Original article

Nutritional value, functional properties and nutraceutical applications of black cumin (*Nigella sativa* L.): an overview

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Summary Non-conventional seeds are being considered because their constituents have unique chemical properties and may augment the supply of nutritional and functional products. Black cumin (*Nigella sativa L.*) seeds and its crude or essential oils have been widely used in traditional nutritional and medicinal applications. Consequently, black cumin has been extensively studied for its nutritional value and biological activities. The black cumin oilseed had been shown to be anticancer, antidiabetic, antiradical and immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepatoprotective, antihypertensive and renal protective. Moreover, black seeds have many antioxidative properties and activities. In consideration of potential utilisation, detailed knowledge on the composition of black cumin oilseed is of major importance. The diversity of applications to which black cumin can be put gives this oilseed great industrial importance. This review summarises the nutritional value, functional properties and nutraceutical applications of black cumin (*N. sativa* L.) oilseeds.

Keywords Antioxidant compounds, bioactive lipids, black cumin, crude seed oil, essential oil, fatty acids, *Nigella sativa* L., radical scavenging activity, thymoquinone.

Introduction

Black cumin (*Nigella sativa* L.) is one of the most revered medicinal seeds in history. The best seeds come from Egypt where they grow under almost perfect conditions in oases where they are watered until the seed pods form. Although black cumin seed is mentioned in the Bible as well as in the words of the Prophet Mohammed, it was not carefully researched until about 40 years ago. Since this time, several studies have been conducted. The popularity of the plant was highly enhanced by the ideological belief in the herb as a cure for multiple diseases. In fact, this plant has occupied special place for its wide range of medicinal value. Consequently, black cumin has been extensively studied particularly, which justifies its broad traditional therapeutic value. The reason might be found in the complex chemical composition of the seeds. Black cumin seed has over 100 different chemical constituents, including abundant sources of all the essential fatty acids (Ramadan & Moersel, 2002a). Although it is the oil that most often used medicinally, the seeds are a bit spicy and are often used whole in cooking curries, pastries and Mediterranean cheeses. *Nigella sativa* seed has very little aroma but are carminative, meaning they tend to aid digestion and relieve gases in the stomach and intestines. They aid peristalsis and elimination. The essential oil of black cumin is antimicrobial and helps to rid the intestines of worms. Black cumin is regarded by many as a panacea and may therefore not be taken seriously by some, but for those inclined to dismiss folklore, it should be noted that these humble seeds have been found superior to almost every other natural remedy when used for autoimmune disorders, conditions in which patients suffer greatly because their own systems attack their bodies (Kapoor, 1990; Evans, 1996; Ramadan & Moersel, 2002a).

Black cumin is very appreciated for its seeds with a strong, hot, peppery taste. Oil is extracted from them, which was a precious remedy of the Egyptian and named for its benefits (Pharaos' oil). A water-retentive protein is extracted from the seeds, which are capable of helping the skin resist free radical aggression (Evans, 1996). The seeds have been used to promote health and fight disease for centuries especially in the Southeast Asia and Middle East. In Arabic countries, it is called Al-Habat-El-Sauda or Haba-Al-Barka. The plant is widely grown as an annual herb in different parts of the world (Nadkarni, 1976, Ramadan & Moersel, 2002a). This plant has been a great focus of research for centuries and has several traditional uses and

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consequently has been extensively studied for its chemical constituents and biological activities.

Traditional applications of black cumin seed

Black cumin has many nutritional and pharmaceutical uses. The seed can be added to tea, coffee, casseroles or breads, used in canning, or extracted in wine or vinegar. The ground seed could be mixed with honey or sprinkled on salads. In addition, most people seeking the benefits of black cumin take the oil in capsule form. However, some people use the oil externally, for beauty as well as for treating skin conditions such as psoriasis and eczema. A mixture of oil with beeswax can be used for burns, skin infections, moisturisers, joint pain reliever, or an anti-wrinkle agent. In addition, black cumin seeds are extensively used as natural remedy and the seeds are extensively used as spice, carminative, condiment and aromatic (Atta-ur-Rahman *et al.*, 1992; Al-Gaby, 1998). Traditionally, they have been used as diuretic, diaphoretic, stomachic, liver tonic and digestive. As a confection with other ingredients, they are used in diarrhoea, indigestion, dyspepsia and sour belching as well as a breath deodorizer. The seeds are given with buttermilk to cure obstinate hiccups and are also useful in loss of appetite, vomiting, dropsy and puerperal diseases. In different combinations with other ingredients, the seeds have been used in obesity and dyspnoea. They have anti-bilious property and are administered internally in intermittent fevers. The herb has been regarded as a valuable remedy (Nadkarni, 1976; Usmanghani *et al.*, 1997) in hepatic and digestive disorders as well as stimulant in a variety of conditions ascribed to cold humours. They have also been used in chronic headache and migraine. They have been useful in mercury poisoning, sores and leprosy. Brayed in water, its application removes swellings from hands and feet. Black cumin seed is also used externally in leucoderma, alopecia, eczema, freckles and pimples. The seeds have also been used as anthelmintic and antibacterial agent (Kapoor, 1990; Evans, 1996; Al-Gaby, 1998, Ramadan & Moersel, 2002a).

