



# IJRASET

International Journal For Research in  
Applied Science and Engineering Technology



---

# INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

---

**Volume: 9      Issue: XII      Month of publication: December 2021**

**DOI: <https://doi.org/10.22214/ijraset.2021.39246>**

**[www.ijraset.com](http://www.ijraset.com)**

**Call:  08813907089**

**E-mail ID: [ijraset@gmail.com](mailto:ijraset@gmail.com)**

# An Overview on Composition and Therapeutic Potentials of the Black Seed (*Nigella sativa*)

Yusra Tafheem S<sup>1</sup>, Dr. Neeta Pattan<sup>2</sup>

<sup>1</sup>PG scholar, Department of Food and Nutrition, Maharani Cluster University, Bangalore, Karnataka, India

<sup>2</sup>Assistant Professor, Department of Food and Nutrition, Maharani Cluster University, Bangalore, Karnataka, India

**Abstract:** *Nigella sativa* is an annual herbaceous plant that belongs to the Ranunculaceae family and produces seeds known as black seed or black cumin. Black seed has been used in various civilization around the world for centuries to treat various ailments. It is widely used in a variety of traditional medical systems, including Unani, Ayurveda, and Siddha. Black seed is considered to be nutritionally dense, with high levels of fat, protein, dietary fibre, calcium, and iron. The seed is known to have a wide range of pharmacological properties which are supported by numerous studies. Extensive research has been carried out over decades to confirm the seed's anti-oxidant, anti-inflammatory, anti-microbial, anti-diabetic, anti-hypertensive, anti-lipidemic, anti-cancer, gastroprotective, hepatoprotective, neuroprotective properties etc. Black seed has earned a position among the top ranked evidence-based herbal medicines due to its marvellous healing properties. Studies have revealed that the presence of thymoquinone, a major bioactive component of the seed essential oil, is responsible for the majority of its therapeutic properties. Consumption of the seeds for an extended period of time has been shown to have significant effects on lowering blood glucose levels, improving lipid profiles, and other biochemical parameters. The minor or negligible toxicological effects of black seed and its active constituent, thymoquinone, support its long-term use in traditional food and medicine. Because of their low toxicity, black seed is frequently used in food as a flavouring agent, additive in breads, and pickles. The current review summarises the composition, important pharmacological studies, dosage and toxicity of the Blackseed and its application in food industry.

## I. INTRODUCTION

*Nigella sativa* seed is known by various names across the globe. In old Latin, it was recognised as 'Panacea,' which meant 'cure all', in Arabic, it is identified as 'Habbat-ul-Barakah,' translated as 'Seeds of blessing'. In India it is known as Kalonji while in English it is termed black cumin or black seed [1]. *Nigella sativa* is an annual herbaceous plant from the family, Ranunculaceae [2]. The plant grows up to 20-90 cm tall and is composed of finely isolated leaves that are barely straight - threadlike. The flowers are delicate, with 5-10 petals and are generally white, yellow, pink, light blue, or pale purple in colour. The natural fruit is a large and expanded capsule made up of 3-7 connected follicles, each containing numerous seeds [3]. The seeds, which contain a significant amount of oil with a pungent and bitter flavour, are the most commonly used part of the plant for its therapeutic purposes in "Alternative Medicinal" systems [2].



*Nigella sativa* is majorly found in the Mediterranean region and Western Asian countries such as India, Pakistan, and Afghanistan [1]. It is widely used in a variety of traditional medicines, including Unani and Tibb, Ayurveda, and Siddha [4]. References to these seeds can be found in some of the oldest religious and medical texts. According to Islamic tradition, blackseed is considered a universal remedy for all ailments except the death [5]. In the Holy Bible, the black seed is also known as the 'curative black cumin' and is described as 'Melanthon' [6].

Black seed has been extensively studied for its biological activities and therapeutic potential, and has been shown to have a wide range of activities such as diuretic, anti-hypertensive, anti-diabetic, anti-cancer, immune-modulatory, antimicrobial, anthelmintic, analgesics, bronchodilator, anti-inflammatory, anti-tussive, gastro-protective and hepatoprotective [3]. Thymoquinone is the major active principle of *Nigella sativa* (Blackseed) and constitutes about 30% of its volatile oil or ether extract [7]. The presence of thymoquinone (TQ) is responsible for the majority of this plant's remedial properties. Moreover, a large body of data analysis clearly shows that TQ has very few side effects and no serious toxicity [8].

Due to various ethnopharmacological uses of Blackseed as a healing herb, an attempt has been made to review the composition, therapeutic potentials, and scientific studies related to their health benefit.

## II. COMPOSITION OF THE BALCK SEED

### A. Nutritional Composition

Several studies have been conducted to investigate the nutritional and chemical composition of the black seed. The seeds are nutritionally rich; they provide high amounts of fat (especially monounsaturated fat), protein, and dietary fibre. Black seed contains 30% to 40% oil and 20% to 30% protein, 3.7%–4.7% ash, and 25%–40% total carbohydrates with antioxidants lignans such as saponin, melanine [9]. The nutritional composition of the black seed grown in Saudi Arabia [10] and Bangladesh [2] have been discussed below (Table 1)

Table 1: Nutritional composition of Black seed.

Nutrient	Composition (%)	
	Saudi Arabia <sup>[10]</sup>	Bangladesh <sup>[2]</sup>
Crude fat	31.95 ± 0.3	37 ± 0.4
Crude protein	20.61 ± 0.3	19.8 ± 0.3
Crude fibre	10.37± 0.1	5.1 ± 0.3
Total Carbohydrate	30.0 ± 1.2	30
Moisture	2.55 ± 0.2	4.2 ± 0.3

Black seed being an oil seed is majorly composed of fat. Studies show that fat is the major nutrient present in the seeds obtained from Saudi Arabia and Bangladesh. Protein is the next major nutrient present in both the varieties of seed. The total protein content of both the varieties is approximately the same. The current findings indicate that seeds are protein-rich enough to meet the protein needs of the consuming population [2]. There is a huge difference in the fibre content of both the varieties. The moisture content of the seeds varies. Knowing a product's moisture content is critical for determining whether it can be stored for an extended period of time without being attacked by bacterial and fungal agents [2].

