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Nigella sativa: A Potential Natural Antidote for Poisoning Cases †

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Abstract: In several cultures, black cumin, also known as *Nigella sativa*, has long been used medicinally. Recent research has revealed that this plant has potent anti-inflammatory and antioxidant qualities, making it a possible treatment for several medical conditions. Additionally, because of its capacity to detoxify the liver and protect it from harm, *Nigella sativa* has demonstrated positive results as an antidote for poisoning. Consumption of hazardous substances by accident or planned poisoning are two prevalent causes of poisoning. The liver is the primary organ in detoxification. According to studies, *Nigella sativa* can help the liver operate better and defend it from toxins' harmful effects. Additionally, it has been demonstrated that *Nigella sativa* protects against heavy metals toxicity. Thymoquinone and thymohydroquinone, the plant's active components, have been demonstrated to bond with heavy metals and stop the body from absorbing them. Further studies are needed to evaluate the efficacy and safety of *Nigella sativa* as an antidote for poisoning cases. *Nigella sativa* presents an interesting natural alternative for treating poisoning cases, potentially complementing traditional medical approaches. The main goal of this review is to explore the potential application of *Nigella sativa* as an antidote for poisoning cases. The article discusses the plant's strong ability to detoxify and protect the liver. The review highlights preclinical studies that have shown promising results but also emphasizes the need for further clinical trials to determine the efficacy and safety of *Nigella sativa* as a natural alternative for treating poisoning cases.

Keywords: *Nigella sativa*; poisoning; liver detoxification; antidote; heavy metals; toxicity; thymoquinone; thymohydroquinone; lead toxicity; mercury toxicity

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1. Introduction

1.1. About Nigella sativa

Medicinal plants have been used for generations in the earliest folk medicine systems to treat illnesses. Most indigenous medicine systems have been reported to use locally grown and harvested herbs and plants. However, a few plants have been well-documented for their therapeutic benefits and have demonstrated efficacy in treating ailments across various civilizations. *Nigella sativa* is one such miraculous plant *Nigella sativa*(Ranunculaceae), also known as black caraway, black cumin, and kalonji in different cultures. It is a treasured plant in traditional medicine and is well-known for its culinary applications. Black cumin is grown in locales, including Egypt, Iran, Greece, Syria, Albania, Turkey, Saudi Arabia, India, and Pakistan. It is native to the eastern Mediterranean, northern Africa, the Indian subcontinent, and Southwest Asia. Black cumin has been recommended in traditional medicine for a variety of illnesses and conditions, including asthma, cough, eczema, anorexia, amenorrhea, arthritis, toothache, backache, diabetes, high blood pressure, dizziness, paralysis, chronic headache, inflammation, infertility, and other

gastrointestinal disorders like diarrhoea, flatulence, dyspepsia, and dysentery to name a few. [1]–[3].Traditional uses of *N. Sativa* seeds are largely attributed to their extensive medicinal properties, including anti-inflammatory, antioxidant, immunomodulatory, cardioprotective, antihypertensive, antidiabetic, gastroprotective, anticancer, neuroprotective, antimicrobial, and hepatoprotective properties [4].

1.2. Significance of N in Traditional and religious culture:

The religious and historical significance of N. sativa is well-known and referenced in several religious writings. The N. sativa plant is called "Habb-e-Sauda" in Traditional Arab and Islamic Medicine (TAIM). Because a prophet mentioned using this seed, it is referred to as prophetic medicine (SAW). Bukhari's book says, "*N. sativa* is a healing of all ailments" (Bukhari 5687). It is mentioned in the Bible's Old Testament and included in the book of Isaiah, referred to as "ketzah," a spice for bread and cake that can be utilized in various ways.[5] Additionally, it is mentioned in both Indian and Chinese traditional medicine. It has been used in Indian medicine for a long time to cure various diseases.[6]

2. Characteristics of *Nigella sativa*

N. sativa (fig 1) is an angiosperm and annual flowering plant. It can reach lengths of up to 40 cm (1'4") and a breadth of about 20 cm (8"). It has long, striated leaves. The flowers have five to ten petals and are fragile, usually white, pink, yellow, light blue, or pale purple. Fruit is a large, expanded capsule comprising 3–7 connected follicles, each with many seeds. Transverse sections of *N. Sativa* seeds show a single-cell epidermis with thick-walled, elliptical cells covered with papillose cuticles. Two to four layers of tangentially elongated parenchyma are seen inside the epidermis, followed by a layer of rectangularly elongated cells with reddish-brown pigment. Inside the reddish-brown walls, the endosperm comprises thin-walled cells with oil globules.[7]

Fig 1. Whole plant and seeds of *N.sativa* [8].

