



Effects of *Nigella sativa* on Mammals' Health and Production

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Abstract | Interests have grown in the use of herbal medicinal plants as feed additives to animal rations in order improve their productive, reproductive and therapeutic performances. *Nigella sativa* seeds and their purified constituents have been shown beneficial effects in several studies on such aforementioned performances. *Nigella sativa* seed contains more than 100 compounds, some of which have not yet been identified or explored. The present review article addresses and discusses the effects of *Nigella sativa* seeds and their purified constituents on productive, reproductive and therapeutic performances on mammals.

Keywords | *Nigella sativa*, Productive, Reproductive and therapeutic

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Herbal medicinal plants and their extracts had been used for different purposes as improvement of body growth and health. The researchers are interested in recent decades in identifying their main constituents and understanding their mechanism of action. Many studies have been carried out to explore the probable beneficial effects of herbal medicine plants as anti-oxidant, anti-inflammatory and immunomodulatory (Salem, 2005). *Nigella sativa* (*N. sativa*) is considered one of such plants.

Nigella sativa (*N. sativa*) or black seed is an annual flowering plant that grows to 20-30 cm tall and planted in Asia and the Middle East (Khare, 2004). The flowers of this plant are very delicate and pale and white coloured. *Nigella sativa* have been used intensively by people in Middle East and are commonly used in the kitchen also in many recipes because they are considered a valuable remedy for several diseases. A number of studies were investigated *Nigella sativa* as feed additives in ruminant diets. The seeds of *Nigella sativa* composed of protein (20-27%), fat (34.5-38.7%), carbohydrates (23.5-33.2%) crude fibre (8.4%) and ash (4.8%) (Babayan et al., 1978). The seeds also contain good amount of various vitamins and minerals like Zn, Cu, P,

and F as well as carotene, which converts by the liver to vitamin A (Ahmad et al., 2013).

The *Nigella sativa* containing an active materials known as nigellicone, thymoquinone, and thymohydroquinone that were shown to possess antimicrobial, antitoxic and pharmacological activities via increasing the defense mechanisms against infectious diseases (Forouzanfar et al., 2014).

FEED INTAKE AND EFFICIENCY

Feed intake and feed efficiency are the prime factors to assess feed quality and growth performances of animals. Incorporating black seeds in animals' rations could be helpful to promote growth performance and improve feed conversion (Abdel-Magid et al., 2007). Forouzanfar et al. (2014) reported that nutritional compositions of *Nigella sativa* include eight or nine essential amino acids. Khatib et al. (2011) found that calves fed ration supplemented with black seed oil had higher nutrient digestibility compared to calves fed free black seed oil diet. Mahmoud and Bendary (2014) carried out a study to evaluate digestibility and growth performance in growing Barki lambs and

calves upon substitution of soybean and cotton seed meal by *Nigella sativa* and sesame seed meal. The results indicated insignificant differences in average daily gain and final body weight of animals upon feeding the two experimental rations. The differences among experiments in feed intake and efficiency using *Nigella sativa* could be related to differences in the species used, ration composition and level and nutrient contents in meals.

GROWTH PERFORMANCE

There are several studies have been carried out on different species of animals to investigate the effect of *Nigella sativa* on growth performance. Mohamed (2007) studied the effect of supplementation 35% of *Nigella sativa* on camel ration. Supplementation of *Nigella sativa* on camel ration has improved animal performance. Abd El-Rahman et al. (2011) indicated that Demeshgi goats fed 20% *Nigella sativa* showed significantly higher average daily gain compared to the control diet. Khattab et al. (2011) studied the immune response and productive performance of dairy buffaloes and their offspring upon supplementation with black seed oil. Animals were given 10 ml black seed oil/head/day. Calves received black seed oil gained more weight and had significantly the highest weaning weight than unsupplemented group. The author indicated that the effect of treating buffaloes before given birth was transferred to offspring and consequently had positive effect on the total gain of calves. They concluded their study that the addition of black seed oil to rations of pregnant buffaloes and their offspring had positive effect on nutrient digestibility, increased immune responses and productive performance of the obtained calves.