With regard to minerals, Black seed is a rich source of Calcium and Iron [2,10]. However, the mineral content varies greatly in different variety. The variety from Bangladesh are richer in Calcium, Copper and Magnesium, whereas the Saudi Arabia variety are rich in Iron and Pottasium. [2,10]

Table 2: Mineral composition of Black seed

Minerals	Composition (mg/100 g dry weight basis)	
	Saudi Arabia <sup>[10]</sup>	Bangladesh <sup>[2]</sup>
Calcium	160.0±10.0	611 ± 3
Copper	0.9±0.1	3.8 ± 0.4
Iron	65.0± 2.5	10.2± 0.3
Zinc	2.5±0.2	6.4 ± 0.3
Potassium	823.0± 30.0	702 ± 2.3
Magnesium	80.0± 10.0	85.2 ± 0.2



Black seed oil is composed of four saturated fatty acids and four unsaturated fatty acids [11]. The seeds contain a higher concentration of unsaturated fatty acids, primarily linoleic acid (50-60%) than saturated fatty acid [12]. The fatty acid composition of the seeds from Saudi Arabia, Bangladesh, and India [10,2,11] has been listed in the table 3

Table 3: Fatty Acid composition of Black seed

Fatty Acid		Composition (%)		
		Saudi Arabia <sup>[10]</sup>	Bangladesh <sup>[2]</sup>	India <sup>[11]</sup>
Unsaturated Fatty Acid	Linoleic acid	68.07	52.6 ± 0.7	55.6
	Oleic acid	16.23	23.5 ± 0.5	23.4
Saturated Fatty Acid	Palmitic acid	10.5	16 ± 0.2	12.5
	Stearic Acid	2.04	4 ± 0.3	--

From the given table it is observed that as the linoleic acid composition decreases the composition of fatty acid in the seed is increased. According to studies performed on various species, consumption of conjugated linoleic acid can lead to total body weight and fat loss, lower levels of total and LDL cholesterol plasma concentrations, and has an anti-inflammatory effect [13]. The fatty acid composition of three different seed oils is slightly different, which could be attributed to genetic factors and environmental conditions during fruit development and maturity [2].

**B. Phytochemical Composition**

Phytochemicals are compounds that are produced by plants ("Phyto" means "plant"). The phytochemicals found in Black seed include tannins and sterols in high concentrations (>75%), flavonoids (50%), and alkaloids (25 %). Tannins, flavonoids, and sterols are found in significant concentrations, while alkaloids were found in the lowest concentrations (25%). The presence of these phytochemicals has made a significant contribution to spices' medicinal value [14].

The most important active compounds of Black seed are Thymoquinone (TQ) (30%–48%), p-cymene (7%–15%), carvacrol (6%–12%), 4-terpineol (2%–7%), t-anethole (1%–4%), sesquiterpene longifolene (1%–8%), α-pinene, and thymol [15]. Most of the biological activity of the seed has been linked to thymoquinone, which is found in both essential and fixed oil [16]. Thymoquinone, which gives the seed its aromatic flavour, is fat-soluble, thus seed oil has more therapeutic potential than aqueous extract or dry powder form [12].

**III. THERAPEUTIC POTENTIALS OF BLACKSEED SEEDS**

**A. Anti-oxidant Properties**

Thymoquinone (TQ) has been studied for a variety of pharmacological actions, one of which is its anti-oxidant properties. Several studies have found that the whole herbal plants, cold pressed or essential oil, extracts, and active molecules, particularly thymoquinone, have antioxidant properties supporting the common folk perception of black cumin as an antioxidant factor [17]. Malondialdehyde (MDA) is a naturally occurring reactive species that is one of the biological markers for oxidative stress [18]. An increase in free radicals causes overproduction of MDA. A study showed that after 8 weeks of consuming black seed, plasma MDA levels in 30 postmenopausal women decreased significantly. This effect could be attributed to increased activity of the antioxidant enzymes Glutathione peroxidase and Superoxide dismutase [19]. In a double-blind placebo-controlled randomised clinical trial, 50 obese volunteers were given a low-calorie diet supplemented with 3 g/day of Black seed oil. At the end of the study, a comparison of red blood cell superoxidase dismutase (SOD) levels showed significant differences in the Black seed group when compared the placebo group [20].

An animal trial revealed that giving TQ (80 mg/kg) orally, to diabetic rats for 45 days reversed the decreased activities of catalase (CAT), glutathione peroxidase (GPx), and glutathione-S-transferase (GST), as well as increased antioxidants like Glutathione (GSH) and vitamin C and E [21]. Pre-treatment of male rats for 30 days with the methanolic extract (500mg) and essential oil (100 mg/kg) of Black seed efficiently replenished the plasma total antioxidant power by an average of 88% against free radicals [22]. Based on these findings, it is possible to conclude that the antioxidant activity of Black seed and thymoquinone as a potential antioxidant agent for health promotion and disease prevention.

### B. Anti-inflammatory Properties

Black seed and its derivatives have been shown to have anti-inflammatory and bronchodilator properties, but the effects have only been studied in a very few clinical trials. Thymoquinone's anti-inflammatory activity could be attributed to its ability to inhibit the oxidative products of arachidonic acid formation, such as thromboxane B<sub>2</sub> and leukotriene, by inhibiting both cyclooxygenase and lipoxygenase enzymes [23,24]. In the model of acute inflammation, i.e., carrageenin-induced paw edema in rats, Black seed demonstrated anti-inflammatory action that was statistically significant when compared to the control group [25]. Furthermore, the effectivity of Blackseed ethanol extract as an anti-inflammation agent was investigated using Wistar rat mast cells. The study revealed that Black seed works as an anti-inflammatory agent on mast cells by inhibiting histamine release and has no toxic effect on mast cells [24].

Black seed demonstrated significant anti-inflammatory activity comparable to aspirin in a formaldehyde-induced arthritis model of chronic inflammation. [25]. Additional study found that 40 female RA patients who were given 500 mg *Blackseed* oil capsules twice a day showed improvement in the number of swollen joints and the duration of morning stiffness [26]. Chronic inflammation has been linked to a variety of chronic illnesses (cancer, cardiovascular disorders, diabetes, rheumatoid arthritis, and asthma) that involve progressive and irreversible damage to the cell and/or neurons. Therefore, the crucial role of anti-inflammatory actions of various Black seed preparations and TQ could serve as a potential anti-inflammatory agent to treat these diverse conditions.

### C. Anti-Microbial Properties

Various crude extracts of Black seed demonstrated antimicrobial efficacy against gram-negative or gram-positive bacterial strains. A study was conducted to look into the effect ground Black seeds on the eradication of *H. pylori* in humans. The findings revealed that a dose of 2 g/d eradicated *H. pylori* in infected patients in a proportion (67%) roughly equivalent to standard triple therapy [27]. A study that looked into the anti-microbial effects of *Nigella sativa* seed oil cold extract against two strains of *Staphylococcus aureus* discovered that the effect of Black seed oil extract is comparable to antibiotics like ceftazidime, cefaclor, cefamandole, and cefuroxime [28].

Another study revealed that Blackseed has an inhibitory effect on Methicillin-resistant *Staphylococcus aureus* (MRSA), which is one of the most common pathogens encountered in clinical and laboratory settings. At a concentration of 4 mg/disc, all MRSA strains tested were sensitive to Black seed extract [29]. Thymoquinone also inhibited the growth of *Aspergillus niger* and *Fusarium solani* in a manner comparable to Amphotericin-B [30] and was found to be effective against *Candida albicans*, *Candida tropicalis*, and *Candida krusei* [31]. According to a study, the active constituents of black seed, such as thymoquinone, thymohydroquinone, and thymol, demonstrated potent antifungal activity against dermatophytes, moulds, and yeasts which were isolated clinically [32].

