

# KALONJI (NIGELLA SATIVA): TRANSFORMATION FROM HERB TO MULTIFUNCTIONAL MEDICINE

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## ABSTRACT

The use of herbal drugs is as old as human beings. Kalonji (*N. sativa*) is a widely used medicinal plant throughout the world. It is very popular in various traditional systems of medicine like Unani, Ayurveda and Siddha. The seeds of Kalonji (*N. sativa*) have been widely used in the treatment of different diseases and ailments. The Prophet Mohammad (PBUH) had described the healing powers of the Black Seeds against a variety of diseases. According to common Islamic and Arabic belief, Habbatul Barakah is a remedy for all ailments (universal healer). Black Seed is also mentioned as the curative "black cummin" in the Holy Bible and is described as Melanthion by Hippocrates and Dioscorides and as Gith by Pliny. It is one of the most common medicinal plants worldwide and contains many useful chemical constituents. It has been widely used as antihypertensive, liver tonic, diuretic, digestive, anti-diarrheal, appetite stimulant, analgesic, anti-bacterial and in skin disorders. Extensive studies on Kalonji (*N. sativa*) have been carried out by various researchers and a wide spectrum of its pharmacological actions have been explored which may include antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepato-protective, nephro protective, gastro-protective, antioxidant properties, etc. The present review is an effort to provide a detailed survey of the literature on scientific researches of pharmacognostical characteristics, chemical composition and pharmacological activities of the seeds of this plant.

**Keywords:** Kalonji, Nigella sativa, Unani System of Medicine

## I. INTRODUCTION

The medicinal plants are being therapeutically exploited throughout the world for treating various ailments, and it is the oldest and the safest method to manage or cure illness. Moreover, medicinal plants are also used in the preparation of herbal medicines as they are considered to be safe as compared to modern allopathic medicines. Many researchers are focusing on medicinal plants since only a few plant species have been thoroughly investigated for their medicinal properties, potential, mechanism of action, safety evaluation and toxicological studies.

Among various medicinal plants, Kalonji (*N. sativa*) (Family Ranunculaceae) is emerging as a multi functional herb with a rich historical and religious background since many researches revealed its wide spectrum of pharmacological potential. Kalonji (*N. sativa*) is commonly known as black seed and is native to Southern Europe, North Africa and Southwest Asia and it is cultivated in many countries in the world like Middle Eastern Mediterranean region, South Europe, India, Pakistan, Syria, Turkey, and Saudi Arabia <sup>[20]</sup>. It was mentioned that black seed is the remedy for all diseases except death in one of the Prophetic hadith.

## II. ETHNO-PHARMACOLOGICAL DESCRIPTION

According to the classical literature, Kalonji (*N. sativa*) is an annual flowering plant which grows to 20-90 cm tall, with finely divided leaves, the leaf segments narrowly linear to threadlike. The flowers are delicate, and usually colored white, yellow, pink, pale blue or pale purple, with 5-10 petals. The fruit is a large and inflated capsule composed of 3-7 united follicles, each containing numerous seeds which are triangular in shape and black in colour. Seeds have a bitter taste and strong smell.<sup>[1], [2]</sup>



Fig. 1 Kalonji Flower



Fig. 2 Kalonji Seeds

The parts used for medicinal purpose are dried fruit and seeds. Specimens of *Kalonji* flower and seeds are shown in figure 1 and 2 respectively.

## III. Mizaj (TEMPERAMENT)

The Mizaj (temperament) of this plant described in Unani classics is Hot and dry in second degree.<sup>[1,28,29]</sup> But, according to some scholars it is Hot and dry in third degree<sup>[12,21]</sup>

## IV. MORPHOLOGICAL DESCRIPTION

The scientific classification of Kalonji (*N. sativa*) is given below in table no. 1. A pretty herb, 30-60 cm high. Leaves 2-3 pinnatisect, 2.5-5 cm long, cut into linear lanceolate segments, flowers pale blue or white on solitary long peduncles, 22.5 cm across. Sepals ovate, acute, clawed. Nectorial petals 8, geniculate with saccate gland in knee, one on the face and one on the apex of each lobe. Carpels 67, inflated, warts at the sides and united to the top, beak as long as the ovary. Seeds are trigonous, rigose tubercular. It is mainly found in Punjab, sometimes cultivated as an occasional weed. Plant occurs for most part of the year while flowering and fruiting from March to May.<sup>[1,2,3]</sup>

Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales
Family	Ranunculaceae
Genus	Nigella
Species	Kalonji

Table no. 1. Scientific classification of NS

## V. MICROSCOPIC DESCRIPTION

Microscopically, transverse segment of seed shows single layered epidermis comprising of oval, thick walled cells, covered externally by a papillose cuticle and filled with dark brown contents Epidermis is trailed by 2-4 layers of thick-walled tangentially extended parenchymatous cells, trailed by a rosy chestnut pigmented layer made out of thick-walled, rectangular amplified cells Inward to the pigment layer, there is a layer that is made out of thick-walled rectangular stretched or almost columnar, extended cells Endosperm comprises of thin-walled, rectangular or polygonal cells mostly loaded with oil globules The microscopy of seed powder shows earthy dark, parenchymatous cells and oil globules.<sup>[1,2,3,31]</sup>

## VI. ACTIONS AND THERAPEUTIC USES OF KALONJI

Various actions and clinical indications of Kalonji are given below in table no. 2.

Actions	Clinical Indications
<i>Kasir-e-riyah (Carminative),</i>	<i>Nafakh-e-shikam (Flatulence)</i>
<i>Muqawwi-e-meda (Stomachic)</i>	<i>Zof-e-meda (Weakness of stomach)</i>
<i>Qatil-e- kirm Shikam (Anthelmintic)</i>	<i>Kirm Shikam (Worms infestation)</i>
<i>Mudir-e-baul (Diuretic),</i>	<i>Qillat-e-baul (Oligouria)</i>
<i>Mudir-e-tams (Emmenagogue),</i>	<i>Ehtebas-e-tams(Amenorrhoea)</i>
<i>Musakkin e Alam (Analgesic)</i>	<i>Asabi dard (Neuralgia), Qulanj (Colic)</i>
<i>Muqavvi Aasab ( Nervine Tonic)</i>	
<i>Dafe taffun (Antiseptic)</i>	
<i>Hazim (Digestive)</i>	<i>Su-e-hazm (Dyspepsia)</i>
<i>Muqawwi Jigar (Liver Tonic)</i>	<i>Amraz-e-kabid (Ailments of liver), Yarqan (Jaundice)</i>
<i>Mushtahi (Appetizer),</i>	<i>Zof e Isthiha ( Loss of Appetite)</i>
<i>Jali ( Detergent),</i>	<i>Skin diseases (Amraz e jild),Bars (Vitiligo)</i>
<i>Munzjij (Coctive),</i>	<i>Nazla (Cold)</i>
<i>Muallid e Labn( Galactagogue)</i>	

[1,4, 12,16,20,21,22,24,25,29,30,31]

**Table no. 2.** Actions and clinical indications of Kalonji.

## VII. IMPORTANT FORMULATIONS

Habb e Hilteet, Jawarish Shoneez, Majoon Kaklaanj. <sup>[1,22,25,30]</sup>

## VIII. DOSAGE:

3-7 gms <sup>[1]</sup>

## IX. SCIENTIFIC STUDIES ON KALONJI

### A. Phytochemical Studies

The most important active constituents are thymoquinone (30%-48%), thymohydroquinone, dithymoquinone, p-cymene (7%-15%), carvacrol (6%-12%), 4-terpineol (2%-7%), tanethol (1%-4%), sesquiterpene longifolene (1%-8%)  $\alpha$ -pinene and thymol etc. 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, Kalonji (*Kalonji*) seeds also contain alpha-hederin, a water soluble pentacyclic triterpene and saponin, a potential anticancer agent <sup>[5]</sup>.

There are some other reported chemical components which includes nigellone,avenasterol-5-ene, avenasterol- 7-ene, campesterol, cholesterol, citrostadienol, lophenol, obtusifoliol, stigmastanol, stigmasterol-7-ene,  $\beta$ -amyryn, butyro- spermol, cycloartenol, 24-methylene-cycloartanol, taraxerol,

