Some Biological and Pharmacological Effects of the Black Cumin (*Nigella sativa*): A Concise Review

S. A. Elnour and E.B. Abdelsalam

Department of Pathology, Faculty of Veterinary Medicine, University of Khartoum, PO box 32, Khartoum North, Code 13314, Sudan
Corresponding author: E.B. Abdelsalam (BVSc, MVSc, PhD)
Email: mahibilal@hotmail.com

Abstract

This review provides a brief account on the various properties and medicinal usage of the black cumin seed (*Nigella sativa*). The literature information indicated that seed was extensively used in ancient and recent history as an effective herbal remedy against a wide spectrum of ailments and disease conditions particularly in rural communities in the Asia, Middle East and some other parts of the world. The seed was reported to have numerous biological and pharmacological properties including antioxidant, antibacterial, antifungal, antiparasitic, antiviral, anti-inflammatory, anticancer, antidiabetic, hepatoprotective, immunomodulatory and so many other beneficial medicinal effects. The therapeutic potential of the black cumin seed is mostly related to the presence of a number of pharmacologically active constituents such as thymoquinone, thymohydroquinone, dithymoquinone, thymol, nigellone and many other phytochemicals. The seed was also found to have a beneficial role in some aspects of poultry production such as improvement of body weight performance, feed conversion rate, carcass characteristics, egg production and egg quality when given as a feed additive.

Key words: Black cumin - black seed – *Nigella sativa* – herbal medicine

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Introduction

There is an increasing awareness of the therapeutic potential of many natural products and medicinal plants that are frequently considered far less toxic and free from side effects than synthetic drugs (Newman and Cragg, 2007). A vivid example of that is the black cumin (*Nigella sativa*), which is probably the most extensively studied medicinal plant in recent literature. The medicinal plant *N. sativa* is an annual spicy herb belonging to the family *Ranunculaceae*. The plant has long been recognized in the Indian subcontinent as an important element in traditional popular medicine but now it is widely cultivated in many other parts of the world including the Mediterranean regions, the Middle East, Far East and several other countries in Asia as well as in Europe (Chevallier, 1969). Historically, the black cumin has been considered a crop of a great medicinal importance in ancient Egyptian and Greek civilizations where it was used for treatment of various ailments such as headache, nasal congestion, toothache, and intestinal worms (Tembhurne *et al*, 2014).The seed is traditionally known in the Middle East as habbat al-Baraka (habbat =seed *in Arabic*; al Baraka = blessing) due to its powerful healing qualities and remarkable therapeutic potentials. It became the most famous and popular medicinal plant among all Muslim communities because it was described by the Prophet Mohammed (PBUH) as a miraculous remedy. The most important active components of the volatile oils of the black seed are thymoquinone (TQ) and dithymoquinoline (DTQ), and both were reported to have anti-inflammatory and antitumor properties (Ivankovic *et al*., 2006; Banerjee *et al.*, 2010).Those two active ingredients (TQ and DTQ) were also reported to have remarkable immunomodulatory and immunotherapeutic potentials (Swamy and Tan, 2000, Salem, 2005). In addition to the traditional use the black cumin in popular folk medicine, it was also reported to have some beneficial effects in several aspects of poultry production such as improvement of body weight performance, food intake, feed conversion ratio, dressing percentage, carcass quality and visceral organ weight (Durrani *et al*, 2007; Miraghaee *et al*, 2011; Abu-Dieyeh and Abu-Darwish 2008). Moreover, the dietary use of the black cumin was also reported to increase egg production, egg mass and egg shell thickness in laying hens (Akhtar *et al*, 2003; Nasir *et al*,2005).