### D. Anti-Diabetic Properties

Despite advancements in the management of diabetes mellitus, the quest for novel agents continues because existing synthetic agents have various limitations [33]. A randomised clinical trial of 70 healthy subjects revealed a significant reduction in fasting blood glucose and HbA<sub>1c</sub> levels in Black seed oil treated patients as compared to the control group by the end of the study. These two groups showed no significant liver, kidney, or gastrointestinal side effects [34]. A one-year non-randomized clinical trial discovered that Black seed supplementation significantly lowered Total Cholesterol (TC), Mean Arterial Pressure (MAP), and heart rate (HR) in type 2 diabetic patients receiving Oral Hypoglycaemic Agents (OHA) [35]. Black seed supplementation may also protect type 2 diabetic patients' heart health from diastolic dysfunction while improving LV systolic function [36]. Another study concluded that administration of 1.5 and 3 mL/day of black seed oil for 20 days resulted in a significant reduction in HbA<sub>1c</sub> levels [37]. Furthermore, the findings of a study suggested that treatment with Black seed seems to have a protective effect by improving lipid profile and blood glucose levels, both of which are elevated during the menopausal period [38].

Black seed has been shown to have postprandial anti-hyperglycaemic activity in type 2 diabetic animal models by reducing or delaying carbohydrate digestion and absorption in the gut and enhancing insulin secretion in response to plasma glucose levels [39]. A study investigating the potential effects of hydroalcoholic extract of Black seed on renal oxidative injury in diabetic rats discovered that long-term administration of Black seed can improve the status of oxidative stress in diabetic rats' renal tissue [40]. Another study confirmed the wound healing properties of hydroethanolic extracts of Black seed in diabetic male rats. The analysis revealed that when Black seed extract was applied topically to full-thickness skin wounds, it reduced inflammation and accelerated wound healing [41]. Moreover, dietary supplementation with Black seed improves fertility in diabetic male rats, with the benefits attributed to its anti-oxidative and androgenic properties [42].

### E. Anti-Lipidemic Properties

Cardio Vascular Diseases (CVD) is projected to remain the single leading cause of death globally and by 2020 almost 23.6 million people are projected to die from CVD particularly heart disease and stroke [43]. Repeated population surveys identify the considerable evidence-treatment gaps for common CVD risk factors such as hypertension and high cholesterol [44]. Studies have shown that Black seed has a high potential for hypoglycemia, hypocholesterolaemia, and antioxidant effects, all of which contribute to its cardioprotective properties [45-47]. In a randomised trial of 40 patients with Hashimoto's thyroiditis, treatment with powdered black seed significantly reduced serum concentrations of low-density lipoprotein cholesterol (LDL) and triglyceride (TG), while serum high density lipoprotein cholesterol (HDL) significantly increased. None of these changes were observed in the placebo-treated group [48]. Another study discovered that patients who received 2 g of Black seeds per day for 12 weeks had a significant decrease in Total Cholesterol (TC), TG, LDL, and a significant increase in HDL/LDL ratio when compared to their baseline data [49]. Additional study examining the hypolipidemic effects of Black seed found a significant decrease in TC, LDL, and TG, as well as a slight increase in HDL, in menopausal women given Black seed powder at a dose of 1 g daily for two months compared to a placebo group. The lipid profiles in the Black seed-treated group tended to return to pre-treatment levels one month after treatment was stopped [50]. Moreover, study discovered that including Black seed in rabbits' diet reduced arterial wall lipid deposition, total cholesterol, and LDL levels, as well as atherogenesis. As a result, the study establishes that Black seed has hypocholesterolaemia and antiatherogenic cardioprotective properties [51].

### F. Anti-Hypertensive Properties

Numerous antihypertensive drugs have been used in clinical practice to manage hypertension and alleviate symptoms. However, the efficacy of these drugs is only 40-60%, and usually two or more antihypertensive drugs from different categories must be combined to achieve the best results. This ultimately increases the likelihood of adverse effects while also increasing the cost of therapy [52]. According to a clinical non-randomized clinical trial, 57 diabetic patients with hypertension and dyslipidaemia who were assigned to receive 2 g of Black seed daily for one year had a significant reduction in systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) when compared to the control group [53]. Similarly in a randomised controlled trial, subjects with mild hypertension who received 100 and 200 mg of Black seed extract twice a day for 8 weeks showed a significant decrease in SBP and DBP values compared to the placebo group [54]. In another study, 70 healthy volunteers with SBPs ranging from 110 to 140 mmHg and DBPs ranging from 60 to 90 mmHg were given 2.5 mL NS oil or a placebo twice a day for eight weeks. At the endpoint, the SBP and DBP in the Black seed oil-treated group were significantly lower than the baseline and the placebo group [55]. In a study of spontaneously hypertensive rats (SHR), oral administration of a dichloromethane extract of Black seed (0.6 ml/kg/day) for 15 days resulted in a 16-30 percent increase in diuresis. This suggests that Black seed, through its diuretic action, may lower blood pressure. The diuretic effect was linked with an increase in urinary excretion of Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, and urea [56]. Moreover, a study on L-NAME-induced hypertensive rats observed that administering Black seed oil at a dose of 2.5 mg/kg for 8 weeks reduced systolic blood pressure, with the effect of the oil appearing to be mediated by a reduction in cardiac lipid peroxidation product and inhibitory activity of Angiotensin Converting Enzyme [57].

### G. Anti-Cancer Properties

Thymoquinone (TQ), which is the major component in Black seed oils, is considered as potent anti-carcinogenic and anti-mutagenic agent [58]. TQ has been shown in studies to play an antioxidant role, improve the body's defence system, induce apoptosis, and control the Akt pathway, which regulates cell survival and proliferation [59]. The effects of TQ on HCT-116 human colon cancer cells were studied, and it was discovered that it acts as an antineoplastic and pro-apoptotic agent against the colon cancer cell line. TQ was also found to inhibit colon cancer cell growth, which was linked to a cell cycle arrest in the G1 phase [60]. Another study revealed that the volatile oil of Black seed has the potential to inhibit colon carcinogenesis in rats in the post-initiation stage, with no obvious harmful effects, and that the inhibition may be associated, in part, with suppression of cell proliferation in the colonic mucosa [61]. A study discovered that oral administration of Black seed protects against methyl nitrosourea (MNU) induced oxidative stress and carcinogenesis by 80%, in Sprague Dawley rats. When honey and Black seed were combined, they provided 100% protection by eliminating malondialdehyde (MDA) and nitric oxide (NO) elevations [62]. Additional study concluded that thymoquinone effectively inhibits endothelial cell migration, invasion, proliferation, and tube formation, as well as tumour-angiogenesis and tumour growth [63]. An extensive study on Thymoquinone as a chemo preventive agent revealed that TQ-induced apoptosis in myeloblastic leukaemia HL-60 cells is associated with the activation of caspases, specifically caspase-8 [64], which are known to be involved in apoptosis [65].

