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MEDICINAL AND THERAPEUTICAL POTENTIAL OF NIGELLA SATIVA

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ABSTRACT

Nigella sativa is a plant. People have used the seed to make medicine for over 2000 years. It was even discovered in the tomb of King Tut. Historically, black seed has been used for headache, toothache, nasal congestion, and intestinal worms. It has also been used for "pink eye" (conjunctivitis), pockets of infection (abscesses), and parasites. Today, black seed is used for treating digestive tract conditions including gas, colic, diarrhea, dysentery, constipation, and hemorrhoids. It is also used for respiratory conditions including asthma, allergies, cough, bronchitis, emphysema, flu, swine flu, and congestion. Other include uses lowering blood pressure, lowering cholesterol levels, treating cancer, and boosting the immune system. You may read that a patent has been issued to cover the use of black seed to improve immunity, but don't be misled. The presence of a patent doesn't mean black seed has been shown to be effective for this use. Women use black seed for birth control, to start menstruation, and to increase milk flow. Black seed is sometimes used in combination with cysteine, vitamin E, and saffron to ease the side effects of a chemotherapy drug called cisplatin. Some people apply black seed directly to the skin for joint pain (rheumatism), headache, and certain skin conditions. In foods, black seed is used as a flavoring or spice. There is some scientific evidence to suggest that black seed might help boost the immune system, fight cancer, prevent pregnancy, and lessen allergic reactions by acting as an antihistamine. For the improvement of human beings. Scientists, researchers should works to know more its other medicinal use in different diseases.

Keywords: Nigella sativa, digestive tract, respiratory conditions, cancer, immune system.

INTRODUCTION:

Nigella sativa is an annual herbaceous plant, black seed (Nigella sativa) is believed to be indigenous to the Mediterranean region but now found widely in india (like Jammu-Kashmir, Himachal Pradesh, Bihar, Assam and Punjab). It has been also cultivated into other parts of the world including Saudi Arabia, northern Africa and parts of Asia ^[1]. It is tiny and hairy being no more than 3 mm in length, black seed originates from the common fennel flower plant (Nigella sativa) of the buttercup (Ranunculaceae) family. Nigella sativa is sometimes mistakenly confused with the fennel herb plant (Foeniculum vulgare) ^[2]. The plant has finely divided foliage and pale bluish purple or white flowers. The flowers grow terminally on its branches while the leaves grow opposite each other in pairs, on either side of the

stem ^[3]. Its lower leaves are small and petiole and the upper leaves are long (6-10 cm). The stalk of the plant reaches a height of twelve to eighteen inches as its fruit, the black seed, matures ^[4].

Nigella sativa reproduces with itself and 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 (black seeds) ^[5]. Nigella sativa and its black seed are known by other names, varying between places. Some call it black caraway; others call it black cumin (Kalonji), or even coriander seeds. In English, the Nigella sativa plant is commonly referred to as "Love in a Mist". Nevertheless, this is Nigella sativa, which has been known and used from ancient times and is also known in Persian as Shonaiz^[6].

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Figure 1: Seeds of N.sativa



Figure 2: Flower of N.sativa

Scientific Classification^[7]

| Kingdom: | Plantae |
|-------------|---------------|
| (unranked): | Angiosperms |
| (unranked): | Eudicots |
| Order: | Ranunculales |
| Family: | Ranunculaceae |
| Genus: | Nigella |
| Species: | sativa |

Morphology

It is small prostrate annual herb about 45 cm high 2-3 slender leaves pinnatisect, 2-4 cm long cut into linear segment, segments oblong ^[8]. Flowers pale, blue on solitary long peduncles, seeds trigonous and black in colour. The plant has a rather stiff, erect, branching stem. bears deeply-cut greyish-green leaves and terminal grayish blue flowers ^[9], followed by odd, toothed seed vessels, filled with small somewhat compressed seeds, usually three-cornered, with two sides flat and one convex, black or brown externally white and oleaginous, strong agreeable aromatic odour, like that of nutmegs, and a spicy, pungent taste ^[10]. The flowers are delicate, and usuallycoloured pale blue and white, with 5-10 petals. The fruit is a large and inflated capsule composed of 3–7 united follicles, each containing numerous seeds. It has a pungent bitter taste and a faint smell of strawberries ^[11].