Profile of phytochemicals

In view of its wide range of medicinal uses, the plant has undergone extensive phytochemical studies and a variety of compounds been isolated. The seeds contain a yellowish volatile oil (0.5–1.6%), a fixed oil (35.6–41.6%), proteins (22.7%), amino acids (e.g. lysine, leucine, isoleucine, valine, glycine, alanine, phenylalanine, cystine, glutamic acid, aspartic acid, proline, serine, threonine, tryptophan and tyrosine), reducing sugars, mucilage, alkaloids, organic acids, tannins, resins, toxic glucoside, metarbin, bitter principles, glycosidal saponins, melanthin resembling helleborin, melanthigenin, ash, moisture and arabic acid (Duke, 1992; Al-Gaby, 1998). The seeds have also been found to contain crude fibre, minerals (e.g. Fe, Na, Cu, Zn, P and Ca) and vitamins like ascorbic acid, thiamine, niacin, pyridoxine and folic acid (Takruri & Dameh, 1998). Black cumin seed contains fatty acids (e.g. palmitic acid, oleic acid and linoleic acid), terpenoids, aliphatic alcohols and unsaturated hydroxy ketones. Moreover, free sterols, steryl esters, steryl glucosides and acylated steryl glucosides were isolated from the seed oil (Menounos *et al.*, 1986; Ramadan & Moersel, 2003). A novel alkaloid (nigellicine), an isoquinoline alkaloid (nigellimine) and an indazole alkaloid (nigellidine) were isolated from the black cumin seeds (Atta-ur-Rahman *et al.*, 1985, 1992, 1995). The seeds also contain lipase (Duke, 1992). The active constituents of the seeds include the volatile oil consisting of carvone, an unsaturated ketone, terpene or *d*-limonene also called carvene, α-pinene and *p*-cymene. The crystalline active principle, nigellone, is the only constituent of the carbonyl fraction of the oil. Pharmacologically, active constituents of volatile oil (Fig. 1) are thymoquinone, dithymoquinone, thymohydroquinone and thymol (Ghosheh *et al.*, 1999).

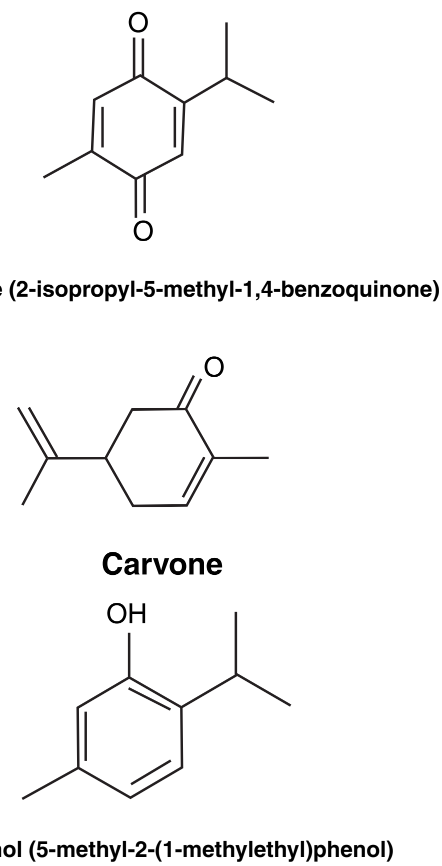

Figure 1 Main active compounds in black cumin volatile oil.

Composition and functional properties of crude fixed oil

In a recent study (Ramadan & Moersel, 2002a,b,c), black cumin seed oil was extracted with two different solvents; *n*-hexane and a mixture of chloroform and methanol (2:1, v/v), the latter was found to contain higher amounts of total lipids. Major fatty acids were linoleic acid, palmitic acid, oleic acid and stearic acid (Table 1). Neutral lipids accounted for about 97% of total crude oil followed by glycolipids and phospholipids, respectively.

Triacylglycerols were the major neutral lipid class (83.1–80.8% of the total neutral lipids), while the neutral lipid profile was characterised by high level of free fatty acids (14.3–16.2% of the total neutral lipids). A good resolution of the triacylglycerol fractions was accomplished employing a gas–liquid chromatography (GLC) equipped with flame ionisation detector (FID). The separation of the triacylglycerol fractions C48:0, C50:1, C52:2 and C54:3 (ECN = 48) as well as C42:0, C48:3 and C54:6 (ECN = 42) has been accomplished. Six triacylglycerol fractions were determined, but two of them, C54:3 (ECN = 48) and C54:6 (ECN = 42), were presented to the extent of 74% or above of the total triacylglycerol content.