Morphology and taxonomy of the plant

The medicinal plant *N. sativa* is an annual flowering herbaceous tree which grows up to 20-90 cm tall, with finely divided leaves, the leaf segments are narrowly linear to threadlike (Khare, 2004; Ahmed *et al*, 2013). The flowers are delicate and usually coloured white, yellow, pink, pale blue or pale purple with 5-10 petals. The fruit has inflated capsule composed of 3 to 7 united follicles, each containing numerous seeds. The seed is dicotyledonous angular, extremely black from outside, white inside, slightly aromatic in odour and bitter in taste (Paarakh, *et al,* 2010; Rajesekhar and kuldeep, 2011). Due to the worldwide distribution of *N.sativa*, the plant has been recognized by different names according to the geographic location and language. For example, in English speaking countries it is known as the black seed, black cumin, black caraway and black coriander. In India, the plant is known as Kalaunji or Kalonji. In Greece, it is named Melanthion or Melaspermm. In Italy it is called Grano nero, and in Arabic it is known as Al Habbeh as-sudah, Habbat al-baraka or Kamun aswad (Tembhurne *et al*, 2014).The botanical classification of the plant according to the International Code of Nomenclature (ICN) for Algae, Fungi and Plants (Sharma *et al*, 2009) is documented to be as follows:

Kingdom: *Plantae*

Division: *Magnoliophyta*

Class: *Magnoliopsida*

Order: *Ranunculales*

Family : *Ranunculaceae*

Genus: *Nigella*

Species: *sativa*

Geographical distribution

The black cumin herbal tree *N.sativa* is originally native to South West Asia and Mediterranean regions but the growth of the plant has further extended to Northern Africa, Eastern Asia and

Southern Europe (Chevallier, 1969). For the past several decades, the plant has also found its way into Eastern Europe, North America and Southern Africa (Rajesekhar and kuldeep, 2011; Assi *et al*, 2016). The black cumin is now cultivated worldwide for medicinal uses and also for cooking purposes as a favourable delicious spice in food industry with a unique taste and flavour. Nevertheless, cultivation of the plant usually thrives much better in South Asia and in the Middle East due to the climate suitability and soil sensitivity (Temburne *et al*, 2014).

Historical background

The black cumin has been regarded since ancient history as a miraculous remedy for various ailments and disease conditions in human patients (Ahmad *et al.*, 2013; Tembhurne *et al.*, 2014**).** In fact, the seed has long been discovered in preserved crops found with Tutankhamun's tomb in Egypt and it was mentioned as a curative substance in the Holy Bible. The Greek physician Dioskorides used black cumin to treat headache, nasal congestion, toothache and intestinal parasites. Hippocrates regarded the black cumin as a valuable remedy for hepatic and digestive disorders. It has been recorded that the black cumin was prescribed by ancient Egyptian physicians to treat the above mentioned ailments in addition to obesity, back pain, hypertension, gastrointestinal problems and bronchial asthma (Salem, 2005; Forouzanfar *et al*, 2014). The black cumin was also used in folk medicine for hundreds of years in the Middle East and Far East as a traditional medicine for a wide range of illnesses. It was frequently used as a diuretic agent and to promote menstruation and increase milk production (Goreja, *et al*., 2003). It is worth mentioning that the black cumin has considerably received a special attention and interest in all Arab and other Muslim communities in which it was extensively used for treatment of various kinds of diseases. The absolute confidence on the curative potential of the black cumin by Muslim communities was due to the fact that the Prophet Mohammed (PBUH) described the black seed as

"a remedy for every illness except death". Moreover, the famous Muslim philosopher and physician Avicenna (980-1037A.D.) stated in his famous legendary book "*The Canon of Medicine"* that the black cumin stimulates the body's energy and helps recovery from fatigue (Chevallier, 1996)**.** He further claimed that the black cumin is good for inner purification of the body by reducing mucous and strengthening lungs, treating fever, coughs, colds, toothache,

headache, skin diseases, infected wounds and intestinal parasites in addition to its ability to protect against poisonous bites and stings (Sayed, 1980; Hajhashemi *et al*., 2004 Ahmed *et al*, 2013).

