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Nigella sativa L.: Uses in traditional and contemporary medicines – An overview

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ABSTRACT

There are several wild and cultivated plants that offer excellent opportunities for being used as herbal and therapeutic agents. The identification of medicinal properties of plants and their effectiveness in treating diseases are important components in medicinal plant research and this can pave ways for further improvements in traditional drug use. Climatic conditions and phytogeography in Pakistan are ideal for naturally occurring diverse flora and managed cultivation of hundreds of plants of medicinal significance. *Nigella sativa* commonly known as the black seed is an important medicinal plant that has been widely used as a multipurpose medicinal agent in different countries since old times. The plant is abundantly cultivated in Pakistan for uses as condiment and medicines. It possesses important classes of bioactive compounds among which thymoquinone has attracted significant attention from the scientific community because of its active role in treating a diverse spectrum of diseases. The black seeds are used for reducing adverse effects of arthritis, asthma, inflammation, liver and gastro disorders besides their potential role in diabetes and cancers. The focus of this review is to highlight the medicinal significance of *N. sativa* in traditional medicine and opportunities for exploitation in contemporary medicine.

Contents

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1. Introduction

Plants are natural sources of food, feed, and medicinal substances besides their role in ecosystem sustenance. Since human beings are often challenged with different diseases, proper identification of the curing agents and subsequent recommendation for the treatment of diseases is crucially required for healthy manpower. There are several plants that possess active biomolecules with either confirmed or potential therapeutic attributes. The utilization of plant resources for treating different human diseases has been in practice since ancient times [1]. In Pakistan, concurrent with contemporary drug uses, traditional and herbal medicines are also commonly used and in most instances, herbal medicines are preferred over modern drugs because of the associated side effects of the later one [2]. Climatic conditions and geographical attire of Pakistan are conducive for the growth of diverse medicinal plants under natural and cultivated environments and during the last few decades, hundreds of plants have been documented with broad-spectrum medicinal properties [3,4]. The efficacy of different plants such as *Coriandrum sativum, Acroptilon repens, Berberis lyceum, Alium* sp., *Opuntia* sp., *Lepidium sativum*, and *Prosopis* sp., among many others has been well established in the literature for treating different diseases in the local population of the country [5–7].

Nigella sativa which is commonly known as black seeds has been long used as a condiment and relieving agent for different ailments in different countries and cultures [8–10]. The plant has been frequently described and recommended in Tibb-e-Nabvi [11,12], Unani medicines [13], African and Eastern medicines [14], Arabic, Chinese and Ayurvedic medicines [15] for different diseases and as a general tonic. Black seeds may be used as directly, active ingredients in herbal medicines or as a herbal tea. Seeds of *N. sativa*, its extracts, and oils in different trials have been proven to control diabetes [14,16], hypertension and oxidative stress [17], epilepsies [18], ulcers [19], asthma [20], inflammatory disorders [21], fatty liver [22], cancers [23,24], and arthritis [25] in model organisms as well as in human beings. Thymoquinone, a major phytochemical in *N. sativa*, is widely considered for the broad spectrum medicinal properties of this valuable plant [26,27]. In Pakistan, *N. sativa* is frequently used in Unani and folk medicine. Considering its health promotion and disease control activities, greater efforts are needed to transform the herbal and local medical system and exploit the plant in modern medicines. This would lead to grasping maximum benefits from black seeds. The aim of this review is to present an update on the medicinal properties of *N. sativa* in traditional medicine systems and opportunities for exploitation in modern medicines.

