NIGELLA SATIVA MEDICINE FOR TREATMENT OF MALIGNANT GROWTH

DR. CHANDRASHEKHAR VERMA
MAGADH UNIVERSITY BODH GAYA, BIHAR

ABSTRACT: Its botanical name is Nigella sativa. It is believed to be indigenous to the Mediterranean region but has been cultivated into other parts of the world including the Arabian peninsula, northern Africa and parts of Asia. The Black seeds originate from the common fennel flower plant (Nigella sativa) of the buttercup (Ranunculaceae) family. It is sometimes mistakenly confused with the fennel herb plant. The Black Seed forms a fruit capsule which consists 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 color. The Black Seed is rich in nutritional values. It contains almost 40% fixed oils and 1.4% volatile oils. It also contains around fifteen amino acids, proteins, calcium, iron, sodium, and potassium. Among its most effective compositions are thymoquinone, dithymoquinone, thymohydroquinone, and thymol. The magazine Food Chemistry found the Black Seed to be high in protein, carbohydrates, essential fatty acids, vitamins A, B1, B2, C and niacin as well as calcium, potassium and iron. These are the very nutrients that modern science has found that we most lack. It also provides many of the same nutrients that the FDA recommends to help prevent disease and slow down the aging process.

It is very popular in various traditional systems of medicine like homeopathy. Seeds and oil have a long history of folklore usage in various systems of medicines and food. The seeds of N. sativa have been widely used in the treatment different types of diseases and ailments. It is considered as one of the greatest forms of healing medicine. It has been recommended for using on regular basis in Tibb-e-Nabwi (Prophetic Medicine). It has been widely used as antihypertensive, liver tonics, diuretics, digestive, anti-diarrheal, appetite stimulant, analgesics, anti-bacterial and in skin disorders. Extensive studies on N. sativa have been carried out by various researchers and a wide spectrum of its pharmacological actions have been explored which may include anti-diabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmylic, bronchodilator, hepato-protective, renal protective, gastro-protective, antioxidiant properties, etc. Due to its miraculous power of healing, N. sativa has got the place among the top ranked evidence based herbal medicines. Cancer is one of the major threats of modern life, which is considered as the second cause of death after myocardial infarction. Millions of people die every year in different types of cancer despite tremendous efforts to find methods of control and cure. In the last century, great advances were made in modern medical science to control disease. Many active ingredients have been found in the seeds of N. sativa. The seeds contain both fixed and essential oils, proteins, alkaloids and saponin Ghosheh (1999) described the quantification of four pharmacologically important components: thymoquinone (TQ), dithymoquinone (DTQ), thymohydroquinone (THQ), and thymol (TH1), in the oil of N. sativa seed by HPLC. Much of the biological activities of the seeds have been shown to be due to thymoquinone, the major component of the essential oil, which is also present in the fixed oil. TQ is considered as potent anti-oxidant anti-carcinogenic and anti-mutagenic agent. Moreover, TQ is a relatively safe compound, particularly when given orally to experimental animals. Alpha (α)-hederin, a pentacyclic triterpene saponin.

Keywords: Nigella sativa, Miracle herb, Ranunculaceae, Habat-ul-Sauda, Thymoquinone, Tibb-e-Nabwi, Black seeds, Anti-cancer, Antioxidant.

INTRODUCTION

Nigella sativa (N. sativa) Family Ranunculaceae is a widely used medicinal plant throughout the world. Nigella sativa is an annual flowering plant. Botanical name is Nigella sativa. It is believed to be indigenous to the Mediterranean region but has been cultivated into other parts of the world including the Arabian peninsula, northern Africa and Asia. Nigella sativa seeds have wide therapeutic effects and have been reported to have significant effects against many ailments such as skin diseases, jaundice, gastrointestinal problems, anorexia, conjunctivitis, dyspepsia, rheumatism, diabetes, hypertension, intrinsic hemorrhage, paralysis, amenorrhea, anorexia, asthma, cough, bronchitis, headache, fever, influenza and eczema. Cancer is one of the major threats of modern life, which is considered as the second cause of death after myocardial infarction (Grundy, 1991). Millions of people die every year in different types of cancer despite tremendous efforts to find methods of control and cure. In the last century, great advances were made in modern medical science to control disease. But many diseases like cancers are not yet curable fully.

Nigella sativa, Hindi name (Mangaraila) and Arabi (Kalonji) is an annual flowering plant. It grows to 25–30 cm tall and has linear lanceolate leaves. The delicate flowers have 5-10 petals and the colors are usually yellow, white, pink, pale blue or pale purple. The fruit of plant is large and inflated capsule composed of 3-7 united follicles, that each of them has numerous seeds. The black colored seeds are flattened, oblong and angular, funnel shaped, with the length of 0.2 cm and 0.1 cm wide.
This plant is known by different names in different countries, for example black cumin (English), black caraway seeds (USA), shonaiz (Persian) and kalajira (Bangali).

