



## Black seed (*Nigella sativa*) used in traditional medicines to treat diseases-a review

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### SUMMARY

*Nigella sativa* has been used and known as medicinal plant on wide range in whole world. Black seeds utilize in different recipes of edible food. Black seed is also utilized to treatment of various ailments has been used on wide range. It has been useful and effective for treatment of diseases like, antihypertensive, diuretics, anti-diarrheal, betterment of appetite by acting as stimulus, antimicrobial, disorders of skin and as liver tonic. Considerable study on *N. sativa* has been conducted by different researchers and large number of pharmacological usefulness has been explored which include anti-covid-19, Immunomodulator, anti-bacterial, bronchodilator, anti-inflammatory, hepato-protective, renal infections, antioxidant, anticancer and antidiabetic properties etc. Black seed has miraculous power because of which it has top ranked evidenced position in herbal medicinal based treatment. It has been explored that plants having thymoquinone compound have effective therapeutic properties. Thymoquinone is a main bioactive component present in essential oil. Current review is conducted to compile a detailed of scientific data conducted about pharmacogenetic properties, chemical manufacturing as well as pharmacological effectively of *N. sativa* seeds.

**Keywords:** Traditional medicines, Black seed, COVID-19, Diabetes

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### INTRODUCTION

Parts of animals (Adil and Tariq, 2020; Aslam and Faiz, 2020; Tariq, 2020; Haidar and Bashir, 2021; Ijaz and Iftikhar, 2021) and plants (Khan *et al.*, 2017; Umair *et al.*, 2017b) have been utilizes since ancient era as medicinal tool for cure of different ailments (Fabricant and Farnsworth, 2001). Local cultures even recent era use plants and animals in their healing services (Umair *et al.*, 2017a; Farooq *et al.*, 2019; Umair *et al.*, 2019; Altaf *et al.*, 2020). It has been found that plants used in medicinal preparation have rich amount of phytochemical ingredients that play major role in new drugs development. *N. sativa* is commonly called “black seed” or “Kalongi”, also known as wonderful herb that has been already used for wide range of ayurvedic benefits. *N. sativa* used in different foods, this herb is also beneficial in historical folklore way of medicines use because it contains curative characteristics in cure of different diseases. From last many centuries, this herb has been extensively

used worldwide for treatment in different ailments so it is a vital drug used in traditional system of medicines like Ayurveda and Unani (Ahmad *et al.*, 2013; Perveen, 2019; Yimer *et al.*, 2019; Belgaumi *et al.*, 2020).

#### CHEMICAL COMPOSITION

Large number of compounds have been extracted, separated, noted and documented in various types of *N. sativa*. Active compounds include 4-terpineol, carvacrol, dithymoquinone, p-cymene, sesquiterpene longifolene, t-anethol, thymohydroquinone, thymol, thymoquinone and  $\alpha$ -pinene etc. which are mostly found in this herb. *N. sativa* seeds also have trace number of other compounds. Isoquinoline alkaloids like niellicimine, nigellicimine N-oxide, pyrazol alkaloids/indazole ring containing alkaloids are found in this herb. Black seeds also have alpha-hederin which is aqua soluble pentacyclic “triterpene” and “saponin” that is powerful agent of anticancer (Al-Jassir, 1992; ATTA-UR-RAHMAN *et al.*, 1995). Other important compounds are also found in trace amount that include carvone, limonene, citronellol. Most important medicinal characteristic of *N. sativa* seed are chiefly linked to quinine constituents. Seed also contain vital large number of different vitamins and minerals i.e. Cu, P, Zn and Fe etc. Seed also have carotene which is changed to vitamin A in liver. In root and shoot part of *N. sativa* vanillic acid is reported (Al-Jassir, 1992; Nickavar *et al.*, 2003). In seeds fatty oil is found which rich with unsaturated fatty acid, mainly dihomolinoleic acid (10%), eicodadienoic acid (3%), linoleic acid (50-60%), oleic acid (20%). In seed saturated fatty acid are also deposited that include palmitic acid, steric acid nearly in amount of 30% or less. Seed also contain alpha-sitosterol, stigmasterol and sterol (Cheikh-Rouhou *et al.*, 2008; Mehta *et al.*, 2008). Moreover, other important chemical components are also documented that include 24-methylene-cycloartanol, aliphatic alcohol, campesterol, cycloartenol, glycosidal saponin, gramisterol, lophenol, hederagenin glycoside, linoleic acid, lipid, melanthin, melathigenin bitter principle, nigellone, avenasterol-7-ene, obtusifoliol, stigmastanol, oleic acid esters protein, reducing sugar, stigmasterol-7-ene, tannin, resin, taraxerol, terpenoids, tirucallol, volatile oil,  $\beta$ -amyirin, butyrospermol, and  $\beta$ -unsaturated hydroxy ketone (Nickavar *et al.*, 2003; Ali *et al.*, 2008; Mehta *et al.*, 2009).

