

Phytochemical Analysis of *Nigella sativa* and its Effect on Reproductive System

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Abstract

Plants and plant-based compounds are the basis of many of the modern pharmaceuticals used today for the treatment of various dreadful diseases. The discovery of medicinal plants has usually depended on the experience of the populace based on long and dangerous self-experiment. Progress over the centuries towards a better understanding of a plant derived medicine has depended on two factors that have gone hand in hand. One has been the development of increasingly strict criteria of proof that a medicine really does what it is claimed to do and the other has been the identification by chemical analysis of the active compound in the plant. *Nigella sativa* L an annual herbaceous plant commonly known as Kalounji or Black cumin has been used from centuries for treatment of various ailments, including infectious diseases which make it one of the important medicines of Tibbe Nabawi. Its seeds have been extensively studied in the last 4-5 decades and these studies have reported it to possess a number of medicinal properties. Medicinal plants have been a major source of therapeutic agents since ancient times to cure human disease. India is considered as "Botanical Garden of the world" and more than 2200 species of medicinal and aromatic plants have been identified after studies. The revival of interest in natural drugs started in last decade mainly because of the wide spread belief that green medicine is healthier than synthetic products. Now-a-days, there is manifold increase in medicinal plant based industries due to the increase in the interest of use of medicinal plants throughout the world which are growing at a rate of 7-15% annually. Despite the major advances in the modern medicine, the development of new drugs from natural products is still considered important. This seems to be even more relevant for the developing countries, where the cost to develop a drug is prohibitive. In Islam, it is regarded as one of the greatest forms of healing medicine available. The Islamic prophet Muhammad once stated that the black seed can heal every disease except death. Avicenna, most famous for his volumes called The Canon of Medicine, refers to *Nigella* as the seed that stimulates the body's energy and helps recovery from fatigue and dispiritedness. It is also included in the list of natural drugs of 'Tibb-e-Nabavi', or "Medicine of the Prophet (Muhammad)", according to the tradition "hold onto the use of the black seeds for healing all diseases. In the Unani Tibb system of medicine, *N. sativa* is regarded as a valuable remedy for a number of diseases. In the Indian system of medicine, the seeds are used as astringent, bitter, stimulant, diuretic, emmenagogue, anthelmintic, jaundice, intermittent fever, dyspepsia, paralysis, piles and skin diseases. The present review is concentrated on nigella sativa seed effect in male fertility.

Key Words – *Nigella Sativa*, Thymoquinone, Nigellone, Reproductive Hormones.

INTRODUCTION

Nigella sativa is an annual herb of the Ranunculaceae family, which grows in countries bordering the Mediterranean Sea, Pakistan and India. This widely distributed plant is native to Arab countries and other parts of the Mediterranean region[1]. For thousands of years, this plant has been used in many Asian, Middle Eastern and Far Eastern Countries as a spice and food preservative as well as a protective and health remedy in traditional folk medicine for the treatment of numerous disorders[2]. The seed of this plant is commonly known as black seed and is referred to by the prophet Mohammed as having healing powers. The seeds are commonly eaten alone or in combination with honey and in many food preparations. The oil prepared by compressing the seeds of *N. sativa* is used for cooking. Black seed is also identified as the curative black cumin in the Holy Bible, and is described as

the Melanthion of Hippocrates and Discroides and as the Gith of Pliny[3]. Other names for the seed include black caraway seed, Habbatu Sawda and Habatul Baraka "the Blessed Seed".

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astringent, bitter, stimulant, diuretic, emmenagogue, anthelmintic, jaundice, intermittent fever, dyspepsia, paralysis, piles and skin diseases[4,5]. *Nigella sativa* seeds, as nutritional and medicinal plant, have traditionally been used for thousands of years as folk medicine and some of its active compounds were reported against many ailments[6]. Different pharmacological effects such as gastric ulcer healing[7], anti-microbial effect[8], anti-cancer activity[9], cardiovascular disorders[10], gastroprotective and antioxidant activity[11], immunomodulatory, anti-inflammatory and antitumor effects[12], antitussive effect[13], anti-anxiety effect[14], anti-asthmatic effect[15], anti-inflammatory effects in pancreatic cancer cells[16], anti-helicobacter activity[17], tumor growth suppression[18], anti-viral activity against cytomegalovirus[16], hepatoprotective activity[19] have been reported for this medicinal plant. The present review aim is to assess the effects of *Nigella Sativa* and Thymoquinone on male infertility.