**Characteristics of the Nigella Sativa Seeds**

Macroscopically, seeds are small dicotyledonous, trigonus, angular, regulose-tubercular, 2-3.5 mm × 1-2 mm, black externally and white inside, odor slightly aromatic and taste bitter. Microscopically, transverse section of seed shows single layered epidermis consisting of elliptical, thick walled cells, covered externally by a papillose cuticle and filled with dark brown contents. Epidermis is followed by 2-4 layers of thick walled tangentially elongated parenchymatous cells, followed by a reddish brown pigmented layer composed of thick walled, rectangular elongated cells. Inner to the pigment layer, is present a layer composed of thick walled rectangular elongated or nearly columnar, elongated cells. Endosperm consists of thin walled, rectangular or polygonal cells mostly filled with oil globules. The powder microscopy of seed powder shows brownish black, parenchymatous cells and oil globules.

**Homoeopathy Drug Proving**

Drug Proving is the method of stupifying the scientific properties of the drug substance i.e. (NIGELLA SATIVA). In other hand we can say that it is the systematic process of investigating the pathogenic power of drug by administering the same to the healthy individuals of different age and both sex, different geographical areas and should be truth worthy, honest, healthy as well as mentally who can narrates symptoms exactly or may be physician as a well provers.

**Background:**

The methodology of drug Proving has evolved considerable since the times of Dr Hahnemann standardisation of Proving process and quality of Proving studies has been a major consideraration for research over years. Proving guidelines have been developed by various international bodies such as Homoeopathic Pharmacopoeia committee of United States (HPCUS), European Commission of Homoeopathy (ECH) and Liga Medicorum Homoeopathica Internationalis (LMHI) and in our country a major research activities of the Central Council for Research in Homoeopathy (CCRH) are also doing vast work. Dr. Hahennmann has clearly indicated his views and given his instructions regarding the preparation of Homoeopathy mother tincture from various sources in his Organon of Medicine at aphorism 269 and 271 including foot notes. We shall examine them here and classified those plant materials in four groups depending upon the quantity of juice. They contained most juicy, moderately juicy, less juicy and dry plant samples. Class I Tincture is prepared with equal parts by weight of juice and alcohol. This mixture is allowed to stand for 8 days in a well-stoppered bottle, in a dark cool place, and is then filtered. This prepared tincture denoted by Q and known by Mother Tincture. The Homoeopathy Medicines are potentised in three scale namely 1. Decimal scale, 2. Centesimal scale, 3. Fifty Millisimal scale. Decimal Scale: As the mother tincture in this method contains 1/10 of drug concentration, it corresponds to 1X potency. One drop of mother tincture and 9 drops of plane alcohol and given 10 downward strokes on the palm in equal proportion, it becomes 1X Potency. The next higher potencies are prepared with one drop of preceding Potency and nine drops of alcohol and do usual process it becomes 2X Potency. The medicine prepare under Decimal Scale are called 1X, 2X, 3X etc. And medicines are prepare under Centesimal Scale called 1, 2, 3, 30, 200, 1M etc. whereas medicines are prepare under the Fifty Millisimal Scale called 0/1, 0/2, 0/3, etc.
Cancer
Cancer is the uncontrolled growth of abnormal cells anywhere in our body. These abnormal cells are termed cancer cells, malignant cells, or tumor cells. These cells can infiltrate normal body tissues. Many cancers and the abnormal cells that compose the cancer tissue are further identified by the name of the tissue that the abnormal cells originated from (for example, breast cancer, lung cancer, colon cancer). Cancer is not confined to humans; animals and other living organisms can get cancer. Below is a schematic that shows normal cell division and how when a cell is damaged or altered without repair to its system, the cell usually dies. Also shown is what occurs when such damaged or unrepaired cells do not die and become cancer cells and show uncontrolled division and growth – a mass of cancer cells develop. Frequently, cancer cells can break away from this original mass of cells, travel through the blood and lymph systems, and lodge in other organs where they can again repeat the uncontrolled growth cycle. This process of cancer cells leaving an area and growing in another body area is termed metastatic spread or metastasis. For example, if breast cancer cells spread to a bone, it means that the individual has metastatic breast cancer to bone. This is not the same as "bone cancer," which would mean the cancer had started in the bone.