tirucallol, 3-O-[ $\beta$ -D-xylopyranosyl(1 $\rightarrow$ 3)- $\alpha$ -L-rhamnopyranosyl(1 $\rightarrow$ 2)- $\alpha$ -L-arabino-pyranosyl]-28-O-[ $\alpha$ -L-rhamnopyranosyl(1 $\rightarrow$ 4)- $\beta$ -D-glucopyranosyl(1 $\rightarrow$ 6)- $\beta$ -D-glucopyranosyl] hederagenin, volatile oil (0.5-1.6%), fatty oil (35.6-41.6%), oleic acid, esters of unsaturated fatty acids with C15 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)- $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranosyl]-11-methoxy-16, 23-dihydroxy-28-methyl-12-enoate, stigma-5, 22-dien- 3- $\beta$ -D-glucopyranoside, cycloart-23-methyl-7, 20, 22- triene-3 $\beta$ , 25-diol, nigellidine-4- O-sulfite, N. mines A3, A4, A5, C, N. mines A1, A2, B1, and B2 [33,34,39].

## B. Physicochemical Studies

The seed of Kalonji (*Kalonji*) contains:

Protein	:	(26.7%)
Fat	:	(28.5%)
Carbohydrates	:	(24.9%)
Crude Fibre	:	(8.4%)
Total ash	:	(4.8 %)
Vitamins and minerals	:	Cu, P, Zn and Fe etc [15,40]
Saturated fatty acids	:	(30% or less)

Fatty oil rich in unsaturated fatty acids, mainly linoleic acid (50-60%), oleic acid (20%), eicodadienoic acid (3%) and dihomolinoleic acid (10%) [11]

## C. Pharmacological Studies

### • Antibacterial activity:

The crude extracts of Kalonji (*N. sativa*) were tested for antimicrobial effectiveness against different bacterial isolates which comprised of 16 gram negative and 6 gram positive representatives. These isolate was showed multiple resistances against antibiotics, especially the gram negative ones. Crude extracts of Kalonji (*N. sativa*) showed a potential effect against some of the test organisms. The most valuable extracts were the crude alkaloid and water extracts. Gram negative isolates were affected more than the gram positive ones [35,37].

In a study, *Hannan et al.* investigated that Kalonji (*N. sativa*) has antibacterial activity against clinical isolates of methicillin resistant *Staphylococcus aureus*. All tested strains of methicillin resistant *Staphylococcus aureus* were sensitive to ethanolic extract of Kalonji (*N. sativa*) at a concentration of 4 mg/disc with an MIC range of 0.2-0.5 mg/mL [26].

In another study, antibacterial activity of Kalonji (*N. sativa*) against and triple therapy in suppression of *Helicobacter Pylori* in patients with non-ulcer dyspepsia was determined. Kalonji (*N. sativa*) seeds exhibited clinically useful anti *H. pylori* activity, comparable to triple therapy [42,43].

### • Antiviral activity:

In a study, *Zafar et al.* found that Kalonji (*N. sativa*) helps to enhance helper T cell (T4) and suppressor T cell (T8) ratio and increased natural killer (NK) cell activity in healthy volunteers [19]. As it improves the

immunity, Kalonji (*N. sativa*) extract have some inhibitory effect on the human immune deficiency virus protease but the active principle(s) responsible for this activity was not identified [36,52].

- **Anti fungal activity:**

In a study, it was found that Kalonji (*N. sativa*) has anti yeast activity of the seed quinines, dithymoquinone, thymohydroquinone, and thymoquinone were evaluated in vitro against six dairy spoilage yeast species. Thymohydroquinone and thymoquinone possessed significant anti yeast activity [44].

In another study, the methanolic extracts of Kalonji (*N. sativa*) showed very strong antifungal effect against different strains of *Candida albicans*. An intravenous inoculum of *Candida albicans* produced colonies of the organism in the liver, spleen and kidneys. Treatment of mice with the plant extract 24 hrs after the inoculation caused a considerable inhibitory effect on the growth of the organism in all organs studied. It was also reported that the aqueous extract of Kalonji (*N. sativa*) exhibits inhibitory effect against candidiasis in mice [13].

- **Anti allergic activity:**

In a study, thymoquinone dimer isolated from Kalonji (*N. sativa*) volatile oil, 'Nigellone' suppressed symptoms when given orally to bronchial asthma patients with effective results without any toxicity [46]. Administration of Kalonji oil to patients with allergic problems, like allergic rhinitis, atopic eczema, and bronchial asthma decreased the immunoglobulin E, and eosinophil count [29].