Chemical Constituents

The medicinal plant *N.sativa* has undergone extensive phytochemical studies which revealed that the seed is fairly affluent and diverse in its chemical composition. (Babayan *et al*, 1978; Al-Homidan *et al*., 2002; Nasir *et al*, 2005; Gharby *et al*, 2015). Basic studies on the proximate analysis of *N. sativa* seeds showed a composition of 21% protein, 35.5% fat, 5.5% moisture, 3.7% ash and the rest being total carbohydrate (Babyan *et al*, 1978). Similar results were also obtained by Aljasir (1992) who showed that the seed contains crude protein (20.9 %) crude fibres (7.94 %) and fat (38.20 %). Further subsequent studies have also shown similar values of crude proteins, fat and crude fibres in addition to carbohydrates and saponin (Nerzig and Otles, 1993; Asdadi *et al*, 2014). The seed also contains some alkaloids such as nigellicimine, nigellicimine, nigellidine and nigellicine in addition to some vitamins and minerals (Babayan *et al*, 1978; Javed *et al*, 2012; Haron *et al*, 2014). However, the most important pharmacologically active ingredients of the black cumin are the fixed and volatile oils. The fixed oil (32-40%) contains several unsaturated fatty acids including arachidonic, eicosadienoic, linoleic, linolenic, oleic, almitoleic, and myristic acid as well as some sterol esters and sterol glucosides (Edris, 2011; Gharby *et al*, 2015). The unsaturated fatty acid amounted to more than 83% of total fatty acid content of lipid extract. It was also shown that lenolic acid and oleic acid represent 59% and 23.58% respectively of total of fatty acid contents (Hajhashemi *et al*., 2004). On the other hand, the volatile oil (0.4-0.45 %) contains saturated fatty acids such as palmitic and stearic acid (Ramadan and Mörsel,2002). However the most important pharmacologically active phytochemicals of the black cumin are thymoquinone, thymohydroquinone , dithymoquinone, thymol and nigellone which are all present in both fixed and volatile oils (Ali and Blunden, 2003; Ahmed et al, 2013; Khan and Afzal, 2016).

Pharmacological and Therapeutic Properties

The black cumin has long been reported to have numerous pharmacological and therapeutic properties due to the presence of several pharmacologically active ingredients in its volatile and fixed oil (Gilani *et al*., 2004).The most important of them include thymoquinone(TQ), dithymoquinone, (DTQ), thymol (THY) and thymohydroquinone (THQ)) in addition to the crystalline active principle nigellone and several pharmacologically active alkaloids (Ghosheh *et al*., 1999; Hajhashemi *et al*., 2004; Khan and Afzal, 2016). However, much of the biological activities of the seed have been shown to be due to thymoquinone, the major component of the essential oil, which is also present in the fixed oil (Ali and Blunden, 2003).The active ingredients of the black cumin were reported to have a wide range of pharmacological and therapeutic activities including anti-oxidant, anti-inflammatory anti-microbial anti-parasitic, immunomodulatory and anti-cancer effects. They were also reported to act as diuretic, antihypertensive, antidiabetic, anticonvulsants, spasmolytic, bronchodilator gastroprotective, hepatoprotective, neuroprotective and renal protective agents (Assi *et al.*,2016).

Antioxidant Effect

The beneficial therapeutic, anti-inflammatory and anticancer effects of the black cumin seed have directly been attributed to the potent antioxidant activity of some its active ingredients particularly thymoquinone. (Burits and Bucar, 2000 ; Mansour *et al*.,2001 ; Ali and Blunden, 2003). In addition, the seed was also found to contain significant amounts of some other well known potent anti-oxidant elements such as selenium, tocopherols (vitamin E) and trans-retinol (vitaminA) (Al-Saleh *et al.*, 2006; Khan and Afzal, 2016). The antioxidant effect of thymoquinone and related compounds was reported to be due to their radical scavenging or anti-oxidative activity of superoxide, hydroxyl radical and singlet molecular oxygen and also to their ability to inhibit the production of 5-lipoxygenase products during inflammation (Mansour *et al.*, 2002 ; Badary *et al.*, 2003).