Phytosterols isolated from the unsaponifiable fractions were β-sitosterol (1135–1182 μg per g oil) as the main component (Table 1) followed by Δ5-avenasterol (925–1025 μg per g oil), and Δ7-avenasterol (615–809 μg per g oil). Stigmasterol, campesterol and lanosterol were detected in small amounts (Ramadan & Moersel, 2002a). Fat-soluble vitamins and pro-vitamin A (β-carotene) are of particular importance in nutrition. An isocratic normal-phase high-performance liquid chromatography (HPLC) method for fat-soluble vitamin and β-carotene analysis using Zorbax-Sil silica column and ultraviolet (UV) detector was performed (Ramadan & Moersel, 2002b). All tocopherol derivatives were identified in black cumin seed oil (Table 1) wherein α- and γ-isomers were the main constituents. β-Carotene was also measured in high level in black cumin (569–593 μg per g oil).

Total glycolipids were separated from black cumin seed oils by Silica gel chromatography. Different glycolipid subclasses were then identified and separated using HPLC with UV adsorption. Separation was accomplished using Zorbax-Sil (5 μm) column with an isocratic elution by mixed solvents of isooctane/2-propanol (1:1, v/v) and detection at 206 nm (Ramadan & Moersel, 2003). Methods are described for the analysis of glycolipid constituents, sugar and sterols, using GLC equipped with FID. A relatively high level of glycolipids was found in black cumin seed (2.59 g per 100 g oil). Six glycolipid subclasses were detected (Fig. 2), wherein diglucosyldiacylglycerol (DGD) was the prevalent component followed by glucocerebroside (CER). The fatty acid profile of glycolipid fractions from black cumin seed oil was generally similar, wherein linoleic acid (C18:2*n*-6) was the dominating fatty acid followed by oleic acid (C18:1*n*-9). Four sterol moieties were identified in black cumin glycolipid fractions. As the component sugars, glucose was the only sugar detected. The average daily intake of glycolipids in human has been reported to be 140 mg of ASG, 65 mg of SG, 50 mg of CER, 90 mg of MGD and 220 mg of DGD (Sugawara & Miyazawa, 1999). Therefore, it is

Table 1 Analysis of fatty acids (as a percentage of total fatty acids), initial peroxide values (PV), unsaponifiables and total phenolics of black cumin crude seed oil[a]

Compound	Black cumin seed oil	Compound	Black cumin seed oil
C16:0	13.0 ± 0.03	PV (meq kg^{-1})	17.8 ± 0.12
C18:0	3.16 ± 0.01	α-Tocopherol (g kg^{-1})	0.284 ± 0.01
C18:1n-12	ND[b]	β–Tocopherol (g kg^{-1})	0.040 ± 0.01
C18:1n-9	24.1 ± 0.03	γ–Tocopherol (g kg^{-1})	0.225 ± 0.02
C18:2n-6	57.3 ± 0.04	δ–Tocopherol (g kg^{-1})	0.048 ± 0.01
C18:3n-6	ND	β–Carotene (g kg^{-1})	0.593 ± 0.03
C20:2n-6	2.44 ± 0.01	Ergosterol (g kg^{-1})	ND[b]
C22:0	Nd	Campesterol (g kg^{-1})	0.226 ± 0.01
C22:1n-9	Nd	Stigmasterol (g kg^{-1})	0.314 ± 0.02
C20:5n-3	Nd	Lanosterol (g kg^{-1})	0.106 ± 0.01
C22:6n-3	Nd	β–Sitosterol (g kg^{-1})	1.182 ± 0.05
ΣSFA[c]	16.1 ± 0.02	Δ5-Avenasterol (g kg^{-1})	1.025 ± 0.04
ΣMUFA[d]	24.1 ± 0.03	Δ7-Avenasterol (g kg^{-1})	0.809 ± 0.02
ΣPUFA[e]	59.7 ± 0.31	Total unsaponifiables (g kg^{-1})	14.9 ± 0.09
S/P[f]	0.269 ± 0.01	Total phenolics (ppm caffeic acid)	24 ± 0.11

Source: Ramadan *et al.* (2003).
[a]Values given are the mean of three replicates ± SD. [b]nd, not detected. [c]Total saturated fatty acids; [d]Total monounsaturated fatty acids; [e]Total polyunsaturated fatty acids; [f]The ratio of saturated to polyunsaturated fatty acids.