Risk factors and causes of cancer
Anything that may cause a normal body cell to develop abnormally potentially can cause cancer. Many things can cause cell abnormalities and have been linked to cancer development. Some cancer causes remain unknown while other cancers have environmental or lifestyle triggers or may develop from more than one known cause. Some may be developmentally influenced by a person's genetic makeup. Many patients develop cancer due to a combination of these factors. Although it is often difficult or impossible to determine the initiating event(s) that cause a cancer to develop in a specific person, research has provided clinicians with a number of likely causes that alone or in concert with other causes, are the likely candidates for initiating cancer. The following is a listing of major causes and is not all-inclusive as specific causes are routinely added as research advances:

Chemical or toxic compound exposures: Benzene, asbestos, nickel, cadmium, vinyl chloride, benzidine, N-nitrosamines, tobacco or cigarette smoke (contains at least 66 known potential carcinogenic chemicals and toxins), asbestos, and aflatoxin

Ionizing radiation: Uranium, radon, ultraviolet rays from sunlight, radiation from alpha, beta, gamma, and X-ray-emitting sources

Pathogens: Human papillomavirus (HPV), EBV or Epstein-Barr virus, hepatitis viruses B and C, Kaposi's sarcoma-associated herpes virus (KSHV), Merkel cell polyomavirus, Schistosoma spp., and Helicobacter pylori; other bacteria are being researched as possible agents.

Genetics: A number of specific cancers have been linked to human genes and are as follows: breast, ovarian, colorectal, prostate, skin and melanoma; the specific genes and other details are beyond the scope of this general article so the reader is referred to the National Cancer Institute for more details about genetics and cancer.

It is important to point out that most everyone has risk factors for cancer and is exposed to cancer-causing substances (for example, sunlight, secondary cigarette smoke, and X-rays) during their lifetime, but many individuals do not develop cancer. In addition, many people have the genes that are linked to cancer but do not develop it. Why? Although researchers may not be able give a satisfactory answer for every individual, it is clear that the higher the amount or level of cancer-causing materials a person is exposed to, the higher the chance the person will develop cancer. In addition, the people with genetic links to cancer may not develop it due to compound stimuli to make the genes function. In addition, some people may have a heightened immune response that controls or eliminates cells that are or potentially may become cancer cells. There is evidence that even certain dietary lifestyles may play a significant role in conjunction with the immune system to allow or prevent cancer cell survival. For these reasons, it is difficult to assign a specific cause of cancer to many individuals.

Recently, other risk factors have been added to the list of items that may increase cancer risk. Specifically, red meat (such as beef, lamb, and pork) was classified by the Research on Cancer as a high-risk agent for potentially causing cancers; in addition processed meats (salted, smoked, preserved, and/or cured meats) were placed on the carcinogenic list. Individuals that eat a lot of barbecued meat may also increase risk due to compounds formed at high temperatures. Other less defined situations that may increase the risk of certain cancers include obesity, lack of exercise, chronic inflammation, and hormones, especially those hormones used for replacement therapy. Other items such as...
cell phones have been heavily studied. In 2011, the World Health Organization classified cell phone low energy radiation as "possibly carcinogenic," but this is a very low risk level that puts cell phones at the same risk as caffeine and pickled vegetables.

**cancer symptoms**

Symptoms of cancer depend on the type of cancer, where it is located, and where the cancer cells have spread. For example, breast cancer may present as a lump in the breast or as nipple discharge while metastatic breast cancer may present with symptoms of pain (if spread to bones), extreme fatigue (lungs), or seizures (brain). A few patients show no signs or symptoms until the cancer is far advanced. Many cancers will present with some of the above general symptoms but often have one or more symptoms that are more specific for the cancer type. For example, lung cancer may present with common symptoms of pain, but usually the pain is located in the chest. The patient may have unusual bleeding, but the bleeding usually occurs when the patient coughs. Lung cancer patients often become short of breath.

**Modern carcinogens**

In 1911 Peyton Rou was discovered a type of cancer in chickens that was caused by Rous sarcoma virus. In 1915, cancer was induced for the first time in rabbits by coal tar applied to skin. 150 years had passed since the most destructive source of chemical carcinogens known to man, tobacco (nicotin) was rediscovered as a carcinogen. As of today more than 100 carcinogens (chemical, physical, and biological) were identified. From many of these carcinogens associations recognized long before, scientists understood the mechanism by which the cancer was produced. The continuing research is discovering new carcinogens, explaining how they cause cancer and providing insight into ways to prevent it.