Anti-inflammatory Effect

The back cumin was reported to have a pronounced anti-inflammatory effect in several inflammatory diseases such as experimental allergic encephalomyelitis (EAE), colitis, and arthritis (Mohamed *et al.*, 2003). When animals with EAE received thymoquinone they showed higher glutathione level, absence of lymphocytic perivascular inflammation and absence of disease symptoms, compared with EAE untreated animals. The aqueous extract of the black cumin was also investigated for anti-inflammatory, analgesic and antipyretic activities in animal models. The extract was found to have an anti-inflammatory effect demonstrated by its inhibitory effects on Carrageenan - induced paw edema in mice (Al-Ghamdi, 2001). The extract was also found to produce significant increase in the hot plate reaction time in mice and thus indicating an analgesic effect. Also, the ethanolic extract of the black cumin was reported to have a significant analgesic effect in mice which were exposed to acetic acid induced writhing test (Bashir and Qureshi 2010)). Furthermore, the black cumin was found to maintain its inflammatory and analgesic activity even during different phases of germination. The mechanism that mediates the inhibitory effect of the black cumin on inflammatory immune responses is probably attributed to alteration of trafficking of the inflammatory cells via modulating expression of chemokines and/or adhesion molecules (Hajhashemi *et al.,* 2004). Even though, there are no reported studies on the effect of the black cumin on the chemokines or adhesion molecules, the inhibition of the inflammatory cytokines IL-1, TNF-α and enhancement of the chemokine IL8 by the black cumin might give a positive indication of the anti-inflammatory effect of its active ingredients (Salem, 2005).

Antimicrobial effect

It is well documented that the black cumin was found to have variable anti-microbial effects including anti-bacterial, anti-fungal, anti-parasitic and anti-viral effects (Agarwal *et al.*, 1979, Khan *et al*., 2003 ; Aljabre *et al*, 2005). Some of these anti-microbial effects have been attributed to the immunomodulatory properties of the active components of the black cumin. The antibacterial effect of the phenolic fraction of the black cumin oil has been recognized for more than half a century (Topozada *et al*., 1965). The authors reported that the black cumin oil extract and the active ingredients thymoquinone and thymohydroquinone isolated from the volatile oil were found to have inhibitory activity against a number of gram positive and gram-negative bacteria. Similar results were also reported by El-Fatatry (1975) who showed that the extract and the oil exhibited a broad spectrum activity against a number of bacterial species. *In vitro* antibacterial studies have shown that the essential oil had a pronounced antibacterial activity against several organisms including *Staphylococcus albus, E. coli, Salmonella typhi* and *Vibrio cholera* even at 1:1000 dilutions. The oil was found to be more effective against gram positive than gram negative organisms (EL-Fatatry, 1975). The antibacterial effect of the black cumin has also been demonstrated by using the plate diffusion method which showed that the essential oil was effective against gram positive bacteria such as *Bacillus substilis* and *Staphylococcus aureus* and some gram negative bacteria such as *E. coli* and *Pseudomonas aeruginosa* (El-Kamali *et al.*,1998). The volatile oil of the black cumin was further tested against 19 microbes (gram positive, gram negative bacteria and fungi). The gram negative bacteria were shown to have the highest sensitivity followed by gram positive bacteria, yeast and dermatophytes. Moreover, the two main components of black cumin essential oil thymoquinone and thymohydroquinone were similarly investigated for their antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa, Shigella flexneri, Salmonella Typhimurium, Salmonella Enteritidis* and *Staphylococcus aureus* (Halawani, 2009).The results showed that both thymoquinone and thymohydroquinone exerted antibacterial activity against gram-positive and gram-negative bacteria regardless to their susceptibility to antibiotics. In addition, diethyl ether extract of the black cumin was also found to have a synergistic effect with streptomycin and gentamicin together with an additive effect with several other antibiotics including spectinomycin, erythromycin, tobramycin, doxycycline, chloramphenicol, nalidixic acid, ampicillin, lincomycin and co- trimoxazole (Hanafy and Hatem, 1991) Furthermore, some multi-drug resistant gram-positive and gram- negative bacterial isolates were found to be susceptible to the crude extracts of the black cumin (Hanafy and Hatem, 1991; Morsi, 2000). The active ingredients of the black cumin were also reported to have a noticeable antimycotic effect against several types of pathogenic fungi including *Aspergillus fumigatus, Epidermophyton floccosum, Candida albicans, Trichphyton megnini* and *Microsporum canis* (Hanafy and Hatem, 1991; Khan *et al*., 2003). Ether extract of the black cumin was also found to inhibit dermatophytes isolated from skin infection of sheep (Kader *et al.*, 1995). Moderate effect of thymoquinone against clinical isolates of the main groups of dermatophytes including *Trichophyton*, *Epidermophyton* and *Microsporum* was further reported by Aljabre *et al.*, (2005).