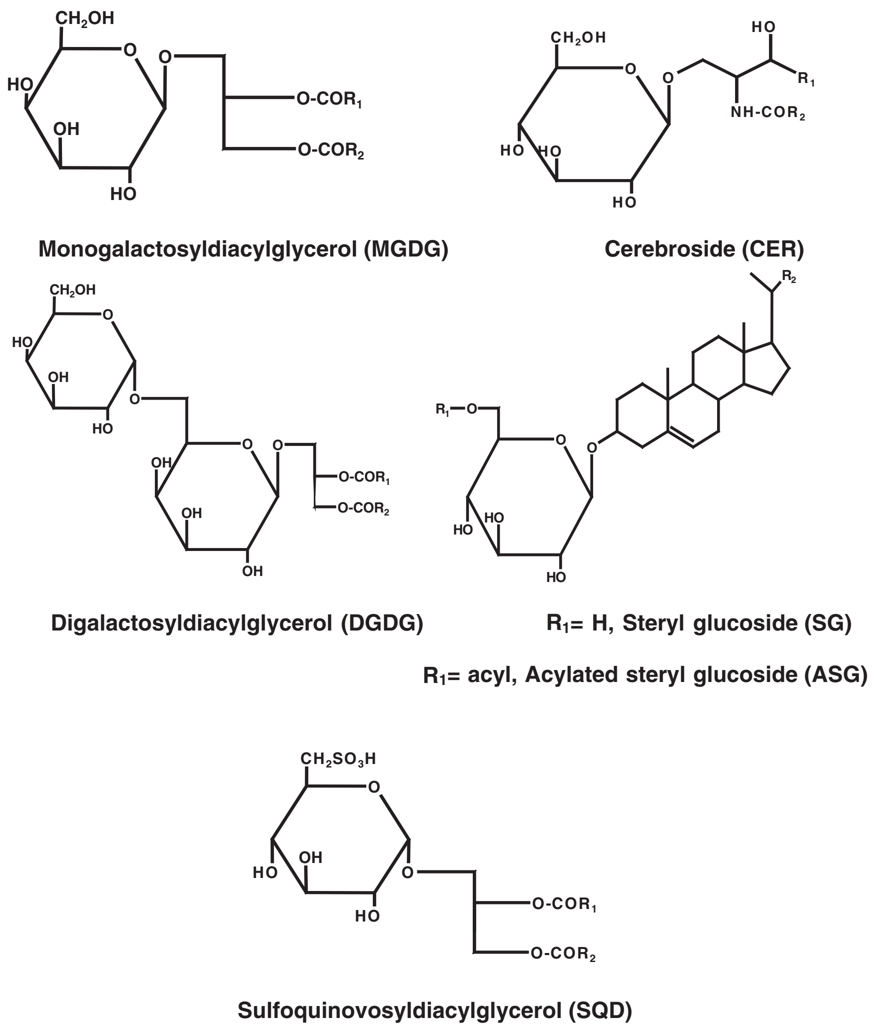

Figure 2 Representative structures of glycolipids subclasses found in black cumin seed oil.

worthy to point out that black cumin seed oil could be an excellent as well as a complete source of glycolipids in diet.

Phospholipid fractions were determined *via* HPLC. Separation was achieved on a silica normal phase column using isooctane/2-propanol/water (6:8:0.6, by volume) as a mobile phase with UV detection at 203 nm. Major phospholipids subclasses were phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine and phosphatidylinositol. Phosphatidylglycerol, *lyso*-phosphatidylethanolamine and *lyso*-phosphatidylcholine were isolated in smaller quantities. The predominant fatty acids present in the individual phospholipid fractions were linoleic, oleic and palmitic acids (Ramadan & Moersel, 2002c). The UV spectra of methanolic solutions of black cumin phenolics exhibited one absorption maxima at 282 nm. The absorption maximum at short wavelength (280 nm) may be due to the presence of *p*-hydroxybenzoic acid and flavone/flavonol derivatives (Ramadan *et al.*, 2003).

Seed oil was stored under accelerated oxidative conditions for 21 days. The progress of oxidation at 60 °C was followed by recording the UV absorptivity and measuring the formation of oxidative products (peroxide and *p*-anisidine values). Inverse relationships were noted between peroxide values and oxidative stabilities and also between secondary oxidation products, measured by *p*-anisidine value and stabilities at termination of the storage. Absorptivity at 232 and 270 nm increased gradually with the increase in time, because of the formation of conjugated dienes and polyenes. In general, oxidative stabilities of the crude oil stronger than its stripped counterparts (Ramadan & Moersel, 2004a).

Moreover, crude black cumin seed oil and its fractions were investigated for their radical scavenging activity (RSA) towards the stable galvinoxyl radical by electron spin resonance spectrometry and towards 1,1-diphenyl-2-picrylhydrazyl radical by spectrophotometric method (Ramadan *et al.*, 2003). Black cumin seed oil and its fractions exhibited the stronger RSA when compared with some crude vegetable oils (Ramadan & Moersel, 2004b). The data correlated well with the total content of polyunsaturated fatty acids, unsaponifiables and phospholipids as well as the initial peroxide values of crude oils. In overall ranking, RSA of oil fractions showed similar patterns wherein the phospholipids exhibited greater activity to scavenge both free radicals followed by glycolipids and triacylglycerols, respectively. The results demonstrate the importance of minor components in crude seed oils on their oxidative stability, which will reflect on their food value and shelf life (Ramadan *et al.*, 2003).