3. Chemical Composition of *Nigella sativa*:

The chemical composition of nigella seeds is comprehensive. A mixture of proteins, carbohydrates, and volatile and fixed oils can be found in the black seed extract. [9]. The quinone components of Nigella seed extracts are responsible for their therapeutic effects. An analysis of the chemical constitution of *N. sativa* seed extract revealed that it contains around 30% fixed oils and 0.5%–1.5% volatile oils[10].

Thymoquinone is present in the volatile oil of Nigella in concentrations of around 54%, followed by a large number of monoterpenes, including a-pinene and p-cymene. Additionally, it includes thymohydroquinone and dithymoquinone. The extract from nigella seeds contains both volatile and nonvolatile oils. These oils have been shown to comprise significant amounts of proteins, unsaturated fatty acids, and terpenoids. And

alkaloids [11]. The primary components of Nigella seed extract include aliphatic fatty acids (63%), fatty acids (23%), monoterpene hydrocarbons (5%), alkane hydrocarbons (3%), and sesquiterpenes (1%). Thymoquinone, dithymoquinone, p-cymene, trans-anethol, carvone, and limonene were found to be among the 32 volatile terpenes and eight fatty acids found in Nigella seed extract, according to GC-MS analysis[12]. In addition, terpene alkaloids, diterpenes, and triterpenes were discovered in the Nigella seed extract. Nigella seed oil also has four unsaturated fatty acids and four saturated fatty acids in a ratio of 87% to 13%. Linoleic acid (56%), oleic acid (23%), and palmitic acid (13%), are the three main fatty acids. Other chemical compounds that have been linked to the plant are nigellone, avenasterol-5-ene, avenasterol-7-ene, campesterol, cholesterol, citrostadienol, cycloeucalenol, gramisterol, lophenol, obtusifoliol, stigmastanol, stigmasterol-7-ene, -amyrin, butyrospermol, cycloartenol, 3-O -[β-D-xylopyranosyl (1.3)-α L-rhamnopyranosyl(1.2)-β-L-arabinopyranosyl] -28-O-[β-L-rhamnopyranosyl (1.4)-β-D-glucopyranosyl(1.6)-β-Dgluco- pyranosyl] hederagenin, hederagenin glycoside, melanin, melanthigenin, bitter principle, tannin, resin, protein, reducing sugar, glycosidalsaponin, 3-O-[β-D-xylopyranosyl (1.2)-α-L-rhamnopyranosyl-(1.2)-β-D-glucopyranosyl] 11-methoxy-16,23-dihydroxy-28-methyl-lolean-12-enoate, stigma-5,22-dien3—D-glucose-pyranoside, cycloart-23-methyl-7,20,22-triene-3,25-diol, nigellidine-4-O-sulfite, N. mines A3, A4, A5, C, N. mines A1, A2, B1, and B2 [13].

4. Antibacterial, anti-inflammatory, and hepatoprotective effects :

4.1. Antibacterial

The antibacterial potency of crude *Nigella sativa* extracts was evaluated against various bacterial isolates, including 16 gram-negative and six gram-positive representatives. These isolates demonstrated a variety of antibiotic resistances, particularly gram-negative antibiotic resistances. According to the results, *Nigella sativa* crude extracts may have some influence on the test organisms. The water and crude alkaloid extracts were the most useful extracts. More gram-negative isolates than gram-positive ones were impacted[14].