#### H. Neuroprotective Properties

There have been numerous cellular, animal, and clinical reports of the Black seeds' beneficial effects in various psychological and neurological models and disorders such as anxiety, depression, psychosis, ischemia, memory impairment, epilepsy, neurotoxicity, neurodegeneration, and pain [66]. A study that looked at the potential effect of Black seed on lipid peroxidation levels after cerebral ischemia-reperfusion injury (IRI) in the rat hippocampus found that pre-treatment with Thymoquinone and Black seed oil resulted in a significant decrease in MDA levels when compared to the ischemic group [67]. Another study that was designed to assess the potential protective effects of Black seed on neuronal injury in the frontal cortex and brain stem after 12 weeks of chronic toluene exposure discovered that Black seed therapy causes morphologic improvement without any histopathological changes on neurodegeneration in the frontal cortex and brain stem [68]. Beta amyloid (A $\beta$ ), a by-product of amyloid precursor protein, has been linked to neurodegeneration in Alzheimer's disease (AD). A study that looked at the neuroprotective effects of Black seed oil and its fractions against beta amyloid (A $\beta$ )-induced cell death in primary rat cerebellar granule neurons found that the water fraction of Black seed was significantly protective against beta amyloid (A $\beta$ )-induced cell death, which was most likely due to the oil's antioxidant properties. However, Black seed oil and its fractions (hexane fraction, ethyl acetate fraction, and water fraction) were found to be marginally protective against cell membrane damage in lactate dehydrogenase (LDH) assays [69]. A study found that extracts of Black seed from different germination stages had substantial anxiolytic, antiepileptic, and antidepressant effects in rats, particularly the 5th day germination extract followed by the 7th day. It could be due to changes in serotonin (5-HT), NO metabolites (nitrite and nitrate), and gamma-aminobutyric acid (GABA) levels. As a result, it was concluded that Black seed has significant neuroprotective effects during germination when compared to ungerminated seed [70].

#### IV. DOSAGE

Black seed is typically supplemented in the form of whole seed, basic seed extract (crushed powder with no further processing or concentration) or seed oil, either of which do not necessitate extensive processing. A 12-week study found that Black seed supplementation at a dose of 2 g/day may improve dyslipidaemia in type 2 diabetic patients. The hypolipidemic effect produced by the 2 g/day dose was not increased by increasing the dose to 3 g/day [49]. Another clinical study showed that a dose of 2 grams/day of Black seed in the form of oral capsules improved total cholesterol, mean arterial pressure and heart rate in type 2 diabetes patients taking oral hypoglycaemic agents [53]. Ground black seeds when combined with 40 mg/d omeprazole, have anti-helicobacter pylori activity that is similar to standard triple therapy [27]. In patients with insulin resistance syndrome, a six-week supplementation of 2.5mL of nigella sativa oil was found to be effective as an add-on therapy [71]. In rats, oral administration of 400 mg/kg body wt of Black seed for 12 days resulted in morphologic improvement in neurodegeneration in the frontal cortex and brain stem following chronic toluene exposure [68].

#### V. TOXICITY

The LD50 in mice was determined to be 104.7 mg/kg after intraperitoneal injection and 870.9 mg/kg after oral ingestion. In contrast, the LD50 in rats was determined to be 57.5 mg/kg after intraperitoneal injection and 794.3 mg/kg after oral ingestion. The LD50 values presented here are approximately 100-150 times greater than the therapeutic dose [72]. A study that looked at the effects of acute and sub chronic administration of thymoquinone (TQ) in male Swiss albino mice discovered that the LD50 value of TQ after acute oral administration is 2.4 g/kg. However, the sub chronic toxicity study in mice treated with 30, 60, and 90 mg/kg/day TQ for 90 days found no mortality or signs of toxicity. Thus, the study concluded that acute oral toxicity of TQ is of a low order and it is safe and well tolerated when given sub chronically.[73]. Daily administration of Black seed aqueous extract (AqE) to mice for six weeks showed no fluctuation in urea and albumin level at 5 doses (2, 6.4, 21, 33, and 60 g/Kg). However, histopathological examination of the liver confirmed hepatotoxicity from 21 g/Kg in the *Mus musculus* mice.[74]. The acute toxicity of Black seed fixed oil was also investigated in mice. The LD50 values were found to be 28.8 ml/kg body wt when given orally and 2.06 ml/kg body wt when given intraperitoneally [75]. As demonstrated by various scientific studies, the minor and/or negligible toxicological effects and wider therapeutic potential of Black seed and its active constituent, thymoquinone support its long-term traditional food and medicinal use.

#### VI. APPLICATION OF BLACK SEED IN FOOD PRODUCTS

##### A. Black seed in Food Industry

Black seed is often used in food as flavouring agents, additive in breads, and pickles due to their low toxicity. Because of the high concentration of fats, proteins, and minerals in the seeds, it is considered a potential candidate for research as a source of these nutrients [76]. Black seed has been used as a spice and food preservative for many years. It is used as a spice in a variety of dishes, including yoghurt, pickles, sauces, and salads [77, 78]. The seed is widely used as a spice for flavouring, particularly in baked goods and cheese. It has been used to make a traditional sweet dish that is eaten with honey and syrup, as well as to sprinkle on bread [79, 80].



### B. Value-added Products

As per studies, Black seed were found to be an excellent source of polyunsaturated fatty acids (PUFAs), phytosterols (PSs), and phospholipids (PhLs). Furthermore, Thymoquinone, the main component, is known to have numerous therapeutic potentials. Because of the seed's composition, it is a potential spice that could be used to develop value-added products that are beneficial to human health. A research was conducted to develop value-added cookies using Black seed oil as a nutraceutical. The findings revealed that it was possible to produce value-added cookies with 6% Black seed oil fortification. [81]

According to a study, chapatis supplemented with Black seeds (5%) and fenugreek seed (0.8%) is a safe and convenient dietary modification to address cardiometabolic risk [82]. In contrast, another study discovered that Metabolic syndrome (MetS) patients who consumed bread with Black seed (3 g powder of black seed and 3 g wheat bran) showed no significant effect on Fasting Blood Glucose (FBG), Blood Pressure (BP), weight, Waist Circumference, and Body Mass Index (BMI), when compared to patients who consumed bread without the seeds [83]. However, one study on obese men found that Black seed reduced these parameters [84]. Thus, it is possible that the effects of black seed on anthropometric parameters are linked to the type of disease that patients suffer from [83].

## VII. CONCLUSION

Plants as medicines have been used from time immemorial for numerous therapeutic purposes and to cure various ailments. Black seed is one such plant whose pharmacological activities were recognised thousands of years ago, but proper scientific research has only recently been conducted. The seed of this traditional medicinal plant have recently gained popularity as dietary supplements because of its very few side effects. Black seed contains numerous phytoconstituents with therapeutic potential, the most important of which is thymoquinone (TQ). Anti-oxidant, anti-inflammatory, anti-microbial, anti-diabetic, anti-hypertensive, anti-lipidemic, anti-cancer, neuroprotective, and other properties of the seed and TQ have been proved in several human and animal trials. Moreover, when combined with various conventional chemotherapeutic agents, the seeds substantially boost the efficacy of the treatment, minimising the dosage of the concurrently used medicines while also combating drug resistance. Certain studies contradict the therapeutic potential of the seeds, but the benefits have always outweighed the drawbacks.

The seeds, which have wider safety margins and commendable efficacy against a wide range of ailments, could be a potential herbal remedy to be analysed in clinical trials for a variety of conditions. Extensive research with Black seed could aid in the development of novel and reliable alternative and/or complementary medicines. Furthermore, including seeds and its various forms, such as powder, extracts, and oils, in the diet at the recommended dosages may enhance its benefits.