Antioxidant action of volatile oil

The volatile oil and its main active constituent, thymoquinone, are reported to inhibit peroxidation in ox brain phospholipid liposomes (Houghton *et al.*, 1995). Similarly, thymoquinone exhibited protective effect against *ter*-butyl-hydro-peroxide-induced hepatotoxicity and hepatoprotective effect against carbon tetrachloride induced toxicity in mice (Nagi *et al.*, 1999) and rats (El-Dakhakhny *et al.*, 2000). Furthermore, thymoquinone exhibited also renal protective effect in rats through its antioxidant activity. The free radical scavenging (Burits & Bucar, 2000) effects of thymol, thymoquinone and dithymoquinone were studied on the reactions generating reactive oxygen species such as superoxide anion radical, hydroxyl 2-radical and singlet oxygen using chemiluminescence and spectrophotometric methods (Kruk *et al.*, 2000). The hepatoprotective effects, protective effect against doxorubicin-induced nephropathy and that against doxorubicin-induced cardiotoxicity of essential oil and thymoquinone were found *via* the antioxidant mechanism (Al-Shabanah *et al.*, 1998; Nagi *et al.*, 1999; Mansour, 2000; Nagi & Mansour, 2000; Mahmoud *et al.*, 2002; Mansour *et al.*, 2002). On the contrary, the modulating effect of thymoquinone on benzopyrene-induced forestomach tumours in mice and its antitumour effect on 20-methylcholanthrene-induced fibrosarcoma tumorigenesis were found to be partly through its antioxidant effect (Badary *et al.*, 1999; Badary & Gamal-El-Din, 2001). The possible mechanism of the protective effect of thymoquinone against acetic acid-induced colitis in rats was also supposed to be partly its antioxidant action (Mahgoub, 2003).

Hypoglycaemic impact of black cumin seed

In view of the folkloric use of plant mixture extracts for treatment of diabetes in the Middle East, Al-Awadi & Gumaa (1987) studied a plant mixture (black cumin, Myrrh, Gum olybanum and Gum asafoetida) for its blood glucose lowering effect in rats and found it effective. Further studies on the plant mixture containing black cumin revealed that the blood glucose lowering effect was due to the inhibition of hepatic gluconeogenesis and the plant extract mixture may prove to be a useful therapeutic agent in the treatment of non-insulin dependent diabetes mellitus. An aqueous decoction of a plant mixture containing black cumin was found to lower the blood glucose level significantly after oral administration (Al-Awadi *et al.*, 1991; Akhtar & Shah, 1993). The intraperitoneal administration of volatile oil produced a hypoglycaemic effect in normal and alloxan-induced diabetic rabbits (Al-Hader *et al.*, 1993). In a more recent study, the seed extract when given orally decreased the elevated glucose levels in alloxan-induced diabetic rabbits after 2 months of treatment (Meral *et al.*, 2001). Another study was designed to investigate the possible insulinotropic properties of seed oil in Streptozotocin plus Nicotinamide-induced diabetes mellitus in hamsters. After 4 weeks of treatment with oil, decrease in blood glucose level together with increase in serum albumin level were observed. The results showed that the hypoglycaemic effect of seed oil was, at least partly, because of a stimulatory effect on beta cell function with consequent increase in serum insulin level and possess insulinotropic properties in type II-like model (Fararh *et al.*, 2002). The hypoglycaemic effect of black cumin was also supposed to be mediated by extrapancreatic actions rather than by stimulated insulin release (El-Dakhakhny *et al.*, 2000). Additionally, the effect of seed oil on blood glucose concentrations was studied in Streptozotocin-induced diabetic rats. The effect of seed oil and other constituents such as nigellone and thymoquinone were studied on insulin secretions of isolated rat pancreatic islets in the presence of 3, 5.6 or 11.1 mM glucose. Oil significantly lowered the blood glucose concentrations in diabetic rats after 2, 4 and 6 weeks, which was, however, not paralleled by a stimulation of insulin release in the presence of oil, nigellone or thymoquinone; thus indicating the extrapancreatic actions to be responsible for hypoglycaemic effects of black cumin oil. A recent clinical study on human volunteers showed that 1 g of black seeds twice daily caused a decrease in blood glucose level after 2 weeks of oral treatment (Bamosa *et al.*, 1997).

Impacts on immune system and cancer

Black cumin seed and its oil have been traditionally used as a tonic to promote health and prevent diseases. They were reported to exhibit immunopotentiating, immunomodulating and interferon-like activities (Hailat *et al.*, 1995). The ethanolic extract was found to inhibit cancer cells and endothelial cells progression *in vitro* (Medenica *et al*., 1997; Swamy & Tan, 2000). The protective effect of black grains as nutraceuticals was studied on the oxidative stress and carcinogenesis induced by methylnitrosourea in Sprague Dawley rats and it was found to produce about 80% protection against methylnitrosourea-induced oxidative stress, inflammatory response and carcinogenesis (Mabrouk *et al*., 2002). The alcoholic extract also showed cytotoxic activity and was found to cure oral cancers (Salomi *et al*., 1989). Mixture of crude gum, a fixed oil and two purified components of black cumin seed, thymoquinone and dithymoquinone were assayed *in vitro* for their cytotoxicity for several parental and multi-drug resistant human tumour cell lines. Although as much as 1% w/v of the gum or oil was devoid of cytotoxicity, both thymoquinone and dithymoquinone were found to be cytotoxic for several types of human tumour cells (Worthen *et al*., 1998).