2. *Nigella sativa* –the plant and its phytoconstituents

N. sativa is an annual herbaceous plant in family Ranunculaceae which grows well on loamy soils in tropical and subtropical regions [28,29]. The plant attains a height of 20–60 cm with thread-like leaves and producing delicate flowers that contain many seeds [30]. The plant is an erect and branched herb which has a tap root system, divided leaves and attractive flowers ranging from yellow to white in color. Generally, the plant is pentamerous with the exception of stamens which are numerous. Seeds are produced in large fruit (https://www.britannica.com/plant/black-cumin). In Asia, Europe, the Middle East, and other Mediterranean countries, *N. sativa* has been regularly and abundantly cultivated for various purposes [31]. The plant is generally cultivated in spring and harvested in the autumn, although a slight variation in the cultivation pattern may follow depending on the geographic locations. The total growth duration of *N. sativa* from sowing till harvest generally comprises six months. It is mainly cultivated for seeds that are used as spices, flavoring agents, and medicinal remedies, especially in South Asia.

Major chemical constituents in *N. sativa* are thymoquinone, thymol, α-phellandrene, oleic acid, proteins, and carbohydrates [28,32]. In previous work, oleic acid, palmitic acid, linoleic acid, and trans-anethole were extracted and identified as the major components of black seeds [33]. In a study conducted by Kumar et al. [31] revealed that the plant contained phenolics and Quinones (thymoquinone, thymol, dithymoquinone, and thymohydroquinone). Harzallah et al. [34] isolated 48 different compounds from the oils of black seed which mainly comprised thymoquinone. Benkaci-Ali et al. [35] reported that seeds of *N. sativa* yielded different compounds dominated by monoterpene hydrocarbons. Piras et al. [36] reported the presence of proteins, oils, phenols and alkaloids in *N. sativa* seeds. More recently, Srinivasan [37] and Mazaheri et al. [38] ascribed that the plant possessed diverse biochemical predominantly phenols, terpenes, and flavonoids.

2.1. N. sativa –uses in herbal medicines

Seeds of *N. sativa* possess several medicinal properties. In herbal medicine, the plant has been widely reported to treat asthma, hypertension, gastric disorders, liver disorders, immune disorders, cancer, neurological disorders, and many other health conditions [28,39]. A comprehensive list of different health disorders and the relevant efficacy of *Nigella* seeds have been presented in Table 1.

2.2. Role in the treatment of asthma

Asthma, a respiratory disorder which may be associated with genetic or environmental factors, affect more than 0.3 billion people throughout the world [40]. Seeds as a whole, oil and herbal tea of *Nigella sativa* have been actively used in different regions for the treatment of acute and chronic asthma. Boskabady et al. [41] suggested that boiled extracts of *N. sativa* seeds efficiently improved asthma-related disorders in asthmatic patients at daily administration for three months. In a similar study, fifteen patients with asthma were given boiled extracts which revealed improved bronchodilatory responses [41]. Partial improvement in asthmatic conditions of patients was observed with 1–2 g day-1 provision of *N. sativa* [42]. Koshak et al. [20] find out that the seed oil contributed to controlled asthma in patients when they were treated with a 500 mg capsule twice per day. In animal trials, ethanolic extracts [43] and oil [44] significantly reduced histamine release and improved asthmatic problems in rats. In guinea pigs treated with *N. sativa* oil, reduced inflammation of airways and asthma was controlled when compared to the control group [45]. Since traditionally used anti-asthmatic medicines act as dilating agents of the airways in addition to owing anti-inflammatory effects, *N. sativa* seems to possess these properties which contribute to considerable control of asthma.

2.3. Effect on diabetes

Diabetes is one of the fatal causes of deteriorated health conditions of humans throughout the world which has generally no cure, but preventive measures and a healthy lifestyle can reduce the risks of secondary associated disorders. Globally, it affects more than 400 million people, which is expected to exceed 600 million by 2050 [46]. Favorable effects of *N. sativa* on diabetic patients is well established. [47] found that oral administration of *N. sativa* capsule significantly retarded blood glucose level and concerned parameters in type 2 diabetic patients. In a similar study, improved glucose concentration and dyslipidemia were observed in patients which were given *N. sativa* as an oral supplementation [48]. In other trials, *N. sativa* oil imparted beneficial effects on lipid profile and glycemic conditions of type 2 diabetes [49]. [50] treated diabetic patients with oral supplementation of *N. sativa* which proved effective in controlling cholesterol and other parameters. Frequent studies of the beneficial influences of seed extracts and oil in diabetic rats and other model organisms have been reported [51–53].