MORPHOLOGY OF *Nigella sativa*

Nigella sativa is a bushy, self branching plant of about 50 to 60 cm in height. Leaves are divided into linear segment 2 to 3 cm long; they are apposite in pairs on either side of the stem. Its lower leaves are small, and petiolate and upper leaves are long. The plant has finely divided foliage and pale bluish or white flowers. The flowers grow terminally on its branches. *Nigella sativa* reproduces with itself and forms a fruit capsule which consist of many white trigonal seeds, once the fruit capsule has matured, it opens up and the seeds contained within are exposed to the air becoming black in colour that is reason it also called as black seeds, seeds are triangular in shape, black in colour and possess a severe pungent smell, contains considerable amount of oil[20].



Figure -1. Showing the flower and seeds of *Nigella Sativa*.

CHEMICAL CONSTITUENTS OF *Nigella sativa* SEEDS

The seeds are very rich and diverse in chemical composition. They contain amino acids, proteins, carbohydrates, fixed and volatile oils[21]. Many of the pharmacological activities mentioned above have been attributed to quinone constituents in the seed. Chopra et al. found that thymoquinone is the main active constituent of the volatile oil of the black seed[22]. Mahfouz and El-Dakhakhny were the first to report on the isolation of 'nigellone' from the oil of *Nigella sativa* seed, using Girard's reagent[23]. Nigellone was later found to possess antihistaminic properties in relatively low concentrations[24]. El-Dakhakhny[25] was able to isolate the constitutive components of *Nigella sativa* seeds from its essential oil, among which Thymoquinone was later shown to be the main constituent of the volatile oil[26]. El Dakhakhny E determined that the 'nigellone' isolated earlier was a dimer of Thymoquinone, which was later named dithymoquinone[25]. The latter compound was shown to be formed via photodimerization of Thymoquinone as a consequence of exposure to sunlight during separation and extraction of the quinones from the seed. El-Fatraty[27] reported the isolation of thymohydroquinone from *Nigella sativa* seed volatile oil. In study of Aboutabl et al.[28] the chemical composition of the black seed of *Nigella sativa* was found to contain a fixed oil (30%) and a volatile oil that is average 0.5%, maximum 1.5%. The volatile oil was found to contain 54% Thymoquinone and many monoterpenes such as p-cymene and α -pinene, dithymoquinone and thymohydroquinone. The review article of Hala Gali-Muhtasib et al[29] concluded that *Nigella sativa* seeds contain fixed oils and volatile oils, which are rich sources of quinones, unsaturated fatty acids, amino acids and proteins and contain traces of alkaloids and terpenoids. Most of the studies on the biological effects of *Nigella sativa* have dealt with its crude extracts in different solvents; however, some studies used its active principles. Among the components isolated from the volatile oil of *Nigella sativa*, Thymoquinone has been shown to be the principal active ingredient and thus is the most studied of all[23].