#### ANTIDIABETIC

Researches documented results depict that medicinal herbs have great affectivity. Black seed is one of those herbs which can control metabolic factors causing “diabetes mellitus”. *N. sativa* medicinal properties has been researched, documented, and narrated several times but despite of all these works there is no such systematic review that can conclude *N. sativa* effect on homeostasis of glucose and fatty acid profile in diabetes mellitus patients. *N. sativa* can bring betterment in “glycemic” and “fatty acid” profile in models of diabetes. Moreover, to reveal benefits of black seed, effective types and useful dose for management of diabetes and problems in clinical trials along more research work is required (Heshmati and Namazi, 2015).

### ANTICANCER

Seeds of *N. sativa* contain important nutritional flavoring agents as well as large number of ailments useful in natural remedy that has been used for centuries in ancient system of medicines like, Chinese, Arabic, Unani, and Ayurveda medicines system. Moreover, some important components present in seed, oil and various black seed extracts has been documented to having impact on immune stimulation, anti-inflammatory, hypoglycemia, antihypertensive, anti-asthmatic, anti-bacterial, antiparasitic, antioxidant anticancer effects. Medicinal characteristics of black seed has been documented by few numbers of authors and reported about little anti-cancerous effectively. Recent research review shows that many searches have been carried out about *N. sativa* effectively for healing of malignant cells disease and active compounds of *N. sativa* like thymoquinone and  $\alpha$ -hederin have anticancer affectivity. Research conducted on acute and chronic toxicity has currently confirmed the safe affectivity of black seed oil and rich with active compounds that include thymoquinone particularly when consumed orally. Current summative literature has been conducted to summarize valuable work till now conducted by researchers on effectiveness of *N. sativa* seed, its extract and active components that work as anti-cancer. Main mechanism linked to effectivity and action of components of black seed, that include derivatives of thymoquinone, nanothymoquinone and mixture of thymoquinone with recently used cytotoxic drugs are more important to discuss. Current study is aimed to review and enhance interest in researchers to perform preclinical and clinical practices to evaluate anti-cancerous effect of *N. sativa*, its active components and their derivative forms as cited by Randhawa and Alghamdi (2011).

### ANTI-COVID-19

Coronaviruses are zoonotic diseases; include COVID-19 (Altaf, 2020). *N. sativa* is a natural nutritive supplement having safe profile that can provide sufficient beneficial antiviral compounds. It has been documented that black seed has compounds like hederagenin, nigelledine, thymohydroquinone, thymoquinone and  $\alpha$ -hederin, had different ranges of affinity to SARS-CoV-2 enzyme and protein. These compounds have ability to actively control SARS-CoV-2 attachment and replication ability with host cell receptor site. It has been revealed by several researches that this herb has great affectivity for phytotherapy candidate for COVID-19. Moreover, preclinical trials results are needed followed by clinical trial in a Phase I (Koshak and Koshak, 2020).

### IMMUNOMODULATOR AND ANTI-INFLAMMATORY

Variety of herbal products is being utilized for cure of different infectious and non-infectious situations. In the East world the herbal and extracted products use is more evidenced, their utilization in Western cultures is also getting enhanced day by day. Immunomodulator effectively of some herbs have been investigated to a large extent, researches about estimated immunomodulatory impact of some herbs have been studied in detail, these researches depict different spices are relatively low effective. Therefore, here a detailed review of immunomodulatory and anti-inflammatory characteristics of *N. sativa*, also called as black seed/black cumin and its main

potentially active compounds like, thymoquinone. Current reviewed literature focused on analysis in vitro as well as in vivo experiments results that were extracted linked to ability of *N. sativa* and thymoquinone to treat inflammation, cellular and hormonal adaptive immune responses and Th1/Th2 paradigm. It has been documented that *N. sativa* has ability to augment cytotoxic activity of natural killer cells as anticancer is also emphasized. *N. sativa* and TQ has immunomodulatory and anti-inflammatory effectiveness at molecular and cellular level. Research conclusions depict that black seed extracts and TQ can actively work in development of beneficial therapeutic compounds that play role in control of immune system which play role in infectious and non-infectious situation may be caused by allergy, autoimmunity and cancerous condition (Majdalawieh and Fayyad, 2015).

#### ANTIMICROBIAL

In last few decades, antimicrobial-resistance ability has been a worldwide health issue, because pathogens have emerged having actively developed rapid resistance ability against multiple drugs. Unique and vital effective medicinal drugs are required to develop to take control over resistant pathogens. To find remedy effective against such pathogens researchers has suggested natural sources which can explore such plants having useful medicinal role in production of new antibiotic drugs. It has been revealed in through ancient civilizations that black seeds have been utilized till now in many areas. Current study shows active use and affectivity of these vital plant products as antimicrobial drug as nominated (Abdallah, 2017).