The proteins of black cumin fractionated by ion-exchange chromatography were also found to possess immunomodulatory effect. The effect of these proteins on the production of cytokines was further evaluated by using specific enzyme-linked immunosorbent assay. The results, however, showed that the fractionated protein was less effective when compared with whole protein (Haq *et al*., 1999). Topical application of the seed lipid extract inhibited skin carcinogenesis in mice and intraperitoneal administration (100 mg kg^{-1} body weight) delayed the onset of 1 papilloma formation (Salomi *et al*., 1991). The active components of black cumin seed containing certain fatty acids was studied for anti-tumour activities against Ehrlich ascites carcinoma, Dalton's lymphoma ascites and Sarcoma-180 cells *in vitro* and *in vivo*. The active principle showed complete inhibition in *in vivo* and 50% cytotoxicity in *in vitro* studies (Salomi *et al*., 1992). In mice bearing Ehrlich ascites carcinoma xenograft, thymoquinone (from volatile oil) significantly enhanced the anti-tumour effect of ifosfamide (analogue of cyclophosphamide). There was also less weight loss and lower mortality rate when compared with ifosfamide single therapy, thus thymoquinone was found to improve the therapeutic efficacy of ifosfamide by both decreasing ifosfamide-induced nephrotoxicity and improving its anti-tumour activity (Badary, 1999). Another investigation also mentioned that thymoquinone inhibited the benzopyrene-induced forestomach carcinogenesis in mice. The possible modes of action were discussed to be through its antioxidant and anti-inflammatory activities coupled with enhancement of detoxification process (Badary *et al*., 1999). In addition, thymoquinone-induced cytotoxicity was investigated in a study using canine osteosarcoma, its cisplatin-resistant variant, human breast adenocarcinoma and human ovarian adenocarcinoma and Madin-Darby canine cell lines. Thymoquinone-induced cytotoxicity was determined using a proliferation assay (MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay) and apoptosis assays. Effects on the cell cycle were determined using flow cytometry and thymoquinone was found to produce cell cycle arrest (Shoieb *et al*., 2003).

The aqueous and alcoholic extracts of black cumin alone or in combination with H_2O_2 as an oxidative stressor, were found to be effective *in vitro* in inactivating MCF-7 breast cancer cells (Farah & Begum, 2003). The fresh aqueous extract augmented natural killer cells (62.3%) in developing cytotoxicity against YAC *in vitro*. Fresh aqueous extracts appeared to be more potent than old dried extracts or ethanolic extracts (Abuharfeil *et al*., 2000). Aqueous extract was also found to significantly augment the splenic natural killer cells in generating cytotoxicity in mice against YAC tumour targets (Abuharfeil *et al*., 2001). In a study using murine cytomegalovirus as a model, intraperitoneal administration of oil substantially decreased the viral load in liver and spleen. There was an increase in interferon, macrophages and CD4+ T cells and decrease in both number and function of NK cells. On day 10, the virus titre was undetectable in the spleen and liver of infected mice, while positive in controls (Salem & Hossain, 2000). A fraction of the ethanolic extract of black seed was studied in mice against intraperitoneally implanted murine P388 leukaemia and subcutaneously implanted Lewis lung carcinoma cells. The life span of treated mice increased by 153% when compared with dimethyl sulphoxide-treated control mice. Hederin, a triterpene saponin isolated from this fraction produced significant tumour inhibition rates; while, the underlying mechanism(s) of anti-tumour activity of Hederin remained to be established (Kumara & Huat, 2001). In a recent study (Jeong & Choi, 2002), the stimulating effect of hederin on the release of nitric oxide and upregulation of inducible nitric oxide synthase gene expression in mouse macrophages were examined. Thus, showing a mechanism responsible for its biological effects including its anti-tumour activities. In another study (Badary & Gamal-El-Din, 2001), the anti-tumour effect of thymoquinone was investigated both *in vivo* and *in vitro* in male Swiss albino rats on fibrosarcoma induced by 20-methylcholanthrene and it was found to inhibit tumour incidence and tumour burden significantly. The possible modes of action were discussed as its antioxidant activity and interference with DNA synthesis coupled with enhancement of detoxification processes.