4.1.1. In vitro studies for antibacterial activity

TQ contains antibacterial properties that antibiotics may enhance, particularly in the case of Staph. aureus. In a study, the antibacterial activity of TQ and HQ against Staph. aureus, Salmonella typhimurium, Shigella flexneri, Pseudo. aeruginosa and E. coli were examined. Staph. aureus was extremely vulnerable to TQ, as 3 and 6 g/ml were sufficient to kill and suppress the bacteria. On the other hand, THQ needed a concentration of 400 and 800 g/ml, or 100 times more than TQ, to inhibit and kill Staph. aureus, respectively. Gram-negative bacteria had lower sensitivity to TQ and THQ; their minimum bactericidal concentration (MBC) ranged from 200 to 1600 g/ml. TQ and THQ demonstrated synergistic effects when combined with antibiotics (ampicillin, cephalexin, chloramphenicol, tetracycline, gentamicin, and ciprofloxacin), particularly in the case of Staph. aureus[15].

4.1.2. In vivo studies for antibacterial activity

In an animal investigation, the total extract (TE) and essential oil (EO) of *N. sativa* seeds were demonstrated to have dose-dependent antibacterial action on both Gram-positive and Gram-negative pathogens. In this study, male mice received intraperitoneal injections of Staph. aureus and Esch. coli (0.1 ml from 106 colony forming units/ml solution). After 24 hours, different doses of TE or EO were administered to infected mice. On a soybean casein digest agar plate surface, the specimens aspirated from intraperitoneal fluid were cultivated, and it was discovered that the EO and TE are efficient against both Gram-positive and Gram-negative bacteria[16].

4.2. Anti-inflammatory activity

While the anti-inflammatory activity of the alcoholic extracts of *N. sativa* seeds and their callus on mixed glial cells of rats about their TQ content was explored, it was discovered that the aqueous extract of *N. sativa* possessed analgesic and anti-inflammatory but not antipyretic effects in animal models. Mixed glial cells inflamed by lipopolysaccharide were put through anti-inflammatory tests while exposed to various concentrations of TQ and alcoholic extracts. According to the results, the TQ content of the leaf's callus was 12 times higher than that found in the seed extract. Studies on the inflamed rat mix glial cells showed that adding 0.2 to 1.6 mg/mL of callus extract and 1.25 to 20 L/mL of seed extract significantly reduced nitric oxide production[17].

4.3. Hepatoprotective effects

According to reports, using *Nigella sativa* prevents the damaging effects of toxic metals like lead and lessens the peroxidation of hepatic lipids after exposure to toxins like carbon tetrachloride.[10] Hepatotoxicity is linked to changes in the concentrations and activities of several enzymes, including glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), serum glutamic oxaloacetic transaminase (SGOT), and serum glutamic-pyruvic transaminase (SGPT). Rat-isolated hepatocytes demonstrated how thymoquinone protects against the hepatotoxin terbutyl hyderoperoxide[18].

5. Poisoning Cases: Overview

5.1. Types and sources of poisoning

5.1.1. Cyclophosphamide-induced pulmonary injury

Several studies were conducted in the past to determine the effectiveness of *Nigella sativa* in treating the toxic symptoms arising from the use of various common drugs. One of these drugs, cyclophosphamide, is known to have significant side effects in the clinical setting, including significant changes in the functions of the liver and kidneys, a decrease in hemoglobin concentration, an increase in blood sugar levels, and an increase in triglyceride, cholesterol, and low-density lipoprotein [19]. Thymoquinone may reduce the pulmonary damage caused by cyclophosphamide by increasing levels of antioxidant enzymes and lowering pro-inflammatory cytokine release and lipid peroxidation in the lung tissues. Thymoquinone also dramatically reduced pulmonary histological alterations, enhanced the relevant serum indicators, and reducednflammatory responses [20].

5.1.2. Cisplatin-induced nephrotoxicity

Thymoquinone may reduce all of the harmful effects of cisplatin on the liver, including the toxic histopathological changes, attenuated NF-B in the liver, increased antioxidant enzyme activity, such as glutathione peroxidase and glutathione-S transferase, and decreased malondialdehyde levels. Additionally, there was a significant improvement in energy metabolism, an acceleration of the regeneration of injured organelles, and a strengthening of the endogenous antioxidant defense mechanism about the expression and concentrations of inflammatory tumor necrosis factor, nitric oxide synthase, and interleukin. On the other hand, additional investigations suggested that thymoquinone might act as a renoprotective agent against the nephrotoxicity caused by cisplatin[21].

