* and silver sulfadiazine on healing of burn wounds in rats. It has been concluded that in a burn wound model in rats, *Nigella sativa* was found to shorten the healing process both histopathologically and statistically as compared to silver sulfadiazine and the control group. Through its antimicrobial, antioxidant, anti-inflammatory and immunomodulatory effects, *Nigella sativa* can be used as an adjunctive or alternative agent to existing wound healing therapies in future (Yaman *et al*., 2010).

Kalonji
***Nigella sativa* Linn**

Flower

Plant

Seeds

CONCLUSION

Nigella sativa (*Kalonji*) has been in use since times immemorial to treat wide range of indications. It has been subjected to quite extensive phytochemical, experimental and clinical investigations. Experimental studies have demonstrated its abortifacient, analgesic, anti-inflammatory, anthelmintic, anti-asthmatic, anti-cancer, anticonvulsant, antiepileptic, antifungal, antihypertensive, antimicrobial, antinociceptive, antioxidant, antioxytocic, anti-rheumatoid arthritis, antispasmolytic, antiurolithatic, anxiolytic, bronchodialator, CNS depressant, contraceptive, diuretic, galactagogue, gastroprotective, hepatoprotective, human neutrophil elastase inhibitor, hypoglycemic, hypolipidemic, immunomodulatory, nephroprotective, wound healing and diabetic embryopathy protective effects. The scientific studies have proved most of the claims of traditional medicines. However, further, detailed clinical research appears worthwhile to explore the full therapeutic potential of this plant in order to establish it as a standard drug.

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