El-Ghamry et al. (2002) reported an increased body weight by incorporating grounded *N. sativa* seed in broiler feed. Improved average daily weight gain and better feed conversion ratio (FCR) in broilers was achieved with feeding 1% *N. sativa* seed in broiler diet (AL-Beitawi and EL-Ghousein, 2008).

On the other hand, Mahmoud and Bendary (2014) carried out a study to evaluate digestibility and growth performance in growing Barki lambs and calves upon substitution of soybean and cotton seed meal by *Nigella sativa* and sesame seed meal. The results indicated insignificant differences in average daily gain and final body weight of animals upon feeding the two experimental rations. Lambs fed ration supplemented with *Nigella sativa* showed no significant difference in term of final body weight and average daily gain.

The favourable effects of *N. sativa* on performance are thought to be due to high nutritive value as well as pharmacologically active substances present in the seeds. Black

cumin seeds contain mixture of essential fatty acids that cannot be synthesized in the body particularly oleic, linoleic and linolenic acids. There are fifteen amino acids comprising the proteins of *N. sativa* out of which eight are essential (Tavruri and Dameh, 1998). Jamroz and Kamel (2002) reported a stimulating effect of black seeds on digestive system, resulting in better absorption and performance. Addition of *N. sativa* in feed increased bile flow rate results in increased emulsification that activates the pancreatic lipases, which then aid in fat digestion and absorption of fat soluble vitamins (Lewis, 1980). Black seed oil and thymoquinone have hepatoprotective effects (Mansour et al., 2002), so *Nigella sativa* oil and its constituent, thymoquinone have been used in a wide range of gastrointestinal disorders against gastric mucosal injury (EL-Abhar et al., 2003). The increased performance might also be due to antimicrobial effects of the active ingredients of black seed (Gilani et al., 2004). Nasir and Grashorn (2010) reported controversial findings related to the performance of broiler. They found no significant effect on body weight gain, average daily weight gain and feed conversion ratio by the addition of 1% *N. sativa* seed. The inclusion of *Nigella sativa* seeds into the diet significantly decreased chickens body weight (EL-Sheikh et al., 1998; Akhtar et al., 2003). The reduced weight gain due to *N. sativa* meal was attributed to high fibre contents of the meal (EL-Bagir et al., 2006).

Heat stressed broilers fed black cumin oil (0.5, 1%), seeds (1, 2%) or meal (10, 20%) in feed showed better results than the control group. Significant improvement was observed of the birds regarding feed conversion ratio, crude protein conversion, calorie conversion ratio and feed consumption (Hermes et al., 2009). The better results of broilers by feeding *N. sativa* under heat stressed conditions can be attributed to the different ways by which black seeds exerted their effects on body metabolism.

Firstly, *N. sativa* exhibits a variety of different components such as thymoquinone and thymohydroquinone and these constituents possess antimicrobial properties and are well known for their pharmacological effects. Secondly, black seed also possess antibacterial and antifungal properties, so showed protective action against hepatotoxicity; all this can result in increased nutrient utilization. It has been observed that *N. sativa* can stimulate thyroid gland directly or indirectly through the pituitary gland. Thyroid hormones are very important for the metabolism of the body as these hormones increase the metabolic rate that can lead to enhanced amino acid utilization by fastening their metabolism.

REPRODUCTIVE ACTIVITY

The effects of *Nigella sativa* on reproductive performances of both males and females have been reported concerning semen quality and ovarian follicle development and preg-

nancy. There are a wide range of studies, which proved the safety of *Nigella sativa* upon administration in animals and human (Babazadeh et al., 2012; Dollah et al., 2013). The beneficial effects of *Nigella sativa* in gynecologic disorders have been reported in several studies.

Parhizkar et al. (2016) investigated the effect of *Nigella sativa* on menopausal parameters of ovariectomized rats. The finding indicated the probable beneficial role for *N. sativa* in the treatment of postmenopausal symptoms and possibility of using *N. sativa* as an alternative to hormone replacement therapy for post menopause in human.

El-harairy et al. (2006) studied the effect of level of feeding (80% or 100 of NRC) and replacing 50% of concentrate feed mixture protein by *Nigella sativa* meal protein on reproductive performance of Rahmani ewe lambs. They concluded that feeding Rahmani ewe lambs on 80% dietary CP or diets with or without 50% replacement of concentrate, feed mixture by *Nigella sativa* proteins had beneficial effect on oestrous activity in terms of length of oestrous cycle and oestrous duration as well as on conception rate.