5.1.3. Doxorubicin-induced hyperlipidemic nephropathy

Thymoquinone's antioxidant capability can greatly reduce doxorubicin-induced hyperlipidemic nephropathy while dramatically reducing proteinuria and albuminuria; this makes it a potentially useful protective treatment for proteinuria and hyperlipidemia linked to nephrotic syndrome.[16] Thymoquinone counteracts the cardiotoxicity caused by doxorubicin by boosting the heart's antioxidant defense system and bringing lipid peroxidation levels back to normal. Thymoquinone could be used as a potential treatment for toxic cardiomyopathy[22].

5.1.4. Paracetamol-induced hepatotoxicity

The protection that *Nigella sativa* offers against paracetamol-induced liver damage and nephrotoxicity[23]. Effects of *Nigella sativa* on hepatotoxicity and oxidative stress caused by acetaminophen. The findings of these studies indicate that thymoquinone, an antioxidant that also increases the activity of other antioxidants like glutathione, catalase, and superoxide dismutase, is responsible for the hepatoprotective effects of *Nigella sativa*. This enhances the body's antioxidant defenses against oxidative stress. On the other hand, *Nigella sativa*'s nephroprotective effects result from increasing prostaglandin synthesis, which results in insufficient renal perfusion, and from detoxifying free radicals by significantly increasing the activities of antioxidant enzymes, which supports the antioxidant mechanism[24].

5.1.5. Sodium nitrite toxicity

Furthermore, sodium nitrite, an inorganic chemical component frequently employed as a color fixative and preservative, is hazardous, and *Nigella sativa* has a protective effect against it. Thymoquinone can prevent extrinsic and intrinsic apoptosis in the kidney tissue, linked to sodium nitrite toxicity, and restore the normal ratio of pro- and anti-inflammatory cytokines[25].

5.1.6. Toluene-induced testicular toxicity

Nigella sativa and the resultant thymoquinone were used in several investigations on chronic toluene exposure and its effects on the CNS, lung, and testis as protective agent to alleviate its toxic symptoms. Chronic exposure to toluene causes neurodegeneration in the hippocampus, which *Nigella sativa* can help reverse [26]. Through a significant decrease in endothelial nitric oxide synthase and an increase in the expression of proliferating cell nuclear antigen in the testicular tissues, *Nigella sativa* showed excellent effectiveness in preventing toluene-induced testicular toxicity and reestablishing spermatogenesis [27].

5.1.7. Aluminum toxicity

Another chemically toxic metal, aluminum, pose substantial risks to human health and can cause hepatotoxicity, nephrotoxicity, and hematological abnormalities when consumed orally. *Nigella sativa* was employed in numerous trials to reduce aluminum risks. These experiments demonstrated that *Nigella sativa* was protective against aluminum toxicity and that hepatic and renal biochemical parameters significantly improved when black seed and aluminum were administered together[28].

6. Conclusion :

In conclusion, black seed, also known as Nigella sativa, has promising potential as a natural antidote in poisoning instances. The various Nigella sativa extracts, especially the crude alkaloid extracts, show antibacterial action against gram-positive and gram-negative bacteria, with a higher efficiency against gram-negative strains. The anti-inflammatory properties of Nigella sativa also help to reduce inflammation and have analgesic effects. Furthermore, it exhibits hepatoprotective properties by reducing the liver's adverse effects from toxins and enhancing antioxidant defense systems. In cases of specific drug-induced toxicities, such as cyclophosphamide-induced pulmonary injury, cisplatin-induced nephrotoxicity, doxorubicin-induced hyperlipidemic nephropathy, paracetamol-induced hepatotoxicity, sodium nitrite toxicity, and toluene-induced testicular toxicity, Nigella sativa and its active component, thymoquinone, exhibit protective effects and aid in restoring normal physiological functions. These results indicate Nigella sativa as a potential natural treatment for poisoning patients, with potential therapeutic advantages that call for additional study and investigation.

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