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Table 1
Uses of *Nigella sativa* seeds in the treatment of different diseases.

Use of seed material	Disease	Target organism	Effect	Reference
Powder; oil	Asthma	Humans	Effective control	[20,42]
ethanol extract	Asthma	Rats	Inhibition in histamine	[43]
Seed oil	Hepatitis C	Humans	Decreased viral load and oxidative stress	[80]
Extracted thymoquinone	Hepatic injury	Rats	Hepatic-protection	[81]
Essential oil	Bacterial toxicity	Carcinogenic bacteria	Anti-carcinogenic effects	[34]
Extracted polyphenols	Pain/inflammation	Rats/mice	Analgesic and anti-inflammatory responses	[82]
Aqueous seed extracts	Epilepsy	Humans	Anti-epileptic effects	[83]
Tymoquinone injection	Hypertension	Rats	Anti-hypertensive effects	[84]
Extract injection	Bacterial infection (*Salmonella typhimurium*)	Rats	Antibacterial activity	[85]
Ethanolic seed extracts	Newcastle Disease Virus	Chicks/eggs	Antiviral effects	[86]
Oil extracts	Diabetes	Humans/rats	Significant reduction in blood glucose level	[87,88]
Seed oil	Fatty liver (non-alcoholic)	Humans	Improve liver performance and reduced hepatic steatosis	[22]
Ethanol extracts	hepatocellular carcinoma	Rats	Antitumor effects	[55]
Seed oil	Nephrotoxicity	Rats	Protection of kidney against induced injury	[89]
Seed powder	Metabolic syndrome	Humans	Improved metabolic profile	[90]
Seed oil	Leishmaniasis	*Leishmania infantum*	Anti-leishmanial effects	[91]
Hydro-ethanolic extract	Wounds	Rats	Effective wound healing	[53]
Oil	osteoarthritis	Humans	Analgesic properties	[92]
Seed extracts	Vascular inflammation	Rats	Anti-hyperlipidemic, and healthy effects on vasoreactivity	[52]
Ethanol extracts	Bacterial rhinosinusitis	Rabbits	Effectively reduced the adverse effects of the disease	[93]
Processed seeds	Polycystic Ovarian Syndrome	Humans	Improvement in menses	[94]
Alcoholic extracts	Liver disorders	Rats	Hepato-protection and improved liver functions	[95]
Carboxy-methyl cellulose extracts	Induced myocardial infarction	Rats	Protective effects	[96]
Oil capsule (500 mg)	Menstrual irregularities	Humans	Significant improvement in menstrual cycle	[97]
Seed extracts	Malaria	Malarial parasite (*Plasmodium falciparum*)	100% growth inhibition of the parasite / Anti-plasmodial activity	[98]
Quadruple-therapy (2 g/day)	*Helicobacter pylori* infection/dyspepsia	Humans	Significantly improved health of patients and an increased eradication level of *H. pylori*	[99]

2.4. Ameliorative effect on different types of cancers

There are many reports concerning the effectiveness of *N. sativa* seeds in different types of cancers, although still sufficient investigation is required to fully understand the underlying mechanisms in the anti-cancer activities of the plant. Studies conducted on rats and rabbits and in some cases on human beings employing *N. sativa* as cancer protection therapy indicate plausible results. Fathy and Nikaido [54] documented that ethanolic extracts had inhibitory effects on tumor growth and carcinoma in rats. In breast cancer cell line (human) study, *N. sativa* exhibited cytotoxic effects on proliferating cell lines indicating anti-cancerous characters [55]. Shanmugam et al. [56] evaluated the role of *N. sativa* in cancer treatments and attributed the anticancer properties of the plant to thymoquinone which is a major constituent of *N. sativa*. In human ovarian cancer cell lines, extracts of *N. sativa* seeds were reported to possess antagonistic potentials against the spreading cells [57]. In a recent study, [58] reported that different extracts of *N. sativa* exhibited antiproliferative effects on HeLa cell lines. In other studies, antioxidative and anticancerous properties of *N. sativa* extracts, oils, and pulp have been documented in model organisms [59–61]. The effectivity of *N. sativa* in cancer is mainly attributed to its chemical constituent 'thymoquinone' which acts as anti-proliferative, anti-oxidant, protectant and gene regulating agent [61,62].