## REFERENCES

- [1] Padhye, S., Banerjee, S., Ahmad, A., Mohammad, R., & Sarkar, F. H. (2008). From here to eternity - the secret of Pharaohs: Therapeutic potential of black cumin seeds and beyond. *Cancer therapy*, 6(b), 495–510.
- [2] Ali, M Abbas & Sayeed, M. & Alam, M. & Yeasmin, Sarmina & Khan, Astaq & Muhamad, Ida. (2012). Characteristics of oils and nutrient contents of *Nigella sativa* Linn. and *Trigonella foenum-graecum* seeds. *Bulletin of the Chemical Society of Ethiopia*. 26. 10.4314/bcese. v26i1.6.
- [3] Beheshti, F., Khazaei, M., & Hosseini, M. (2016). Neuropharmacological effects of *Nigella sativa*. *Avicenna journal of phytomedicine*, 6(1), 104–116.
- [4] Ali, S. A., Parveen, N., & Ali, A. S. (2018). Links between the Prophet Muhammad (PBUH) recommended foods and disease management: A review in the light of modern superfoods. *International journal of health sciences*, 12(2), 61–69.
- [5] Sahih al-Bukhari 5687, Chapter 7: (To treat with) black cumin (*Nigella* seeds), Book 76: Medicine <https://sunnah.com/bukhari:5687>
- [6] New King James Version, 1982, Isaiah 28:25 <https://www.biblegateway.com/passage/?search=Isaiah%2028%3A25&version=NKJV>
- [7] Al-Ali, A., Alkhawajah, A. A., Randhawa, M. A., & Shaikh, N. A. (2008). Oral and intraperitoneal LD50 of thymoquinone, an active principle of *Nigella sativa*, in mice and rats. *Journal of Ayub Medical College, Abbottabad: JAMC*, 20(2), 25–27.
- [8] Darakhshan, S., Bidmeshki Pour, A., Hosseinzadeh Colagar, A., & Sisakhtezhad, S. (2015). Thymoquinone and its therapeutic potentials. *Pharmacological research*, 95-96, 138–158. <https://doi.org/10.1016/j.phrs.2015.03.011>
- [9] Atta MB. Some characteristics of nigella (*Nigella sativa* L.) seed cultivated in Egypt and its lipid profile. *Food Chemistry*. 2003;83(1):63–68
- [10] Al-Jasass, F. M., & Al-Jasser, M. S. (2012). Chemical composition and fatty acid content of some spices and herbs under Saudi Arabia conditions. *The ScientificWorldJournal*, 2012, 859892. <https://doi.org/10.1100/2012/859892>
- [11] Dinaganar S, Sridhar S and Eganathan P: Chemical composition and antioxidant activities of black seed oil (*Nigella sativa* L.). *Int J Pharm Sci Res* 2016; 7(11): 4473-79. doi: 10.13040/IJPSR.0975-8232.7(11).4473-79.
- [12] Mohamed Ezzat Abd El-Hack, Mahmoud Alagawany, Mayada Ragab Farag, Ruchi Tiwari, Kumaragurubaran Karthik and Kuldeep Dhama, 2016. Nutritional, Healthical and Therapeutic Efficacy of Black Cumin (*Nigella sativa*) in Animals, Poultry and Humans. *International Journal of Pharmacology*, 12: 232-248. DOI: [10.3923/ijp.2016.232.248](https://doi.org/10.3923/ijp.2016.232.248)
- [13] Salas-Salvadó, J., Márquez-Sandoval, F., & Bulló, M. (2006). Conjugated linoleic acid intake in humans: a systematic review focusing on its effect on body composition, glucose, and lipid metabolism. *Critical reviews in food science and nutrition*, 46(6), 479–488. <https://doi.org/10.1080/10408390600723953>
- [14] Javed, S., Shahid, A.A., Haider, M., Umeera, A., Ahmad, R., & Mushtaq, S. (2012). Nutritional, phytochemical potential and pharmacological evaluation of *Nigella Sativa* (Kalonji) and *Trachyspermum Ammi* (Ajwain). *Journal of Medicinal Plants Research*, 6, 768-775.