Zanouny et al. (2013) studied the effect of supplementing *Nigella sativa* at a rate of 100 and 200 mg/kg body weight on male lamb performance. The results indicated that supplementation of *Nigella sativa* increased serum testosterone concentrations. In a study carried out on male broiler breeder birds fed diet containing 0.5% and 1% *N. sativa* oil and seeds showed that the addition of either seed or oil resulted in best semen characteristics. The treated groups showed an increase in ejaculation volume, sperm mass motility, progressive motility, count, and total sperm output as well as viability percentage. On the other hand, breeders exhibited a decrease in time of ejaculation and sperm abnormalities. In the second part of this study, inclusion of black cumin in the diet of cocks significantly improved the fertility and hatchability of the treated cock groups, as compared to non-back cumin diets (Abdulkarim et al., 2009). In general, the surplus availability of nutrients is the reason of reproductive enhancement upon *Nigella sativa* administration.

BLOOD BIOCHEMISTRY

Levels of blood metabolites are an indicative of body's condition. Zanouny et al. (2013) studied the effect of supplementing *Nigella sativa* at a rate of 100 and 200 mg/kg body weight on male lamb performance. Supplementation of *Nigella sativa* increased serum total protein, albumin, and globulin, and testosterone concentrations while decreased triglycerides and cholesterol. They concluded that lambs supplemented with *Nigella sativa* showed a positive response in term of blood metabolites.

Khattab et al. (2011) studied the immune response and productive performance of dairy buffalos and their offspring supplemented with black seed oil. Animals were given 10 ml black seed oil/head/day. Total plasma protein, albumin, and plasma immunoglobulin were significantly higher upon black seed oil administration. Also, adding *Negalla sativa* oil in calve diet showed no significant differences in term of plasma total protein, albumin, urea, creatin, total lipids, glucose, glutamate pyruvate transaminase (GPT), glutamate oxaloacetate transaminase (GOT), triglyceride concentrations. In contrast, plasma cholesterol was significantly higher for calves fed black seed oil compared to unsupplemented group which may be attributed to high amounts of unsaturated fatty acids in black seeds that stimulate the uptake of cholesterol by intestine and can be oxidized to bile acids (Khodary et al., 1996). Zeweil et al. (2008) found that the addition of *Nigalla sativa* to rabbit diets increased plasma total protein, albumin, and globulin. The higher concentration of total protein and their fractions may be attributed to increased activity of hepatic functions when *Negalla sativa* seeds were fed (Tousson et al, 2011). However, Daghash et al. (1999) reported that the addition of *Nigalla sativa* seeds on rabbit diet showed significant decrease of serum cholesterol, total lipids and triglycerides. Mohamed (2007) studied the effect of supplementation *Nigella sativa* on camel rations. The control group received no *Nigella sativa* and the treatment group had 35% of *Nigella sativa* substituted control ration. The author found that supplementation of *Nigella sativa* on camel rations improved animal performance compared to the control animals. Lambs fed ration supplemented with *Nigella sativa* showed no significant difference in term of final body weight and average daily gain (Mahmoud and Bendery, 2014). On contrary, Abd El-Rahman et al. (2011) indicated that Demeshgi goats fed 20% *Nigella sativa* showed significantly higher average daily gain compared to the control diet.

The feeding of 3% crushed and non-crushed *N. sativa* seeds reduced plasma cholesterol, triglycerides concentration and increased the plasma High Density Lipoprotein (HDL) concentrations compared to 1.5, 2 and 2.5% crushed *N. sativa* seeds (AL-Beitawi et al., 2009). The reduction in the triglycerides and cholesterol level might be due to the active ingredients such as thymoquinone and compounds like monounsaturated fatty acids that lower the cholesterol synthesis by hepatocytes and decrease the fractional absorption of cholesterol from small intestine (Brunton, 1998). Studies conducted on broiler chicks have shown that replacing bacitracin methylene disalicylate by ground black cumin seeds decreased serum cholesterol and triglycerides levels while HDL concentration increased (AL-Beitawi et al., 2009). The decrease in serum cholesterol levels might be due to enhanced bile production as reported by El-Dakhkhny et al. (2000). EL-Kaiaty et al. (2002) documented