The antiviral effect of the black cumin has been investigated with certain types of viruses such as Murine Cytomegalovirus (MCMV) which is a herpes virus that causes disseminated and fatal disease in immunodeficient animals (Salem and Hossain, 2000). *In vivo* treatment with the black cumin oil induced a striking anti-viral effect against the disease in experimentally infected mice. In this context, the intreaperitonneal administration of the oil substantially decreased the viral load in the liver and spleen. It was also reported that the administration of the ethanolic extract of the black cumin exhibited potential therapeutic effect against Hepatitis C Virus (HCV) infection via decreasing viral load and alleviating the altered liver function (Abdel-Moneim *et al*., 2013).

Antiparasitic Effect

The antiparasitic effect of the black cumin has been demonstrated with several protozoan and helminthic parasites (Forouzanfar *et al*., 2014; Tembhurne *et al.*, 2014). For example, the black cumin oil was found to have trypanocidal properties by reducing parasitaemia and severity of the disease in *Trypansoma bruci* infected rats (Ekanem and Yusuf, 2008). Various extracts of the black cumin were also found to have antimalarial activity against both *in vivo* and *in vitro* plasmodia infections (Ahmed *et al.*, 2010). A hundred percent inhibition of the protozoan parasite *Plasmodium falciparum* growth was observed at a concentration of 50 µg/ml (Abdulelah and Zainal Abidin, 2007). The black cumin was also shown to have an anti-coccidian effect against *Eimeria tenella* experimentally infected chickens as evident by a significant reduction in oocyst count (Deyab and Laji, 2007). The anti-coccidian effect of the black cumin was also demonstrated in *Eimeria stiedae* infected rabbits (Baghdadi and Al-Mathal , 2011;Seddiek and Metewally,2013). The black cumin extracts and thymoquinon were also found to have a potential protective effect against *Schistosoma mansoni* infection in mice (Aboul-Ela,2002; Mahmoud *et al.*, 2002; El-Shenawy *et al.*, 2008). Treatment of *S. mansoni* -infected mice with the black cumin oil induced a significant reduction in the number of worms in the liver which coincided with a decrease in the egg burden in both the liver and intestine. In addition, the black cumin oil showed a pronounced anti-helminthic activity against tapeworms, earthworms, nematodes and cestode parasites (Akhter and Riffat, 1991).

Immunomodulatory Effect

The effect of the black cumin on the immune system has been investigated by several authors (Haq *et al*., 1995; Houghton *et al*., 1995; El-Dakhakhny *et al*., 2000).The whole seed or its extracts were found to have a remarkable stimulatory effect on the immune system in man and experimental animals. For example, the administration of one gramme of the black cumin twice daily enhanced the immune functions in human volunteers as reflected by a 72% increase in T helper cell to T suppressor cell ratio and improved natural killer cell activity (El-Kadi and Kandil, 1986). However, there was a decrease in the immunoglobulins IgA, IgG and IgM levels. Moreover, the black cumin enhanced the production of cytokines interleukin-3 and tumour necrosis factor-alpha by human lymphocytes when cultured with pooled allogenic cells or without any added stimulator. The black cumin seed was also found to produce a significant increase in interleukin-1 beta, suggesting that the seed might also have an effect on macrophages as well (Haq *et al*, 1995). In addition, whole black cumin seed and its purified proteins demonstrated a stimulatory effect on mixed lymphocyte culture, as well as a suppressive effects depending upon the donor and the concentration used (Haq *et al.*, 1995).