- [15] Krishnapura Srinivasan, Cumin (*Cuminum cyminum*) and black cumin (*Nigella sativa*) seeds: traditional uses, chemical constituents, and nutraceutical effects, *Food Quality and Safety*, Volume 2, Issue 1, March 2018, Pages 1–16, <https://doi.org/10.1093/fqsafe/fvx031>
- [16] Ali, B. H., & Blunden, G. (2003). Pharmacological and toxicological properties of *Nigella sativa*. *Phytotherapy research: PTR*, 17(4), 299–305. <https://doi.org/10.1002/ptr.1309>
- [17] Amin, B., & Hosseinzadeh, H. (2016). Black Cumin (*Nigella sativa*) and Its Active Constituent, Thymoquinone: An Overview on the Analgesic and Anti-inflammatory Effects. *Planta medica*, 82(1-2), 8–16. <https://doi.org/10.1055/s-0035-1557838>
- [18] Dzoyem, Jean & Kuete, Victor & Eloff, Jacobus. (2014). Biochemical Parameters in Toxicological Studies in Africa: Significance, Principle of Methods, Data Interpretation and Use in Plant Screenings. 10.1016/B978-0-12-800018-2.00023-6.
- [19] Mostafa, R. M., Moustafa, Y. M., Mirghani, Z., AlKusayer, G. M., & Moustafa, K. M. (2013). Antioxidant effect of garlic (*Allium sativum*) and black seeds (*Nigella sativa*) in healthy postmenopausal women. *SAGE open medicine*, 1, 2050312113517501. <https://doi.org/10.1177/2050312113517501>
- [20] Namazi, N., Mahdavi, R., Alizadeh, M., & Farajnia, S. (2015). Oxidative Stress Responses to *Nigella sativa* Oil Concurrent with a Low-Calorie Diet in Obese Women: A Randomized, Double-Blind Controlled Clinical Trial. *Phytotherapy research: PTR*, 29(11), 1722–1728. <https://doi.org/10.1002/ptr.5417>
- [21] Sankaranarayanan, C., & Pari, L. (2011). Thymoquinone ameliorates chemical induced oxidative stress and  $\beta$ -cell damage in experimental hyperglycemic rats. *Chemo-biological interactions*, 190(2-3), 148–154. <https://doi.org/10.1016/j.cbi.2011.02.029>
- [22] Ahmad, S., & Beg, Z. H. (2016). Evaluation of therapeutic effect of omega-6 linoleic acid and thymoquinone enriched extracts from *Nigella sativa* oil in the mitigation of lipidemic oxidative stress in rats. *Nutrition (Burbank, Los Angeles County, Calif.)*, 32(6), 649–655. <https://doi.org/10.1016/j.nut.2015.12.003>
- [23] Houghton, P. J., Zarka, R., de las Heras, B., & Hoult, J. R. (1995). Fixed oil of *Nigella sativa* and derived thymoquinone inhibit eicosanoid generation in leukocytes and membrane lipid peroxidation. *Planta medica*, 61(1), 33–36. <https://doi.org/10.1055/s-2006-957994>
- [24] Ikhsan, M., Hidayati, N., Maeyama, K., & Nurwidya, F. (2018). *Nigella sativa* as an anti-inflammatory agent in asthma. *BMC research notes*, 11(1), 744. <https://doi.org/10.1186/s13104-018-3858-8>
- [25] Harshal N Pise, Sudhir L Padwal (2017) Evaluation of anti-inflammatory activity of *Nigella sativa*: An experimental study. *National Journal of Physiology, Pharmacy and Pharmacology*, 7 (7), 707-711. doi:10.5455/njppp.2017.7.0204705032017
- [26] Gheita, T. A., & Kenawy, S. A. (2012). Effectiveness of *Nigella sativa* oil in the management of rheumatoid arthritis patients: a placebo-controlled study. *Phytotherapy research: PTR*, 26(8), 1246–1248. <https://doi.org/10.1002/ptr.3679>
- [27] Salem, E. M., Yar, T., Bamosa, A. O., Al-Quorain, A., Yasawy, M. I., Alsulaiman, R. M., & Randhawa, M. A. (2010). Comparative study of *Nigella Sativa* and triple therapy in eradication of *Helicobacter Pylori* in patients with non-ulcer dyspepsia. *Saudi journal of gastroenterology : official journal of the Saudi Gastroenterology Association*, 16(3), 207–214. <https://doi.org/10.4103/1319-3767.65201>
- [28] Niakan, M., & Miri, S., & Naseri, M., & Karimi, M., & Mansouri, S. (2006). In Vitro Anti-Staphylococcus Aureus Activity of *Nigella Sativa* L. Seed Oil Extract, Compared with Cxm, Cec, Man and Caz Antibiotics. *Journal Of Medicinal Plants*, 5(19), 29-33. <https://www.sid.ir/en/journal/ViewPaper.aspx?id=60560>
- [29] Hannan, A., Saleem, S., Chaudhary, S., Barkaat, M., & Arshad, M. U. (2008). Anti bacterial activity of *Nigella sativa* against clinical isolates of methicillin resistant *Staphylococcus aureus*. *Journal of Ayub Medical College, Abbottabad : JAMC*, 20(3), 72–74.
- [30] Mahmoudvand, H., Sepahvand, A., Jahanbakhsh, S., Ezatpour, B., & Ayatollahi Mousavi, S. A. (2014). Evaluation of antifungal activities of the essential oil and various extracts of *Nigella sativa* and its main component, thymoquinone against pathogenic dermatophyte strains. *Journal de mycologie medicale*, 24(4), e155–e161. <https://doi.org/10.1016/j.mycmed.2014.06.048>
- [31] Piras, A., Rosa, A., Marongiu, B., Porcedda, S., Falconieri, D., Dessi, MA, ... Ozcelik, B.(2013). Chemical composition and in vitro bioactivity of the volatile and fixed oils of *Nigella sativa* L. extracted by supercritical carbon dioxide. *Industrial Crops and Products*, vol.46, 317-323.
- [32] Taha, M., Azeiz, A.A., & Saudi, W. (2010). Antifungal Effect of Thymol, Thymoquinone and Thymohydroquinone Against Yeasts, Dermatophytes And Non-Dermatophyte Molds Isolated From Skin And Nails Fungal Infections. *The Egyptian Journal of Biochemistry and Molecular Biology*, 28.
- [33] Daryabeygi-Khotbehsara, R., Golzarand, M., Ghaffari, M. P., & Djafarian, K. (2017). *Nigella sativa* improves glucose homeostasis and serum lipids in type 2 diabetes: A systematic review and meta-analysis. *Complementary therapies in medicine*, 35, 6–13. <https://doi.org/10.1016/j.ctim.2017.08.016>
- [34] R. Mohtashami , Blood glucose lowering effects of *Nigella sativa* l.seeds oil in healthy volunteers:a randomized, double-blind, placebo-controlled clinical trial, *J. Med. Plants*. 2011; 10 (39): 90-94
- [35] Badar, A., Kaatabi, H., Bamosa, A., Al-Elq, A., Abou-Hozzaifa, B., Lebda, F., Alkhadra, A., & Al-Almaie, S. (2017). Effect of *Nigella sativa* supplementation over a one-year period on lipid levels, blood pressure and heart rate in type-2 diabetic patients receiving oral hypoglycemic agents: nonrandomized clinical trial. *Annals of Saudi medicine*, 37(1), 56–63. <https://doi.org/10.5144/0256-4947.2017.56>
- [36] Bamosa, A., Kaatabi, H., Badar, A., Al-Khadra, A., Al Elq, A., Abou-Hozzaifa, B., Lebda, F., & Al-Almaie, S. (2015). *Nigella sativa*: A potential natural protective agent against cardiac dysfunction in patients with type 2 diabetes mellitus. *Journal of family & community medicine*, 22(2), 88–95. <https://doi.org/10.4103/2230-8229.155380>
- [37] Rachman, Pradika & Akrom, Akrom & Darmawan, E. (2017). The efficacy of black cumin seed (*Nigella sativa*) oil and hypoglycemic drug combination to reduce HbA1c level in patients with metabolic syndrome risk. *IOP Conference Series: Materials Science and Engineering*, 259. 012018. 10.1088/1757-899X/259/1/012018.
- [38] Ibrahim, R. M., Hamdan, N. S., Ismail, M., Saini, S. M., Abd Rashid, S. N., Abd Latiff, L., & Mahmud, R. (2014). Protective Effects of *Nigella sativa* on Metabolic Syndrome in Menopausal Women. *Advanced pharmaceutical bulletin*, 4(1), 29–33. <https://doi.org/10.5681/apb.2014.005>
- [39] Hannan, J., Ansari, P., Haque, A., Sanju, A., Huzaifa, A., Rahman, A., Ghosh, A., & Azam, S. (2019). *Nigella sativa* stimulates insulin secretion from isolated rat islets and inhibits the digestion and absorption of (CH<sub>2</sub>O)<sub>n</sub> in the gut. *Bioscience reports*, 39(8), BSR20190723. <https://doi.org/10.1042/BSR20190723>
- [40] Mohebbati R, Abbasnezhad A, Havakhah S, Mousavi M. The Effect of *Nigella Sativa* on Renal Oxidative Injury in Diabetic Rats. *Saudi J Kidney Dis Transpl* 2020;31:775-86
- [41] Nourbar, E., Mirazi, N., Yari, S., Rafieian-Kopaei, M., & Nasri, H. (2019). Effect of Hydroethanolic Extract of *Nigella sativa* L. on Skin Wound Healing Process in Diabetic Male Rats. *International journal of preventive medicine*, 10, 18. [https://doi.org/10.4103/ijpvm.IJPVM\\_276\\_18](https://doi.org/10.4103/ijpvm.IJPVM_276_18)
- [42] Ghilissi, Zohra & Hamden, Khaled & Saoudi, Mongi & Sahnoun, Zouheir & Zeghal, Khaled & El Feki, Abdelfattah & Hakim, Ahmed. (2012). Effect of *Nigella sativa* seeds on reproductive system of male diabetic rats. *African Journal of Pharmacy and Pharmacology*. 6.