Etymology

The scientific name is a derivative of Latin *niger* (black).^[12] The Common names are: In English, *Nigella sativa* seed is variously called fennel flower, nutmeg flower, black caraway, Roman coriander, and black cumin.^[13] Other names used, sometimes misleadingly, are onion seed and black sesame, both of which are similar-looking, but

unrelated. Blackseed and black caraway may also refer to Bunium persicum.^[14] The seeds are frequently referred to as black cumin (asin Assamese: kaljeera or kolajeera or Bengali kalo jeeray), but black cumin (kala jeera) is different from Nigella sativa (kali jeeri). In Kannada, it is called Krishna jeerige, but this is also used for a different spice, Buniumpersicum[15]. It is used as part of the spice mixture paanch phoran or panch phoron (meaning a mixture of five spices) and by itself in a great many recipes in Bengali cookery and most recognizably in naan bread [16]. The Turkish name corek otu literally means "bun's herb" from its use in flavouring the corek buns. Such braided-dough buns are widespread in the cuisines of Turkey and its neighbours (Tsoureki τσουρέκι). In Bosnian, the Turkish name for N. sativa is spelled asčurekot[17]. The seed is used in Bosnia, and particularly its capital Sarajevo, to flavour pastries (Bosnian: somun) often baked on Muslim religious holidays.

History of Nigella sativa

Earliest written reference to black seed was first found in the book of Isaiah in the Old Testament. Isaiah explains: "For the black cumin is not threshed with a threshing Sledge, nor is a cart wheel rolled over the cumin, but the black cumin is beaten out with a stick, and the cumin with a rod ^[18]. Easton's Bible Dictionary explains that the



Hebrew word for Black Cumin, "ketsah", refers to "doubt the Nigella sativa, is the order Ranunculaceae which grows wild in Mediterranean countries, and cultivated in Egypt and Syria^[19].

Dioscoredes, Greek physicist at unity century, reported that black seed is used to treat headaches, nasal congestion, toothache, and intestinal worms. In addition, also be used to promote menstruation and increase milk production in nursing mothers ^[20]. The Muslim scholar al-Biruni (973-1048), which combine drugs ancestral India and China mentioned that Black seed is a kind of sesame seeds, called alwanak in Sigzi dialect ^[21]. Later, this statement is justified by the Suhar Bakht who explained that the black seed as habb-i-Sajzi (viz. Grains Sigzi). Reference "grain" This allows people to use it as a nutritional ingredient in the 10th century and the 11th AD. In a medical system in Greco-Arab/Unani-Tibb, which originated from Hippocrates, Galen and Ibn Sina, black seed is a valuable remedy in treating gastrointestinal dysfunction, and hepatitis and is described as a stimulant to different conditions, high fever reliever^[22].

Ibn Sina (980-1037), in his greatest "The Canon of Medicine," regarded by many as the most famous books in medicine, in the East or West, said the black seed as "stimulating the body's energy and helps recovery from fatigue or lack of spirit^[23]. "Black seed is also included in the list of natural medicines Al-Tibb al-Nabawi, and according to tradition, "Wearing black seed can cure all diseases except death." Prophetic reference in describing black seed as "the healer of all diseases" are not too exaggerated exaggerated when it first appeared. Previous studies have provided evidence indicating that the black seed has a real ability to improve the human immune system if used all the time ^[24]. Words of the Prophet "to rely on the use of seed" also advocated for the use of seed consistently.