Anticancer effect

The antitumour effect of the black cumin has long been recognized in ancient and recent history (Ahmed *et al.*, 2013; Tembhurne *et al.*, 2014). The active principles in black cumin have been found to exert anti-neoplastic effects both *in vitro* and *in vivo* using various models of carcinogenesis (Salim and Fukushima, 2003). For example, the topical application of black cumin inhibited the growth of experimentally induced skin tumours in mice (Salomi *et al.*, 1991). The onset of papilloma formation was delayed, and the mean number of papillomas was reduced. The oral administration of the ethanolic extract of the black cumin to mice with Ehrlish ascites tumor (EAT) resulted in a significant reduction in cell proliferation, DNA synthesis , mitotic percentage and prolongation of life span of the tumour bearing mice (Musa *et al.*, 2004). Further studies have also indicated that black cumin or its oil and active principles particularly thymoquinone and alpha-hederin, possess remarkable *in vitro* and *in vivo* activities against a large variety of cancers (Salim, 2010; Randhawa and Alghamdi, 2011). Thymoquinone has been reported to inhibit the proliferation of several types of human colon cancer cells (Ivankovic *et al*., 2006; Norwood *et al.*, 2007; Gali-Muhtasib *et al*., 2008; El- Najjar *et al*., 2010) without exhibiting cytotoxicity to normal human intestinal cells. Thymoquinone was also found to reduce mouse colon tumour cell invasion and inhibit tumour growth in murine colon cancer models (Gali-Muhtasib *et al*., 2006). In addition, El-Mahdy *et al* (2005) reported that thymoquinone exhibited an anti-proliferative effect in human myeloblastic leukemia HL-60 cells. It has been suggested that the antioxidant and anti- inflammatory activities of the black cumin contribute to the prevention and reduction of the complications of neoplasms (Khan, *et al*., 2011). Although the precise mechanism of the anticancer properties of the black cumin is not fully understood but the protective effect of the active ingredients of the seed, particularly thymoquinone, against cancer is probably attributed to their potent antioxidant activity and interference with DNA synthesis coupled with enhancement of the detoxification processes (Badary and Gamal El-Din, 2001).

Other beneficial medicinal effects

In addition to the above mentioned properties of the black cumin seed, it was also found to have some beneficial and therapeutic effects against a number of non-specific disease conditions in human patients. For example, the seed was found to be effective in diminishing the risk of atherosclerosis by decreasing the serum low density lipoprotein cholesterol level and increasing the serum high density lipoprotein cholesterol levels (Dahri *et al*., 2005; Nader *et al*., 2010). The black cumin and its active ingredients were also reported to exert therapeutic and protective effects in diabetic patients by decreasing abnormal morphological changes and preserving pancreatic beta-cell integrity (Al-Hader *et al*., 1993; Kanter *et al*., 2009) and by beneficially changing the hepatic enzyme activities (Pari and Sankaranarayanan, 2009). The seed was also reported to be effective against hypertension (Khattab and Nagi, 2007; Dehkordi and Kamkhah, 2008) and it was found to have a potent antihistaminic effect on the pulmonary airways of asthmatic patients (Boskabady et al., 2010). The aqueous suspension of the black cumin seed was found to have a protective effect against carbon tetrachloride induced hepatotoxicity in rats

(Al-Ghamdi, 2003). In addition, the protective effect of the seed and its active components against toxic injury of some vital organs such as the liver, heart, kidneys , bone, pancreas and the nervous system has also been reported (El-Dakhakhny *et al.*, 2000; Ahmed *et al*., 2013).