#### RENAL DISEASES

It has been observed that kidney stone diseases are spreading continuously. After first exposure to such kidney infection risk of such renal problem is greater and time duration between such relapses is short. Urinary stone can cause intense pain and require great economic need for treatment. Renal stone disease may cause increase chances of getting infected by other diseases like renal failure. Medicinal plants have been found with excessive number of antioxidants which have been used for edible purpose as ingredient for safety, benefits, and low-cost source. Plant of *N. sativa* is used as spice to prohibit and cure of ailments in Muslim inhabited areas and globally as well. This review also shows that *N. sativa* is effective on renal wound and stone formation. *Nigella sativa* and its main compounds that include thymoquinone have beneficial affectivity to prevent and treatment of kidney stones especially herbal melanin which require more research and experimental evidences to prove (Mollazadeh and Hosseinzadeh, 2014).

#### ASTHMA

*N. sativa* seeds also called black seed are used as spice and traditional herbal plant used in medicine to treat diseases like bronchial asthma. Purpose of current review is to find supportive research work conductive by medicinal use of black seed for asthma and to highlight future research goals. To find affectivity of black seed large number of medicinal databases was used and active secondary metabolites having potential about asthma inflammation and outputs. Nearly fourteen preclinical research studies were noted that showed number of effects of black seed in animals or cellular

models of asthma involving bronchodilation, anti-histaminic, anti-inflammation, anti-leukotrienes, and immunomodulatory effects. Moreover, nearly seven clinical practices depict that it causes improvement in various asthma patients, betterment include symptoms, pulmonary function and laboratory parameters. Furthermore, generally these researches are not highly profiled and less defined manufacturing mechanism. In results it can be summarized that *N. sativa* can cause therapeutic benefits in alleviating air passage inflammation and regulate asthma symptoms, however remained less evidences supported and based on inappropriate preparation methods. Koshaket *al* also highlighted that well designed clinical studies at large level using well chemical properties containing *N. sativa* preparation is required (2017).

#### ANTIOXIDANT PROPERTIES

During last three decades, large number of researches has been conducted to substantiate folklore characteristics, identification of plants-derived natural compounds and to find their mechanism during action in body during use. Black seed also causes improvement in action of antioxidant enzymes like catalase, glutathione peroxidase and glutathione-S-transferase and work as free radical scavenger. Since it has anticancer activity, it causes effect on targeted molecules that include p53, p73, PTEN, STAT3, PPAR-g, caspases activation and ROS generation had been explained. It contains anti-inflammatory and immunomodulatory ingredient so it causes suppression of inflammatory mediators, prostaglandins, leukotrienes as well as B-cell mediated immune response and causes balance in ratio of Th1/Th2 also provides potential to Tcells and naturally available killer cell-mediated immune response. Purpose of this review is summarize literature and experimental evidences obtained through scientific research methodology based on fundamental and traditional clinical therapeutically evidences obtained from *N. sativa* and its components as preventive for treatment of inflammation, use as antioxidant, immunoregulator and bronchodilator as well on obstructive respiratory diseases (Gholamnezhad *et al.*, 2015).

#### CONCLUSION

Medicinally important traditional plants have been got great attention because of many factors like low price, easily accessible and less side effects as compared to synthetic medicines. Besides, different medicinal plants use directly their products are used in religious and cultural traditions. Among different plants, black cumin has been utilized by various human cultures globally since centuries especially in Muslim communities who used to cure number of ailments. Number of researches has documented show that component of black seed include Thymoquinone have remarkable active effectivity as natural therapy to treat great number of diseases that include chronic noninfectious like neural disorders, DM, hypertension, dyslipidemia, inflammation, cancer etc and other infectious diseases caused by bacteria, fungus, viruses and parasites. It has been revealed by researches conducted on animals and plants that *N. sativa* and Thymoquinone have active ability to cure infertility of male and antioxidant ingredient have gained attention because of their role in dietary supplements having less side effects. Moreover, when mixture along different

traditional chemotherapeutic agents is used they causes synergizing effect which decreases dosage of concomitantly used medicines dose and optimize efficacy level as versus toxic level that can be proved as remedy to get rid problem of drug resistivity. Furthermore, it enhances safe use with maximum efficacy against wide range of diseases; *N. sativa* use in natural herbal remedies would prove efficient in number of clinical trial conditions. Extraction of vital bioactive components from black cumin and its oil use by keeping in view affectivity more research study for different clinical therapies models are recommended.

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