- **Antioxidant and antiarthritic activity:**

In a study, it was evaluated that thymoquinone component of Kalonji (*N. sativa*) showed the antioxidant and antiarthritic activity in Wistar rat by collagen induced arthritis. Oral administration of thymoquinone significantly reduced the levels of pro-inflammatory mediators [IL-1 $\beta$ , IL-6, TNF- $\alpha$ , IFN- $\gamma$  and PGE (2)] and increased level of IL-10 [47].

In another study, it was found that methanol extracts of Kalonji (*N. sativa*) have strong antioxidant activity using the oxygen radical absorbance capacity method and a cell-based assay [14]. It was suggested that dietary supplementation of black seeds powder inhibits the oxidative stress caused by oxidized corn oil in rats [9].

- **Immunomodulatory activity:**

In a study, immunomodulating and cytotoxic properties of volatile oil of Kalonji seeds was investigated in a Long-Evans rat model designed to examine the effect of Kalonji seeds on selected immune components with a specific antigen (typhoid TH). The results indicated that treatment with Kalonji oil induced about 2-fold decrease in the antibody production in response to typhoid vaccination. [46].

- **Antidiabetic activity:**

In a study, which was conducted to determine the effects of Kalonji (*N. sativa*) seed ethanol extract on insulin secretion in INS832/13 and  $\beta$  TC-tet lines of pancreatic  $\beta$ -cells and on glucose disposal by C2C12 skeletal muscle cells and 3T3-L1 adipocytes. Treatment with Kalonji (*N. sativa*) increased glucose-stimulated insulin secretion by more than 35% without affecting sensitivity to glucose. The treatment also accelerated  $\beta$ -cell proliferation. Kalonji (*N. sativa*) increased basal glucose uptake by 55% in muscle cells and approximately 400% in adipocytes. It is concluded that in vivo. Anti hyperglycemic effects of Kalonji

(*N. sativa*) seed extract are attributable to a combination of therapeutically relevant insulinotropic and insulin-like properties [50].

In another study, it was found that effect of the seeds of Kalonji (*N. sativa*) have glucose lowering effect in rats. Further study on the plant mixture containing Kalonji (*N. sativa*) revealed that the blood glucose lowering effect was due to the inhibition of hepatic gluconeogenesis and the plant extract mixture may prove to be useful therapeutic agent in the treatment of non-insulin dependent diabetes mellitus [8, 35].

- **Cardiovascular activity:**

In a study, the acute effects of diesel exhaust particles on cardiopulmonary parameters in mice and the protective effect of thymoquinone were evaluated. The particles were given to mice, intratracheally. They produced systemic inflammation characterized by leucocytosis, increased IL-6 concentrations and reduced systolic blood pressure. Pretreatment of mice with Thymoquinone prevented diesel exhaust particles induced decrease of systolic blood pressure and leucocytosis, increased IL-6 concentration. [41].

In another study, the effects of Kalonji (*N. sativa*) and its active constituent thymoquinone on the arterial blood pressure and heart of anaesthetized rats was evaluated. Both agents produce a dose dependent decrease in the arterial blood pressure and heart rates. These effects were significantly antagonized by atropine, mainly via the involvement of 5-hydroxy tryptaminergic and muscarinic mechanism. These findings were significantly comparable with the standard antihypertensive drug nifedipine [51]. The effect of the drug was concluded to be partially due to its diuretic effect which was comparable to frusemide.

In another study, Kalonji (*N. sativa*) extract to normal rats has shown a homogenous cardiac hypertrophy and enhanced cardiac contractility at baseline conditions. The hearts of Kalonji treated rats developed a moderate hypertrophy which was evident by an increase in the heart weight to body weight ratio. The observed Kalonji induced cardiac hypertrophy was associated with an increase in the baseline cardiac inotropic properties [49].

- **Contraceptive and anti-fertility activity:**

In a study, it was found that hexane extract of Kalonji seeds when administered orally, prevented pregnancy in experimental rats at a dose of 2 g/kg daily on day's 1-10 postcoitum. [32].

In another study, the ethanolic extract of Kalonji (*N. sativa*) seeds was found to possess an anti-fertility activity in male rats which might be due to inherent estrogenic activity of Kalonji. [23].

- **Antioxytotic activity:**

In a study, it was found that Kalonji (*N. sativa*) seeds oil inhibit the uterine smooth muscle contraction induced by oxytocin stimulation in rat and guinea pig uterine smooth muscles suggest the anti-oxytotic potential of *N. sativa* seeds oil [6].