Toxicological effect

It is well established the routine administration of the black cumin seed or its oil and other active ingredients for therapeutic purposes did not produce any adverse effect in human patients and experimental animals (Ali and Blunden, 2003; Ahmad *et al*., 2013; Tembhurne *et al*., 2014). In addition, experimental evidence has consistently shown that the seed appears to have an extremely low toxicity and a wide margin of safety when used for therapeutic purposes. The lack of harmful effect of the seed when given at therapeutic levels was probably due to the fact that the size of the doses selected for treatment of various diseases was apparently far below the actual toxic level which has not yet been determined with full precision. So far, limited information is currently available on the real magnitude of the toxic dose of the medicinal plant *N.sativa* whether in the form of seed, crude oil or other active ingredients. In some previous toxicological studies, the LD_{50} of the fixed oil of the black cumin was found to be 28.8 ml/Kg bwt when given by the oral route and 2ml/Kg bwt when administered by the intraperitoneal route in rats and mice (Zaoui *et al*., 2002). Such a high LD_{50} is considered a clear evince of safety for the oil when given by the oral route. The acute toxicity of thymoquinone, which is the most important active ingredient of the black seed was investigated by Abu khadar (2002b) in male and female rats. The author used extremely high oral doses starting from 200, 300 and 500mg/kg bwt and intraperitoneal doses of 20, 30 and 40 mg/ kg bwt. His results showed that thymoquinone was well tolerated when given orally at 200 mg/Kg. However, it produced transient clinical signs such as diarrhoea, loss of weight, reduced activity and a slight abdominal distention and dypsnoea when given at 300 and 500mg/kg bwt. On the other hand, the intraperitoneal injection of thymoquinone induced noticeable toxicity signs which were mostly related to acute pancreatitis. Further toxicological studies have recently shown that the daily administration of the black cumin seed in the form of dietary powder did not produce any adverse clinical, histological or plasma biochemical alterations when given at increasing concentrations for up to 1gm/kg/day in the diet for 28 days in rats (Dollah *et al*., 2013).

Effects on Animal Production

In addition to the traditional use the black cumin as a curative agent in popular folk medicine, it was also reported to have some beneficial effects in certain aspects of poultry production (Azeem *et al*., 2014). For example, incorporation of the black cumin seed in poultry ration at 4.0% concentration resulted in significant increase in body weight performance, food intake, feed conversion ratio, dressing percentage and visceral organ weight (Durrani *et al.*, 2007). It was also reported that supplementation of poultry diet with 1% black seed has significantly improved body weight gain (BWG) and feed conversion ratio (FCR) in broiler chicks at starter and grower periods (Miraghaee *et al*., 2011). In addition, the dietary supplementation with the black seed was found to improve the carcass quality of broiler chicks (Al-Beitawi and El-Ghousein, 2008; Nasir and Grashorn 2010; Abbas and Ahmed, 2010). Moreover, the use the black seed powder as a natural feed additive at a rate of 1.5% was reported to produce significant beneficial effects on the performance and survivability of broiler chicks (Abu-Dieyeh and Abu-Darwish, 2008). The dietary use of powdered black seed was also reported to increase egg production, egg mass and egg shell thickness in laying hens (Akhtar *et al*., 2003; Nasir *et al*., 2005). It is worth mentioning that the European Union has imposed a strict ban on the use of growth-promoting antibiotics and hormones in poultry production due to their potential hazards on human health (Bedford, 2000; Casewell *et al*., 2003). As a possible effective alternative, the dietary supplementation of the black seed has been recommended by several authors to replace antibiotics and hormones that are routinely used as growth promoters in broiler chicks (Nasir and Grashorn , 2006 ; Guler *et al*., 2006 ; Attia and Al-Harthi, 2015).

Concluding Remarks

It is clearly obvious from the above literature that the black cumin has great potentials and capabilities as a medicinal plant of versatile physiological, biochemical and pharmacological properties. In fact, it is the most widely used medicinal herbal product because of its high efficacy against a wide range of ailments and disease conditions. However, the therapeutic and prophylactic use of the black cumin is still limited to the level of folk medicine. Therefore, more research is essentially required on the possible incorporation of the seed and its active ingredients in modern pharmaceutical products for future clinical use in the field of human and veterinary medicine. Also, the worldwide ban of the use of antibiotics and hormones as growth promoters in poultry industry necessitates an urgent search for a suitable effective alternative. In this respect, the black cumin would probably be a novel candidate for that purpose.

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