Antimicrobial effects

Black cumin extract and its constituents have been extensively studied for its their antimicrobial effect against a wide range of bacterial, fungal and parasitic organisms. The essential oil at various dilutions was screened *in vitro* against some microbes and helminths and it was found to exhibit promising activity against *Shigella flexneri* (Chowdhury *et al*., 1998). It also showed anthelmintic activity against hookworms and nodular worms (Agarwal *et al*., 1979). The methanolic extract was found to exhibit anti-plaque action by potently inhibiting *Streptococcus mutans*, thus also preventing dental caries (Ferdous *et al*., 1992). Alcoholic extracts showed also antibacterial activity against *Micrococcus pyogenes var. aureus* (Kapoor, 1990). It was also found to possess antibacterial activity against *Shigella dysenteriae*, *Shigella sonnei*, *Shigella boydii*, *Vibrio cholerae* and *Escherichia coli* (El-Kamali *et al*., 1998). The ether extracts showed *in vitro* antimicrobial activity against Gram-positive bacteria; e.g. *Staphylococcus aureus*, Gram-negative bacteria; e.g. *Pseudomonas aeruginosa* and *E. coli* (Sokmen *et al*., 1999). The ethanolic extract was found to possess anticestodal effect in children (Akhtar & Riffat, 1991). It was found also that the aqueous extract possess potent *in vivo* antifungal activity against candidiasis in mice (Khan *et al*., 2003a). The protective effect of black seed extract and its main constituent, thymoquinone, was studied on mouse cells infected with schistosomiasis (Aboul-Ela, 2002). Bone marrow cells and spleen cells were used *in vivo* and *in vitro*, respectively, to evaluate the protective effects of these compounds against chromosomal aberrations induced as a result of schistosomiasis.

Anti-inflammatory impact

The topical application of black cumin crude seed oil is of great use in skin eruptions, paralysis, hemiplegia, back pain, rheumatism and related inflammatory diseases. The crude oil and thymoquinone both have been found to inhibit the eicosanoid generation and membrane lipid peroxidation, through the inhibition of cyclooxygenase and 5-lipoxygenase (5-LO) pathways of arachidonate metabolism, thus responsible for the anti-inflammatory activity (Houghton *et al*., 1995). The aqueous extract was investigated for anti-inflammatory, analgesic and antipyretic activities in animal models. The anti-inflammatory effect was demonstrated by its inhibitory effect on carrageenan-induced paw oedema and analgesic effect by significant increase in hot plate reaction time in mice (Khan *et al*., 1999). However, it showed no effect on yeast-induced pyrexia (Al-Ghamdi, 2001). Essential oil and its active principle thymoquinone were found to possess dose-dependent anti-inflammatory activities and inhibited oedema and granuloma formation (Mutabagani & El-Mehdy, 1997). In a recent study, black seed oil, nigellone (polythymoquinone) and derived thymoquinone were studied to evaluate their effect on the formation of 5-LO products from polymorphonuclear leukocytes. They were found to produce concentration-dependent inhibition of 5-LO products and 5-hydroxy eicosatetraenoic acid production, probably as a result of an antioxidant action; thus, showing in part their role in ameliorating inflammatory diseases (El-Dakhakhny *et al*., 2002).

Impact on the gastrointestinal system

Black cumin seed has been widely used as gastrointestinal disorders. The aqueous extract of the seeds was reported to exhibit anti-ulcer activity by decreasing the volume of acid in gastric juice in acetylsalicylic acid-treated rats (Akhtar *et al*., 1996). The alcoholic extract was investigated in rats to evaluate the anti-ulcer activity by using two models, i.e. pyloric ligation and aspirin-induced gastric ulcer. The volume of gastric acid secretion, free acidity, total acidity and ulcer index were significantly reduced (Rajkapoor *et al*., 2002). Administration of black seed oil in rats produced a significant increase in mucin content and glutathione level and a significant decrease in mucosal histamine content in the stomach, leading to significant protection against ethanol-induced ulcer in rats (El-Dakhakhny *et al*., 2000). Recently, seed oil and thymoquinone were found to possess gastroprotective effect against gastric lesions, which may be related to the conservation of the gastric mucosal redox state (El-Abhar *et al*., 2003). Moreover, the aqueous seed extract 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). The volatile oil and ethanolic extract inhibited spontaneous movements of the rabbit jejunum as well as agonist-induced contractions and the spasmolytic effect involved calcium channel blockade (Aqel, 1993). The aqueous-methanolic extract also showed spasmolytic effect mediated through calcium antagonist effect thus providing scientific basis for its traditional use in diarrhoea (Gilani *et al*., 2001). In addition, the hepatoprotective effect of seed oil was shown in some models of liver toxicity. In *Schistosoma mansoni* infected mice, the oil succeeded partially to correct the previous changes in L-alanine aminotransferase (ALT), Gamma-glutamyl-transferase (GGT) and alkaline phosphatase (ALP) activity as well as the albumin content in serum. The oil was suggested to play a role against the alterations caused by *S. mansoni* infection, an effect which may be induced partly by improving the immunological host system and to some extent with its antioxidant effect (Mahmoud *et al*., 2002). Thymoquinone was found to be hepatoprotective against ter-butyl-hydroperoxide-induced hepatotoxicity (Daba & Abdel-Rahman, 1998) and protecting liver also against carbon tetrachloride-induced hepatotoxicity in mice *via* its antioxidant mechanism (Nagi *et al*., 1999). More recently, it has been shown that thymol, one of the constituents of black seeds volatile oil, also exhibits hepatoprotective effect in rodents (Janbaz *et al.*, 2003). Another study showed the possible effects of thymoquinone on acetic acid-induced colitis in rats. The smaller dose of thymoquinone (5 mg kg^{-1}) produced partial protection; whereas, higher dose (10 mg kg^{-1}) was found to give complete protection even significantly higher than sulfasalazine. The possible mechanism of the protective effects might be partly because of an antioxidant action (Mahgoub, 2003).