- [43] World Health Organization Institute for Public Health: Global status report on noncommunicable diseases. The third national health and morbidity survey. 2010, Geneva: World Health Organization Press
- [44] Mc Namara, K., Alzubaidi, H., & Jackson, J. K. (2019). Cardiovascular disease as a leading cause of death: how are pharmacists getting involved?. *Integrated pharmacy research & practice*, 8, 1–11. <https://doi.org/10.2147/IPRP.S133088>
- [45] Gilani AH, Jabeen Q, Khan MA: A review of medicinal uses and pharmacological activities of Nigella sativa. *Pak J Biol Sci*. 2004, 7: 441–451.
- [46] Sabzghabae AM, Dianatkah M, Sarrafzadegan N, Asgary S, Ghannadi A: Clinical evaluation of nigella sativa seeds for the treatment of hyperlipidemia: a randomized, placebo controlled clinical trial. *Med Arh*. 2012, 66: 198–200. 10.5455/medarh.2012.66.198-200.
- [47] Sen N, Kar Y, Tekeli Y: Antioxidant activities of black cumin (Nigella sativa L.) seed cultivating in different regions in Turkey. *J Food Biochem*. 2010, 34: 105–119.
- [48] Farhangi, M. A., Dehghan, P., & Tajmiri, S. (2018). Powdered black cumin seeds strongly improves serum lipids, atherogenic index of plasma and modulates anthropometric features in patients with Hashimoto's thyroiditis. *Lipids in health and disease*, 17(1), 59. <https://doi.org/10.1186/s12944-018-0704-x>
- [49] Kaatabi, H., Bamosa, A. O., Lebda, F. M., Al Elq, A. H., & Al-Sultan, A. I. (2012). Favorable impact of Nigella sativa seeds on lipid profile in type 2 diabetic patients. *Journal of family & community medicine*, 19(3), 155–161. <https://doi.org/10.4103/2230-8229.102311>
- [50] Ibrahim, R.M., Hamdan, N.S., Mahmud, R. et al. A randomised controlled trial on hypolipidemic effects of Nigella Sativa seeds powder in menopausal women. *J Transl Med* 12, 82 (2014). <https://doi.org/10.1186/1479-5876-12-82>
- [51] Al-Naqeep, G., Al-Zubairi, A. S., Ismail, M., Amom, Z. H., & Esa, N. M. (2011). Antiatherogenic Potential of Nigella sativa Seeds and Oil in Diet-Induced Hypercholesterolemia in Rabbits. Evidence-based complementary and alternative medicine : eCAM, 2011, 213628. <https://doi.org/10.1093/ecam/neaq071>
- [52] Vasant, O. K., Vijay, B. G., Virbhadrappa, S. R., Dilip, N. T., Ramahari, M. V., & Laxamanrao, B. S. (2012). Antihypertensive and Diuretic Effects of the Aqueous Extract of Colocasia esculenta Linn. Leaves in Experimental Paradigms. *Iranian journal of pharmaceutical research : IJPR*, 11(2), 621–634.
- [53] Badar, A., Kaatabi, H., Bamosa, A., Al-Elq, A., Abou-Hozafa, B., Lebda, F., Alkhadra, A., & Al-Almaie, S. (2017). Effect of Nigella sativa supplementation over a one-year period on lipid levels, blood pressure and heart rate in type-2 diabetic patients receiving oral hypoglycemic agents: nonrandomized clinical trial. *Annals of Saudi medicine*, 37(1), 56–63. <https://doi.org/10.5144/0256-4947.2017.56>
- [54] Dehkordi, F. R., & Kamkhah, A. F. (2008). Antihypertensive effect of Nigella sativa seed extract in patients with mild hypertension. *Fundamental & clinical pharmacology*, 22(4), 447–452. <https://doi.org/10.1111/j.1472-8206.2008.00607.x>
- [55] Fallah Huseini, H., Amini, M., Mohtashami, R., Ghamarchehre, M. E., Sadeqi, Z., Kianbakht, S., & Fallah Huseini, A. (2013). Blood pressure lowering effect of Nigella sativa L. seed oil in healthy volunteers: a randomized, double-blind, placebo-controlled clinical trial. *Phytotherapy research : PTR*, 27(12), 1849–1853. <https://doi.org/10.1002/ptr.4944>
- [56] Zaoui, A., Cherrah, Y., Lacaille-Dubois, M. A., Settaf, A., Amarouch, H., & Hassar, M. (2000). Effets diurétiques et hypotenseurs de Nigella sativa chez le rat spontanément hypertendu [Diuretic and hypotensive effects of Nigella sativa in the spontaneously hypertensive rat]. *Therapie*, 55(3), 379–382.
- [57] Jaarin, K., Foong, W. D., Yeoh, M. H., Kamarul, Z. Y., Qodriyah, H. M., Azman, A., Zuhair, J. S., Juliana, A. H., & Kamisah, Y. (2015). Mechanisms of the antihypertensive effects of Nigella sativa oil in L-NAME-induced hypertensive rats. *Clinics (Sao Paulo, Brazil)*, 70(11), 751–757. [https://doi.org/10.6061/clinics/2015\(11\)07](https://doi.org/10.6061/clinics/2015(11)07)
- [58] Bourgou, S., Ksouri, R., Bellila, A., Skandrani, I., Falleh, H., & Marzouk, B. (2008). Phenolic composition and biological activities of Tunisian Nigella sativa L. shoots and roots. *Comptes rendus biologiques*, 331(1), 48–55. <https://doi.org/10.1016/j.crv.2007.11.001>
- [59] Khan, M. A., Chen, H. C., Tania, M., & Zhang, D. Z. (2011). Anticancer activities of Nigella sativa (black cumin). *African journal of traditional, complementary, and alternative medicines : AJTCAM*, 8(5 Suppl), 226–232. <https://doi.org/10.4314/ajtcam.v8i5S.10>
- [60] Gali-Muhtasib, H., Diab-Assaf, M., Boltze, C., Al-Hmaira, J., Hartig, R., Roessner, A., & Schneider-Stock, R. (2004). Thymoquinone extracted from black seed triggers apoptotic cell death in human colorectal cancer cells via a p53-dependent mechanism. *International journal of oncology*, 25(4), 857–866.
- [61] Salim, E. I., & Fukushima, S. (2003). Chemopreventive potential of volatile oil from black cumin (Nigella sativa L.) seeds against rat colon carcinogenesis. *Nutrition and cancer*, 45(2), 195–202. [https://doi.org/10.1207/S15327914NC4502\\_09](https://doi.org/10.1207/S15327914NC4502_09)
- [62] Mabrouk, G. M., Moselhy, S. S., Zohny, S. F., Ali, E. M., Helal, T. E., Amin, A. A., & Khalifa, A. A. (2002). Inhibition of methylnitrosourea (MNU) induced oxidative stress and carcinogenesis by orally administered bee honey and Nigella grains in Sprague Dawley rats. *Journal of experimental & clinical cancer research: CR*, 21(3), 341–346.
- [63] Yi, T., Cho, S. G., Yi, Z., Pang, X., Rodriguez, M., Wang, Y., Sethi, G., Aggarwal, B. B., & Liu, M. (2008). Thymoquinone inhibits tumor angiogenesis and tumor growth through suppressing AKT and extracellular signal-regulated kinase signaling pathways. *Molecular cancer therapeutics*, 7(7), 1789–1796. <https://doi.org/10.1158/1535-7163.MCT-08-0124>
- [64] El-Mahdy, M. A., Zhu, Q., Wang, Q. E., Wani, G., & Wani, A. A. (2005). Thymoquinone induces apoptosis through activation of caspase-8 and mitochondrial events in p53-null myeloblastic leukemia HL-60 cells. *International journal of cancer*, 117(3), 409–417. <https://doi.org/10.1002/ijc.21205>
- [65] Kruidering, M., & Evan, G. I. (2000). Caspase-8 in apoptosis: the beginning of "the end"? *IUBMB life*, 50(2), 85–90. <https://doi.org/10.1080/713803693>
- [66] Alireza Tavakkoli, Hossein Hosseinzadeh, Chapter 21 - Nigella sativa L. and thymoquinone as neuroprotective antioxidants, Oxidative Stress and Dietary Antioxidants in Neurological Diseases, Academic Press, 2020, Pages 325–341, ISBN 9780128177808, <https://doi.org/10.1016/B978-0-12-817780-8.00021-9>.
- [67] Hosseinzadeh, H., Parvardeh, S., Asl, M. N., Sadeghnia, H. R., & Ziaee, T. (2007). Effect of thymoquinone and Nigella sativa seeds oil on lipid peroxidation level during global cerebral ischemia-reperfusion injury in rat hippocampus. *Phytotherapy medicine : international journal of phytotherapy and phytopharmacology*, 14(9), 621–627. <https://doi.org/10.1016/j.phymed.2006.12.005>
- [68] Kanter, M. Protective Effects of Nigella sativa on the Neuronal Injury in Frontal Cortex and Brain Stem After Chronic Toluene Exposure. *Neurochem Res* 33, 2241 (2008). <https://doi.org/10.1007/s11064-008-9702-0>
- [69] Ismail, Norsharina & Ismail, Maznah & Latiff, Latiffah & Mazlan, Musalmah & Mariod, Abdalbasit. (2008). Black cumin seed (Nigella Sativa Linn.) Oil and its fractions protect against beta amyloid peptide induced toxicity in primary cerebellar granule neurons. *Journal of Food Lipids*. 15. 519 - 533. 10.1111/j.1745-4522.2008.00137.x.
- [70] Islam, M. H., Ahmad, I. Z., & Salman, M. T. (2015). Neuroprotective effects of Nigella sativa extracts during germination on central nervous system. *Pharmacognosy magazine*, 11(Suppl 1), S182–S189. <https://doi.org/10.4103/0973-1296.157729>