**Cancer causing viruses**

(1) Hepatitis B or C viruses cause liver cancer. (2) Epstein–Barr viruses cause non-Hodgkin lymphomas and nasopharyngeal cancer. (3) The human immunodeficiency virus (HIV) is associated with Kaposi Sarcoma and non–Hodgkin lymphoma. (4) Human papilloma viruses (HPVs) are associated with cervix, vulva and penis cancers.

**Cancer screening and early detection**

The first cancer screening test to be widely used was the Pap test. The test was first developed by George Papanicolaou as a method in understanding the menstrual cycle. He also identified Pap tests potential for early detection of cervical cancer. In 1960s mammography was developed for identification of breast cancer. Later early detection of cervix, breast, colon, rectum, endometrium, prostate, thyroid, oral cavity, skin, lymph nodes, testes, and ovaries cancers were identified and practiced in the clinic.

**Cancer in childrens**

Cancer is the second most common cause of death among children ages 1 to 14 years in the United States, surpassed only by accidents; 1,320 children died from cancer in 2009. Leukemia accounts for almost one-third of all cancers (including benign brain tumors) diagnosed in children aged 0 to 14 years, 77% of which are acute lymphocytic leukemias. Cancers of the brain and other nervous system are the second most common cancer type (25%), followed by soft tissue sarcomas (7%, half of which are rhabdomyosarcoma), neuroblastoma (6%), renal (Wilms) tumors (5%), and Hodgkin and non–Hodgkin lymphomas (4% each). From 2005 to 2009, the overall incidence rate for cancer in children aged 14 years and younger increased slightly by 0.5% per year, a trend that has been consistent since 1975. The death rate for childhood cancer has decreased by more than half over the past 3 decades, from 4.9 (per 100,000) in 1975 to 2.1 in 2009. Table 13 provides trends in survival rates for the most common childhood cancers. The 5-year relative survival rate for all cancer sites combined improved from 58% for children diagnosed between 1975 and 1977 to 83% for those diagnosed between 2002 and 2008. The substantial progress for all of the major childhood cancers reflects both improvements in treatment and high levels of participation in clinical trials.

**Role of N. Sativa as an anticancer agent**

Many active ingredients have been found in the seeds of *N. sativa*. The seeds contain both fixed and essential oils, proteins, alkaloids and saponin. described the quantification of four pharmacologically important components: thymoquinone (TQ), dithymoquinone (DTQ), thymohydroquinone (THQ), and thymol (THY), in the oil of *N. sativa* seed by HPLC. Much of the biological activities of the seeds have been shown to be due to thymoquinone, the major component of the essential oil, which is also present in the fixed oil (Ali and Blunden, 2003). TQ is considered as potent anti-oxidant (Badary et al., 2003), anti-carcinogenic and anti-mutagenic. Moreover, TQ is a relatively safe
compound, particularly when given orally to experimental animals. Alpha (α)-hederin, a pentacyclic triterpene saponin isolated from the seeds of *N. sativa*.

**Molecular mechanisms of *N. sativa* against cancer**

Cancers are the abnormal cell growth caused by genetic alteration. So, any agent which has anti-cancer activity, either protect genetic material from alteration or kill the genetically altered cancer cells. The active ingredients (mainly TQ) from *N. sativa* act on cancer cell to help to kill them by several molecular pathways.

El-Mahdy et al. (2005) suggested the apoptotic mechanisms behind the anti-proliferative effect of TQ (from *N. sativa*) on myeloblastic leukemia HL-60 cells. They reported that TQ induces apoptosis, disrupts mitochondrial membrane potential and triggers the activation of caspases 8, 9 and 3 in HL-60 cells. The apoptosis induced by TQ was inhibited by a general caspase inhibitor, z-VAD-FMK; a caspase-3-specific inhibitor, z-DEVD-FMK; as well as a caspase-8-specific inhibitor, z-IETD-FMK. Moreover, the caspase-8 inhibitor blocked the TQ-induced activation of caspase-3, PARP cleavage and the release of cytochrome c from mitochondria into the cytoplasm. In addition, TQ treatment of HL-60 cells caused a marked increase in Bax/Bcl2 ratios due to upregulation of Bax and downregulation of Bcl2 proteins. Their results indicated that TQ-induced apoptosis is associated with the activation of caspases 8, 9 and 3, with caspase-8 acting as an upstream activator and activated caspase-8 initiates the release of cytochrome c during TQ-induced apoptosis. TQ action was also found as pro-apoptotic against colon cancer cell line HCT116 (Gali-Muhtasib et al., 2004). It was showed that the apoptotic effects of TQ are modulated by Bcl-2 protein and are linked to and dependent on p53. TQ also down-regulates the expression of NF-kappa B-regulated anti-apoptotic (IAP1, IAP2, XIAP Bcl-2, Bcl-xL, and survivin) gene products (Sethi et al., 2008). Torres et al. (2010) found TQ inducing apoptosis by the activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase pathways in pancreatic cancer cell.