decrease in serum glucose levels up to 16% by adding the black cumin in the diet. EL-Ghamry et al. (2002) found that by the incorporation of 4 g/kg black seeds, total plasma protein, albumin as well as globulin values were close to control birds. However, the addition of 2% *N. sativa* seeds in broiler diet resulted in increased total plasma protein (AL-Beitawi and EL-Ghousein, 2008). The research on rats indicated a significant increase in RBC, WBC, PCV and Hb of *Trypanosoma brucei* infected rats when treated with black seed oil as compared to control rats (Justine and Oluwatosin, 2008).

IMMUNITY

Residual of antibiotic and drug resistance are common upon antibiotics administration against pathogenic organisms. Therefore, using natural and effective alternatives might be helpful compared to synthetic antibiotics. The seeds of *Nigella sativa* and their purified constituents have been widely used in the treatment of different diseases. *Nigella sativa* not only promote animal's health and productive performance, but also plays a significant role as a natural antioxidant and immuno-stimulant.

Zeweil et al. (2008) found that the addition of *Nigella sativa* to rabbit diets increased plasma total protein, albumin, and globulin. The higher concentration of total protein and their fractions may be attributed to increased activity of hepatic functions when *Nigella sativa* seeds were fed (Tousson et al, 2011). *Nigella sativa* has immunomodulatory (Hadjzadeh et al., 2012), antibacterial (Bita et al., 2012) characteristics. Therefore, *Nigella sativa* may modulate microorganisms of rumen and their capabilities of rumen digestion. *Nigella sativa* seed extract was enhanced sheep macrophage immune functions *in vitro* (Elmowalid et al., 2013). Zeweil et al. (2008) and Khat tab et al. (2011) found the significant increase of plasma immunoglobulin in rabbits and buffaloes respectively upon supplementation with *Nigella sativa*.

Al-Mufarrej (2014) investigated the immune-responsiveness and performance of broiler chickens fed black cumin powder. This study showed that dietary supplement of black cumin seed at the level of 1% or 1.4% would enhance immune responsiveness in broiler chickens. Ghasemi et al. (2014) found that *Nigella sativa* given to male broilers improved growth performance, immune responses and blood characteristics. Khan et al. (2013) found that supplementation of newly evolved crossbred laying hens with 4 or 5% *N. sativa* seed enhanced immunity against Newcastle disease virus. Supplementation of broiler diet with *N. sativa* strengthened the immunity by preventing liver damage and lipid peroxidation (Tuluze et al., 2009). AL-Jabre et al. (2003) found that volatile oils in *N. sativa* exhibit 67 constituents capable of inducing beneficial and pharma-

cological effects against bacteria such as *Staphylococcus* and *E. coli*. Active components of black seed possessing antibacterial, antioxidant, and anti-inflammatory activities induced positive effects on the immunity and organs involved (Al-Saleh et al., 2006).

ANTIOXIDANT ACTIVITY

Oxygen molecule (O_2) is essential for the production of energy through the process of oxidative phosphorylation within mitochondria in all species. Oxidative phosphorylation process resulted in production of adenosine triphosphate (ATP), water and carbon dioxide. Through the consequence of normal oxygen metabolism, very small amounts of reactive oxygen species (ROS) or free radicals are continuously produced. When reactive oxygen species or free radicals become overabundant, they may toxically damage cells and need to be biochemically neutralized or extruded from the cells. Antioxidants are substances capable of delaying or inhibiting production of ROS intermediates. The cells can either synthesize antioxidants endogenously or given to them through the diets. *Nigella sativa* decrease the production of superoxide (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl (OH) radicals.