- [71] Najmi, A., Nasiruddin, M., Khan, R. A., & Haque, S. F. (2008). Effect of *Nigella sativa* oil on various clinical and biochemical parameters of insulin resistance syndrome. *International journal of diabetes in developing countries*, 28(1), 11–14. <https://doi.org/10.4103/0973-3930.41980>
- [72] Al-Ali, A., Alkhwajah, A. A., Randhawa, M. A., & Shaikh, N. A. (2008). Oral and intraperitoneal LD50 of thymoquinone, an active principle of *Nigella sativa*, in mice and rats. *Journal of Ayub Medical College, Abbottabad : JAMC*, 20(2), 25–27.
- [73] Badary O. A., Al-Shabanah O. A., Nagi M. N., Al-Bekairi A. M., Elmazar M. M. A. Acute and subchronic toxicity of thymoquinone in mice. *Drug Development Research*. 1998;44(2-3):56–61.
- [74] Bensiamer-Touati, K., Kacimi, G., Haffaf, E. M., Berdja, S., & Aouichat-Bouguerra, S. (2017). In Vivo Subacute Toxicity and Antidiabetic Effect of Aqueous Extract of *Nigella sativa*. *Evidence-based complementary and alternative medicine : eCAM*, 2017, 8427034. <https://doi.org/10.1155/2017/8427034>
- [75] Zaoui, A., Cherrah, Y., Mahassini, N., Alaoui, K., Amarouch, H., & Hassar, M. (2002). Acute and chronic toxicity of *Nigella sativa* fixed oil. *Phytomedicine : international journal of phytotherapy and phytopharmacology*, 9(1), 69–74. <https://doi.org/10.1078/0944-7113-00084>
- [76] Dubey, P.N. & Singh, Balraj & Mishra, Brijesh & Kant, Krishna & Solanki, Ramesh. (2016). *Nigella (Nigella sativa)*: A high value seed spice with immense medicinal potential. *Indian Journal of Agricultural Sciences*. 86. 967-979.
- [77] Hajhashemi, V., Ghannadi, A., & Jafarabadi, H. (2004). Black cumin seed essential oil, as a potent analgesic and antiinflammatory drug. *Phytotherapy research : PTR*, 18(3), 195–199. <https://doi.org/10.1002/ptr.1390>
- [78] Tiruppur Venkatachallam, S. K., Pattekan, H., Divakar, S., & Kadimi, U. S. (2010). Chemical composition of *Nigella sativa* L. seed extracts obtained by supercritical carbon dioxide. *Journal of food science and technology*, 47(6), 598–605. <https://doi.org/10.1007/s13197-010-0109-y>
- [79] Hamrouni-Sellami I, Kchouk ME, Marzoul B. Lipid and aroma composition of black cumin (*Nigella sativa* L.) Seeds from Tunisia. *J Food Biochem*. 2008;32:335–352. doi: 10.1111/j.1745-4514.2008.00161.x.
- [80] Cheikh-Rouhou S, Besbes S, Hentati B, Blecker C, Deroanne C, Attia H. *Nigella sativa* L.: chemical composition and physicochemical characteristics of lipid fraction. *Food Chem*. 2007;101:673–681. doi: 10.1016/j.foodchem.2006.02.022.
- [81] D. T. Bornare, jafir y. Pathan, shaikh tausif ahmed, 2015, extraction and utilization of *nigella sativa* l. Oil in development of value-added cookies, *international journal of engineering research & technology (ijert)* volume 04, issue 08 (august 2015), <http://dx.doi.org/10.17577/ijertv4is080417>
- [82] Rao, A. S., Hegde, S., Pacioretty, L. M., DeBenedetto, J., & Babish, J. G. (2020). *Nigella sativa* and *Trigonella foenum-graecum* Supplemented Chapatis Safely Improve HbA1c, Body Weight, Waist Circumference, Blood Lipids, and Fatty Liver in Overweight and Diabetic Subjects: A Twelve-Week Safety and Efficacy Study. *Journal of medicinal food*, 23(9), 905–919. <https://doi.org/10.1089/jmf.2020.0075>
- [83] Mohtashami A. (2019). Effects of Bread with *Nigella Sativa* on Blood Glucose, Blood Pressure and Anthropometric Indices in Patients with Metabolic Syndrome. *Clinical nutrition research*, 8(2), 138–147. <https://doi.org/10.7762/cnr.2019.8.2.138>
- [84] Datau, E. A., Wardhana, Surachmanto, E. E., Pandelaki, K., Langi, J. A., & Fias (2010). Efficacy of *Nigella sativa* on serum free testosterone and metabolic disturbances in central obese male. *Acta medica Indonesiana*, 42(3), 130–134.





10.22214/IJRASET



45.98



IMPACT FACTOR:  
7.129



IMPACT FACTOR:  
7.429



# INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Call : 08813907089  (24\*7 Support on Whatsapp)