TQ has also been reported to be active in controlling Akt pathway. Yi et al. (2008) found that TQ effectively inhibited human umbilical vein endothelial cell migration, invasion, and tube formation by suppressing the activation of AKT and extracellular signal-regulated kinase. Xuan et al. (2010) found that LPS (lipopolysaccharides: a bacterial component)-induced phosphorylation of prosurvival kinases Akt and ERK1/2 was abrogated by TQ in dendritic cells.

NF-kappa B plays a key role in regulating the immune response, and incorrect regulation of NF-kappa B has been found to be linked to cancer (Albensi and Mattson, 2000). Sethi et al. (2008) found that TQ suppressed tumor necrosis factor-induced NF-kappa B activation in a dose- and time-dependent manner and inhibited NF-kappa B activation induced by various carcinogens and inflammatory stimuli. The suppression of NF-kappa B activation is correlated with sequential inhibition of the activation of I kappa B alpha kinase, I kappa B alpha phosphorylation, I kappa B-alpha degradation, p65 phosphorylation, p65 nuclear translocation, and the NF-kappa B-dependent reporter gene expression. Also Oberg et al. (2009) reported that a herbal melatonin (HM) from *N. sativa* modulates cytokine production and suggested it as a ligand for TLR4 (toll-like receptor 4). They investigated the possibility that the HM-induced cytokine production is via an NF-kappa B signaling pathway and found that HM induced the degradation of I kappa B-alpha, a key step in the activation of NF-kappa B. Moreover, addition of I kappa B kinase (IKK) specific inhibitors effectively inhibited the observed HM-induced production of IL-8 and IL-6 by TLR4-transfected HEK293 (embryonic kidney 293) cells and THP-1 (Human acute monocytic leukemia) cells (Oberg et al., 2009).

Many studies showed that *N. sativa* oil or TQ has antioxidant activity and increases the activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) etc (Ismail et al., 2010). And antioxidant enzymes are clearly related to cancer- mostly their increased activities are beneficial against different types of cancer (Khan et al., 2010). Administration of *N. sativa* oil or TQ can lower the toxicity of other anticancer drugs (for example, cyclophosphamide) by an up-regulation of antioxidants mechanisms, indicating a potential clinical application for these agents to minimize the toxic effects of treatment with anticancer drugs (Alenzi et al., 2010).

In addition to these cancer inhibiting properties, components of *N. sativa* have cancer protective roles. Ibrahim et al. (2008) reported that *N. sativa* oil administration has a protective effect against the CCl4-mediated suppression of CYP (drug-metabolizing cytochrome P450 enzymes). And genetic abnormalities and polymorphisms of CYP enzymes are associated with cancer (Chen et al., 2008). Radiotherapy is one of the most common strategies for treating human cancers but this treatment is somehow risky for normal tissue. Cemek et al. (2006) showed that *N. sativa* and glutathione treatment significantly antagonize the effects of radiation. Therefore, *N. sativa* may be a beneficial agent in protection against ionizing radiation-related tissue injury. Assayed (2010) investigated the radio-protective potential of *N. sativa* crude oil against hemopoietic adverse effects of gamma irradiation. He found that irradiation resulted in significant reduction in hemolysin antibodies titers and delayed type hypersensitivity reaction of irradiated rats, in addition to significant leukopenia and significant decrease in plasma total protein and globulin concentration and depletion of lymphoid follicles of spleen and thymus gland. Furthermore, there was a significant increase in malondialdehyde concentration with a significant decrease in plasma GPx, CAT and erythrocyte SOD activities. But oral administration of *N. sativa* oil before irradiation considerably normalized all the above-mentioned criteria; and produced significant regeneration in spleen and thymus lymphoid follicles. Thus *N. sativa* oil is recognized as a promising natural radioprotective agent against immunosuppressive and oxidative effects of ionizing radiation.
Conclusion

The use of herbal drugs as complementary medicine is prevalent and gaining worldwide popularity. Many drugs are derived directly from plants; while the others are chemically modified natural products. The original research articles published so far have confirmed the pharmacological potential of *N. sativa* and extracts and some of its active principles, particularly TQ and alpha-hederin possess remarkable *in vitro* and *in vivo* pharmacological activities against a large variety of diseases and found to be relatively. But I found during my research according to principle of Homoeopathy many miracles action found, especially in carcinoma, GIT disorder, neuropathy and non-healing ulcer recover very rapidly, gently and easily comprehensible principle including restoration of health.

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