Impacts on the cardiovascular system

Volatile oil of black cumin seed exhibited a depressant action on the frog heart and a relaxant effect on isolated smooth muscles of rat. The volatile oil from the seeds and its constituent thymoquinone induced the cardiovascular depressant effects, which were mediated mainly centrally *via* indirect and direct mechanisms and involved both 5-hydroxytryptaminergic and muscarinic mechanisms (El-Tahir *et al.*, 1993a). On the contrary, the unsaponifiable matter of the fixed oil showed a marked depressant effect on heart and produced bradycardia (El-Tahir *et al.*, 1993b). In another study, the crude extract of black cumin seed was found to significantly lower the blood pressure in spontaneously hypertensive rats similar to that of nifedipine (Zaoui *et al.*, 2000). Recently, it was observed that the active ingredients of black seeds, such as thymol lower blood pressure through blockade of calcium channels (Gilani *et al.*, 2001). These studies showed that the plant contains multiple chemicals with antihypertensive effect acting at multiple sites. Black cumin seed treatment was also found to lower the levels of serum cholesterol (Hassanin & Hassan, 1996). In addition, supporting the traditional use of black seeds as a treatment of dyslipidaemia and hyperglycaemia, the effects of the fixed oil in rats were investigated by monitoring blood homeostasis and body weight as well as toxicity. The serum cholesterol, triglycerides and glucose levels and the count of leukocytes and platelets decreased while haematocrit and haemoglobin levels increased significantly (Zaoui *et al.*, 2002). Recently, the effect of crushed seeds and total oil were studied on serum levels of glucose, cholesterol, triglycerides, creatine kinase, prolactin, red blood cells, white blood cells, platelets, haemoglobin and some liver enzymes such as ALT, aspartate aminotransferase (AST), ALP and GGT in healthy female volunteers. Both crushed seeds and total oil decreased glucose, prolactins, triglycerides and cholesterol level. Crushed seeds produced a significant increase in RBCs, WBCs and haemoglobin levels, while total oils increased haemoglobin levels. Only the total oil produced a significant increase in ALT and AST. Both total oil and crushed seeds showed a significant increase in GGT and ALP (Ibraheim, 2002). The black cumin seed extract was found to produce protection against cisplatin-induced falls in haemoglobin levels and leukocyte counts. In a recent study, Bamosa *et al.* (2002) studied the effect of thymoquinone on the blood levels of cholesterol, triglycerides and high- and low-density lipoproteins (HDL and LDL) in albino rats. After 4 days, a reducing effect on triglycerides, HDL and LDL were commenced (Bamosa *et al.*, 2002). Moreover, methanolic soluble portion of black cumin oil, showed inhibitory effects on arachidonic acid-induced platelet aggregation and blood coagulation. Methanolic soluble part was purified to isolate a new compound 2-(2-methoxypropyl)-5-methyl-1,1,4-benenediol and two known compounds, thymol and carvacrol, having very strong inhibitory activity (Enomoto *et al.*, 2001).

Conclusion

Interest in newer sources of oilseeds has recently grown. Oilseeds are important sources of oils of nutritional, industrial and pharmaceutical importance. Among the various oilseeds, black cumin (*N. sativa* L.) is of particular interest because it may utilise for the production of formulations containing phytochemicals with significant antioxidant properties and health benefits. Although black cumin has been part of a supplemental diet in many parts of the world and their consumption is also becoming increasingly popular in the non-producer countries, information on the phytochemicals in these oils is limited. Yet, these phytochemicals may bring nutraceutical and functional benefits to food systems. These points out the fact that black cumin seed contains both active proteins and lipid soluble elements; thus, proving the multiple mechanisms of action behind this phytotherapeutic agent. Crude fixed seed oil is a valuable source of essential fatty acids, phytosterols, glycolipids and phospholipids. The high levels of those bioactive lipids are of importance in nutritional applications. On the contrary, black cumin has significant effects on multiple biological systems. Both ethanolic and aqueous extracts as well as the volatile oil have been proved to possess beneficial effects. Most of the pharmacological activities are attributed to the presence of thymoquinone as an active component. Lately black seed has become an important topic for research world wide, but more studies need to be conducted to find new possible activities of this versatile phytotherapeutic agent as well as clinical trials to prove the therapeutic efficiency of the plant.

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