Folk Medicine

Nigella sativa has been used for medicinal purposes for centuries, both as an herb and pressed into oil, in Asia, Middle East, and Africa. It has been traditionally used for a variety of conditions and treatments related to respiratory health, stomach and intestinal health, kidney and liver function, circulatory and immune system support, and for general well-being^[25]. 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 theUnani Tibb system of medicine, N. sativa is regarded as a valuable remedy for a number of diseases ^[26]. The seeds have been traditionally used in the Middle East and Southeast Asian countries to treat ailments including asthma, bronchitis, rheumatism and related inflammatory diseases, to increase milk production in nursing mothers, to promote digestion and to fight parasitic infections^[27]. Its oil has been used to treat skin conditions such as eczema and boils and to treat cold symptoms. Its many uses have earned Nigella the Arabic approbation 'Habbatul barakah', meaning the seed of blessing^[28]. Karayal seeds and their oil have a long history of folklore usage in Arabian and Indian civilisation and are used in food as well as medicine. The seeds are used as flavouring, to improve digestion and produce warmth, especially in cold climates. They are sometimes scattered in the folds of woollen fabrics to preserve them from insect damage [29, 30, 31]

In India the seeds are used as a carminative and stimulant to ease bowel and indigestion problems and are given to treat intestinal worms and nerve defects to reduce flatulence, and induce sweating. Dried pods are sniffed to restore a lost sense of smell. It is also used to repel some insects, much like mothballs.

Traditional medicine:

In the Unani Tibb system of medicine, black cumin (*Bunium bulbocastanum*) is regarded as a valuable remedy for a number of diseases ^[32]. In Islamic writing, a *hadith* narrated byAbu Hurairah says "I heard Allah's Apostle saying, 'There is healing in black seed (haba sowda) for all diseases except death^[33]. Nestlé has reportedly filed a patent application covering use of *N. sativa* as a food allergy treatment.^[34] Yet the firm denies the claim of patenting the plant, stating that the patent would only cover "the specific way that thymoquinone - a compound that can be extracted from the seed of the fennel flower - interacts with opioid receptors in the body and helps to reduce allergic reactions to food ^[35].

Chemistry composition seeds of Nigella sativa:

Seeds of nigella contain numerous esters of structurally unusual unsaturated fatty acids with terpene alcohols (7%); furthermore, traces of alkaloids are found which belong to two different types: isochinoline alkaloids are represented by nigellimin and nigellimin-N-oxide, andpyrazol alkaloids include nigellidin and nigellicin. In essential (avr. 0.5%, max. 1.5%), the oil thymoquinone was identified as the main component (up to 50%) besides p-cymene (40%), pinene (up to 15%), dithymoguinone and thymohydroguinone.

Other terpene derivatives were found only in trace amounts:Carvacrol, carvone, limonene, 4-terpineol, citronellol^[36]. The essential oil contains significant (10%) amounts of fatty acid ethyl esters. On storage, thymoquinone yields dithymoquinonene and higher oligocondensation products. The seeds also contain a fatty oil rich in unsaturated fatty acids, mainly linoleicacid (50 60%), oleic acid (20%), eicodadienoic acid (3%) and dihomolinoleic acid (10%) ^[37].Saturated fatty acids (palmitic, stearic acid) amount to about 30% or less. Also contain parts of the essential oil, mostly thymoquinone, by which it acquires an aromatic flavor ^[38].

The seeds give on steam-distillation a yellowish brown volatile oil with an unpleasant odor. The oil contains carvone, d -limonene, and a carbonyl compound, nigellone.