2.5. General therapeutic effects

The presence of pharmaceutically important constituents such as thymoquinone, thymol, and nigellone make *N. sativa* as a potential therapeutic source for managing different diseases. Its extracts, oil, and supplementation have been documented for possessing anti-analgesic, anti-inflammatory, wound healing, anti-oxidative, anti-asthmatic, corrective-rheumatoid arthritis and immune-stimulant properties [63,64]. Positive roles of *N. sativa* extracts and oil on obesity, lipid profile, and insulin regulation have been proven in animal trials [65–67]. Al Mofleh et al. [68] confirmed the anti-ulcerative potentials of *N. sativa* in rats. Recent studies suggest that seeds of *N. sativa* exhibit healthy effects on cardiovascular disorders and cardiotoxicity in animals [53,69]. Parhizkar et al. [70] indicated the role of *N. sativa* in improving menstruation and post-menopause cycle in rats. The linear correlation between *N. sativa* oil and increased reproductive capacity, including an increased sperm count in male rats were observed by [71]. In a study over a period of five weeks, *N. sativa* uses significantly improved kidney function in rats and prevented cytotoxicity [72]. Ilhan et al. [73] documented that treatment of mice with *N. sativa* oil resulted in protecting them against reactive oxygen species and induced seizures. In other studies, protective effects of black seed on neurotoxicity, hepatic injury, fatty liver, colon cancer, and gastrointestinal disorders have been proven [74–77].

3. Opportunities for exploitation as a contemporary medicine

Contemporary medicines which are also generally referred to as chemical medicines, drugs, pharmaceutical products, and orthodox medicines have been widely used to treat different diseases effectively. Nonetheless, adverse effects associated with the use of such medicines have attracted million people throughout the world to opt for herbal and natural remedies as alternative healing agents. Long use of contemporary medicine in chronic diseases has certain undesirable effects which most patients try to avoid and hence adopt herbal therapy [78]. Directing the aspired role of *N. sativa* in diverse medical conditions, the contemporary medicinal system needs to fully exploit this valuable plant as a registered drug on a wide scale because beneficial influences of different herbal medicines have already been established [79]. The formulations of synthetic medicines involve several phases ranging from the initial test for efficacy in model organisms, toxicity, and tolerance evaluation, human trials to final production. Considering the affectivity trials, and toxicity assessment, the same phases may be followed in modern medicine systems for *N. sativa*. There are potentials in the modern drug system to make capsules, tablets, and extracted oils from *N. sativa* seeds and may be exploited as allopathic drugs.

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4. Conclusions

N. sativa is an important medicinal plant in family Ranunculaceae which has several health benefits and confirmed therapeutic effects against different disorders. The seeds as a whole, in extracted forms and its oils, have been used for treating different diseases since ancient times. It possesses several active ingredients specifically thymoquinone which has been found in many studies to exhibit anticancer, antidiabetic and hepato-protective effects. The literature reports clearly indicate that *N. sativa* is useful in asthmatic, analgesic, ulcerative, gastro, wound healing, obesity, hypertension, and cardiovascular disorders. Based on its wide spectrum therapeutic potentials, a wide-scale exploitation of *N. sativa*, in both traditional and modern drug systems, is suggested.

Ethical standards and human studies

Not applicable.

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Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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