- **Hepato-protective activity:**

In a study, it was reported that Kalonji (*N. sativa*) administration protects hepatic tissue from deleterious effects of toxic metals such as lead. [33]. The protective action of thymoquinone against the hepatotoxin: tertbutyl hyderoperoxide has also been demonstrated using isolated rat hepatocytes [16].

In another study, aqueous extract of the seeds of Kalonji were evaluated for hepatoprotective activity in male Wistar rats against carbon tetrachloride induced hepatotoxicity. A number of biochemical parameters were studied to determine the hepatoprotective potential. Aqueous extract showed significant hepatoprotective effect against carbon tetrachloride-induced toxicity on the liver indicating the hepatoprotective activity<sup>[38]</sup>.

- **Nephroprotective activity:**

In a study, Nephro-protective effect of vitamin C and Kalonji oil was observed against gentamicin (GM) associated nephrotoxicity in rabbits. Serum creatinine, blood urea nitrogen, and antioxidant activity were measured as indicators of nephrotoxicity for all the groups of rabbits. It was found that Kalonji oil and vitamin C both had nephroprotective effect as they lowered the values of serum creatinine, blood urea nitrogen, and antioxidant activity as compared to GM control group values. When these two antioxidants were given as combination, they proved to have synergistic nephroprotective effect<sup>[42]</sup>.

- **Gastro-protective activity:**

In a study, the anti-ulcer potential of Kalonji (*N. sativa*) aqueous suspension on experimentally induced gastric ulcers and basal gastric secretion in rats was examined and it was found that Kalonji has anti-ulcer effect due to possibly prostaglandin-mediated and/or through its antioxidant and anti-secretory activities<sup>[10]</sup>.

In another study, Ischaemia/reperfusion (I/R) induced gastric lesion, model was used to assess the antioxidant effects of Kalonji oil and thymoquinone on gastric mucosal redox state and gastric lesions, 1 and 24 h after reperfusion. Kalonji oil normalizes the level of lactate dehydrogenase, reduced glutathione and superoxide dismutase. These results indicate that both Kalonji oil and thymoquinone possess gastroprotective effect against gastric lesions which may be related to the conservation of the gastric mucosal redox state<sup>[18]</sup>.

- **Anticancer activity:**

A study was conducted in vitro and in vivo; to evaluate the anti-cancer effects of Kalonji (*N. sativa*) seed extracts. In the study the essential oil and ethyl acetate extracts were showed more cytotoxic effects against the P815 cell line than the butanol extract. Extracts showed a comparable cytotoxic effect against the ICO1 cell line, with IC50 values ranging from 0.2 to 0.26% (v/v), but tests on the BSR cell line revealed a high cytotoxic effect of the ethyl acetate extract (IC50 = 0.2%) compared to the essential oil (IC50 = 1.2%)<sup>[27]</sup>.

In another study, antitumor activity of thymoquinone and thymohydroquinone was demonstrated using tumor cell lines and fibrosarcoma, murine and squamous cell carcinoma<sup>[26]</sup>. In a mouse xeno-graft model, a combination of thymoquinone and diosgenin significantly reduced tumor volume, mass and increased apoptosis<sup>[17]</sup>.

- **Antispasmodic activity:**

In a study, the effect of nigellone and Thymoquinone on trachea (antispasmodic effect) and their influence on respiratory clearance was evaluated. It was found that nigellone possesses an antispasmodic effect and an increase in mucociliary clearance but Thymoquinone do not have such effects. Therefore, it is suggested that nigellone may be useful in treatment of different respiratory diseases<sup>[48]</sup>.

## Conclusion

With the increasing health consciousness day by day and with increasing side effects of conventional therapies, the trend is shifting towards non-conventional systems of medicine namely Unani Tibb. In recent

years, there has been a growing interest in the potential of various plants which provide health benefits other than their nutritional benefits. Thus, the use of herbal plants like Kalonji is rapidly gaining momentum. Traditionally, Kalonji has been used for both culinary as well as medicinal purposes. This review provides extensive information on the medicinal uses of Kalonji and supports the potential of Kalonji as a promising health promoting herbal plant. Hence, more researches can be done to exploit the unexplored potentials of Kalonji which have already been mentioned in Unani classical literature. Also, more clinical trials are warranted to validate the therapeutic efficacy of this Unani herb.

### Conflict of Interest

There is no conflict of interest to declare.

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