Nutritional value of Nigella sativa:

Black seed is rich in nutritional values. Monosaccharides (single molecule sugars) in the form of glucose, rhamnose, xylose, and arabinose are found in the black seed. The black seed contains a non-starch polysaccharide component which is a useful source of dietary fiber. It is rich in fatty acids, particularly the unsaturated and essential fatty acids (Linoleic and Linoleic acid) ^[39]. Essential fatty acids cannot be manufactured by the body alone, and therefore we acquire these from food. Fifteen amino acids make up the protein content of the black seed, including eight of the nine essential amino acids. Essential amino acids cannot be synthesized within our body in sufficient quantities and are thus required from our diet. Black seed contains Arginine which is essential for infant growth ^[40]. Chemical analysis has further revealed that the black seed contains carotene, which is converted by the liver into vitamin A, the vitamin known for its anti-cancer activity. The black seed is also a source of calcium, iron, sodium, and potassium. Required only in small amounts by the body, these elements' main function is to act as essential cofactors in various enzyme functions^[41].

Pharmacological action of Nigella sativa:

Antimicrobial activity: Nigella *sativa* exhibited strong antimicrobial activity against Salmonella *typhi*, Pseudomonas *aeruginosa* and others. The essential oil has been shown to have activity against Gram-positive and Gram-negative bacteria ^[42]. However, sensitivity against Gram-positive bacteria such as Staphylococcus *aureus* and Vibrio *cholerae* was found to be stronger. Bacteria like Staphylococcus *aureus, S. pyogenes* and *S. viridans* are more susceptible to *Nigella sativa*. In an invitro study, volatile oil showed activity comparable to ampicillin^[43]. The activity of the volatile oil also extended to drug-resistant strains of *Shigella spp*,

Vibrio cholerae and *Escherichia coli* and was found to have a synergistic action with streptomycin and gentamycin.

Hepatoprotective activity: Thymoquinone, one of the active constituents of *Nigella sativa*, is reported to havehepatoprotective activity." An in-vitro study showed the protective effect against tert-butyl hydroperoxide (TBHP)-induced oxidative damage to hepatocytes. The activity was demonstrated by a decreased leakage of alanine transaminase (ALT), aspartic transaminase (AST) and decreased trypan blue uptake^[44].

Immune system strengthening

Studies begun just over a decade ago suggest that if used on an ongoing basis, black seed can play an important role to enhance human immunity, particularly in immunocompromise patients.

In 1986, Drs. El-Kadi and Kandil conducted a study with human volunteers to test the efficiency of black seed as a natural immune enhancer. The first group of volunteers received black seed capsules (1 gram twice daily) for four weeks and the second group were given a placebo. A complete lymphocyte count carried out in all volunteers before and four weeks after administration of black seed and the placebo revealed that the majority of subjects who took black seed displayed a 72% increase in helper to suppresser T-cells ratio, as well as an increase in natural killer cell functional activity. The control group who received the placebo experienced a net decline in ratio of 7%. They reported, "These findings may be of great practical significance since a natural immune enhancer like the black seed could play an important role in the treatment of cancer, AIDS, and other disease conditions associated with immune deficiency states." These results were confirmed by a study published in the Saudi Pharmaceutical Journal in 1993 by Dr. Basil Ali and his colleagues from the College of Medicine at Kin Faisal University^[45,46].

In the field of AIDS research specifically, tests carried out by Dr. Haq on human volunteers at the Department of Biological and Medical Research Center in Riyadh, Saudi Arabia (1997) showed that black seed enhanced the ratio between helper T-cells and suppresser T-cells by 55% with a 30% average enhancement of the natural killer (NK) cell activity.

Anti-histamine activity

Histamine is a substance released by bodily tissues, sometimes creating allergic reactions and is associated with conditions such as bronchial asthma.

In 1960, scientists Badr-El-Din and Mahfouz found that dimer dithymoquinone isolated from black seed's volatile oil, under the name of "Nigellone," and given by mouth to some patients suffering from bronchial asthma, suppressed the symptoms of the condition in the majority of patients^[47].