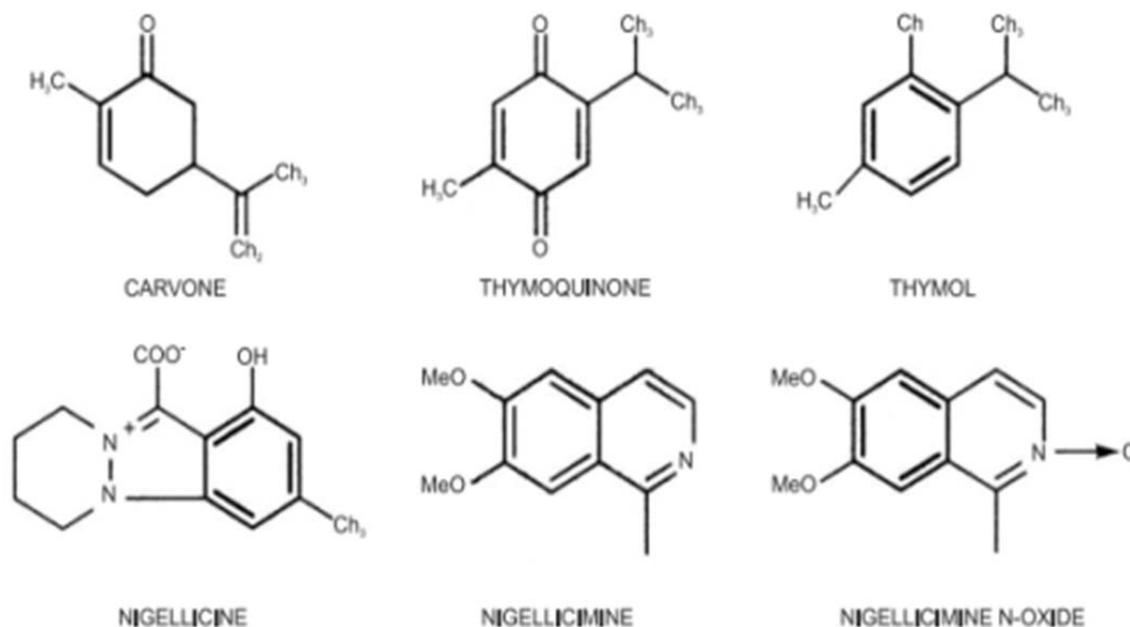


Figure 1 – Showing different chemical composition of *Nigella sativa* seeds

EFFECT ON REPRODUCTIVE SYSTEM

In a studies of Mukhallad et al and Al-Sa'a'idi et al. Sixty days study of *Nigella sativa* seeds shows to increase in the weight of reproductive organs, sperm motility and count in cauda epididimides and testicular ducts. Spermatogenesis was found to increase at primary and secondary spermatocyte. While in fertility, there was increase in number of female pregnant rats[30,31]. In a study of administration of 1ml/kg/day of *Nigella sativa* oil stimulated the secretion of sexual hormones that led to improve protein synthesis of hepatic enzymes, white blood cells count and decrease the serum cholesterol concentration in blood [32]. In a study to evaluate the probable effect of *Nigella sativa* L. seed extract on reproductive organs of male albino rats, the thickness of germinal layer of seminiferous tubules increased significantly while the thickness of epithelial layer which lying the tubules decreased significantly.[33]. In another Similar study in mice showed a significant increase in the weight of seminal vesicle in mice administrated with 0.3 ml of crude oil of *Nigella sativa* as compare with control and group[34]. in a study of Histometry of reproductive organs, revealed a significant increase in the wall thickness of testicular seminiferous tubules in mice administrated with 0.3 ml of crude oil *Nigella sativa* , in contrast to control group [35]. Alcoholic extract of black seed caused significant increase in body weight gain, reproductive parameters like eminiferous tubules thickness and diameters, account of spermatogonia[36]. The protective role of thymoquinone on testicular toxicity of methotrexate on male C57BL/6 mice (6 weeks old, 20±2 g) was investigated. Thymoquinone treatment decreased TAC and prevented the increasein the myeloperoxidase activity. Light microscopy showed in mice that receiving methotrexate resulted in interstitial space dilatation, edema, severe disruption of the seminiferous epithelium and

reduced diameter of the seminiferous tubules. Administration of thymoquinone reversed histological changes of methotrexate significantly. It was suggested that thymoquinone use may decrease the destructive effects of methotrexate on testicular tissue of patients using this agent[37]. In study of Ng Cho Ping[38] Testis Histological Features of *Nigella sativa* Treated Rats had a significantly smaller lumen diameter ($67.53 \pm 2.34 \mu\text{m}$) and thinner spermatogonia layer ($17.67 \pm 0.32 \mu\text{m}$), although a significantly thicker spermatidsperm layer ($36.95 \pm 0.79 \mu\text{m}$) as compared to the control rats group was observed ($P < 0.05$). No significant difference was detected for both the diameter of seminiferous tubule and the thickness of the permatocytes layer. In the same study results of testis histological features save indications to the spermatogenesis process. In this research, rats treated with nicotine demonstrated less mature sperm in the seminiferous tubule. The similar Findings found in other study that slight decrease in spermatogenic series and sperm count in seminiferous tubules of male Swiss albino mice treated with nicotine for durations of both one week and two weeks [39]. in study of Ng Cho Ping as for testis parameters of rats treated with *Nigella sativa* oil wasincreased spearmatids and same finding found in another study also [40]. In a previous study proved the protective effects of thymoquinone on testicular parameters[41]. In another study experimented and reported that, coadministration of cisplatin and *Nigella sativa* oil on rats for a period of 21 days showed an evident improvement in the structure of testes [42]. According to A.Al-Ali study thymoquinone is the major constituent found in *Nigella sativa*, it was believed to have protective effects on testicular parameters [43]. After reviewing the limited available articles on *Nigella sativa* effect on reproductive system we conclude that nigella sativa has positive effect on male reproductive paramets.

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