Several studies have carried in different species shown the antioxidants activities of *Nigella sativa* when supplemented to animals' rations and human diets. El-Far et al. (2014) investigated antioxidant and antinematodal effects of *Nigella sativa* and zingiber officinale supplementations in ewes. They found increase of the antioxidant activity in serum. Badary et al. (2003) concluded that *N. sativa* is an excellent superoxide anion scavenger for free radicals. The antioxidant potential of *N. sativa* oil was captured free radicals when given against pentylenetetrazol-induced killing in mice (Ilhan et al., 2005). These antioxidant effects of *N. sativa* seeds might be due to the active constituents like thymoquinone, carvacole, anethole and 4-terepinol (Guler et al., 2007). The study carried out on broilers using 3, 5 and 7% black cumin showed that the *N. sativa* decreased the hepatic liver peroxidation and increased the activities of several enzymes such as glutathione, catalase, myeloperoxidase and adenosine deaminase (Sogut et al., 2008). In another studies, black seed oil reduced the lipid peroxidation activities of liver enzymes and contributed to the antioxidant defense system in CCl_4 treated rats.

ANTI-CANCEROUS ACTIVITY

Nigella sativa seed has been used as an important natural remedy for many diseases. There are many active components such as thymoquinone and alphahederin isolated from *N. sativa* and identified to cause anticancer effects (Aljabre et al., 2015). Several studies were performed using mice and rats for investigating the anti-cancerous effects

CONCLUSION

of *N. sativa*. The anti-cancerous activity of *N. sativa* was observed when researchers found an increased activity of natural killer cells to 200-300% in patients with advanced cancer who were receiving immunotherapy contained black seeds (Salim, 2010).

The published original research articles on the effects of *N. sativa* and its constituents strongly indicate its positive effects on health and production.

Aqueous extract of *N. sativa* exhibited low free radical scavenging activity and induced gingival fibroblast proliferation with accelerated wound closure activity despite its non-significant effect on collagen synthesis. It also resulted in elevation of basic fibroblast growth factor and transforming growth factor beta (Ab Rahman et al., 2014). *In vitro* studies indicated that the *N. sativa* possess marked growth inhibiting properties of two leukemic cell lines and five solid tumor cell lines (Iddamaldeniya et al., 2003). Ethanol extracts of *N. sativa* were capable of inhibiting ehrlich ascites tumor growth by reducing cell count as well as inhibit tumor development (Iddamaldeniya et al., 2003). Different extracts of *N. sativa* produced different levels of cytotoxic effects on different cell lines when tested *in vitro*.

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ANTIMICROBIAL, ANTIVIRAL AND ANTIPARASITIC ACTIVITY

It has been indicated that *Nigella sativa* has antimicrobial, antiviral and antiparasitic activity. *N. sativa* seeds were reported to exhibit antibacterial effect against many species of Gram-negative and Gram-positive bacteria. Thymoquinone extract of *N. sativa* has antibacterial, antifungal, antiviral and antiparasitic activities (Abdel Azeiz et al., 2013; Forouzanfar et al., 2014; Ratz-Lyko et al., 2014). Moreover, *Nigella sativa* oil has strong activity against Gram-positive *Staphylococcus aureus* and *L. monocytogenes* involved in mastitis (Monika et al., 2013). Ishtiaq et al. (2013) reported that bioactive molecules or extracts of *Nigella sativa* can act as strong inhibitor of growth against wide range of infectious disease caused by harmful and pathogenic bacteria.

CONFLICT OF INTEREST

There is no conflict of interest in this review to declare.

AUTHORS' CONTRIBUTION

All persons who have made substantial contributions to the work reported in the manuscript.

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Concerning the antiviral effects of *Nigella sativa*; it was found in the absence of any viral infection that intake of *Nigella sativa* improve the function of natural killer cell along with augmenting the ratio of helper T cell to suppressor T cell (T4/T8), hence boosts the cell mediated immunity (Abdel-Shafi, 2013; El-Kadi and Kandil, 1986). Active principles of *N. sativa* especially thymoquinone ((TQ), thymol (THY) and thymohydroquinone (THQ) have demonstrated their antifungal potential against various fungal species (Harzallah et al., 2012). Studies from animals experimentally infected or studies from in vitro conditions stated the antiviral effects of active components of *N. sativa* (Ahmad et al., 2013; Sunita and Meenakshi, 2013). Moreover, *Nigella sativa* seed and oil have anti-coccidial, antimalarial and antiparasitic activities against different stages of life of parasite (Baghdadi and Al-Mathal, 2011; Okeola et al., 2011).

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