Following the results of this early study, crystalline nigellone was administered to children and adults in the treatment of bronchial asthma with effective results and no sign of toxicity. It was observed, however, that although effective, crystalline nigellone displayed a delayed reaction [48]. In 1993, Nirmal Chakravarty, M.D., conducted a study to see if this delay could be attributed to the possibility of crystalline nigellone being an inhibitory agent on histamine. His hypothesis proved correct. Dr. Chakravarty's study found that the actual mechanism behind the suppressive effect of crystalline nigellone on histamine is that crystalline nigellone inhibits protein kinase C, a substance known to trigger the release of histamine [49]. In addition, his study showed that crystalline nigellone decreased the uptake of calcium in mast cells, which also inhibits histamine release.

The importance of these results are that people who suffer from bronchial asthma and other allergic diseases may benefit from taking crystalline nigellone.

Anti-tumor activity

A study of black seed's potential anti-tumor principles by the Amala Research Center in Amala Nagar, Kerala (India) in 1991 lent further impetus to Dr. Chakravarty's suggestion for the possible use of black seed in the treatment of cancer. Using an active principle of fatty acids derived from black seed, studies with Swiss albino mice showed that this active principle could completely inhibit the development of a common type of cancer cells called Ehrlich ascites carcinoma (EAC). A second common type of cancer cells, Dalton's lymphoma ascites (DLA) cells were also used. Mice which had received the EAC cells and black seed remained normal without any tumor formation, illustrating that the active principle was 100% effective in preventing EAC tumor development. Results in mice who received DLA cells and black seed showed that the active principle had inhibited tumor development by 50% less compared to mice not given the active principle. The study concluded, "It is evident that the active principle isolated from nigella sativa seeds is a potent anti-tumor agent, and the constituent long chain fatty acid may be the main active component^[50]. Anti diabetic activity

Significant hypoglycaemic activity has been reported and is thought to be due to the essential oil present. Clinical studies have confirmed these results and suggest that the antidiabetic action of the plant extract^[51].

Anti inflammatory activity

Asthma and arthritis are chronic inflammatory disorders involving a variety of inflammatory mediators and different pathways. The fixed oil and thymoquinone from the seeds were found to inhibit eicosanoid generation in leucocytes and membrane lipid peroxidation and a significant reduction in rat paw edema and a reduction in granuloma pouch weight were also observed ^[52]. Nigella in low concentration is effective in inhibiting the histamine release from the mast cells, which supports an antiasthmatic role for the plant ^[52].

Antifertility activity

The antfertility activity of *Nigella sativa* in male rats has been established, shown by an inhibition of spermatogenesis and a significant reduction in sialic acid content of the testis, epididymis, seminal vesicles and prostate^[53].

Antioxytocic activity

Preliminary reports suggest antioxytocic properties, in that a reversible inhibition of spontaneous smooth muscle contraction and inhibition of uterine smooth muscle contraction induced by oxytocin stimulation have been observed ^[54].

Cytotoxic activity

Cytotoxic and immunopotentiating effects

of *Nigella sativa* have been established. The long chain fatty acids are thought to contribute to the antitumour activity. The extract shows a modulatory effect in cisplatin-induced toxicity in mice and a protective effect against cisplatin-induced falls in haemoglobin levels and leucocyte counts^[55].

Anthelmintic activity

Nigella *sativa* was found to have an anthelmintic activity against tapeworm comparable to that of piperazine^[56].

Analgesic activity: The essential oil produced significant analgesic activity using chemical and thermal noxious stimuli methods such as acetic acid-induced writhing, hot plate and tail flick tests^[57].

Promotes lactation:

A study by Agarwhal (1979) showed that black seed oil increases the milk output of breastfeeding mothers. A literature search by the University of Potchefstroom (1989), including biological abstracts, revealed that black seed's capacity to increase the milk flow of nursing mothers could be attributed to a combination of lipid portion and hormonal structures found in the black seed^[58].

Other activites: Other reports include hypocholesterolaemic, antihypertensive and galactagogue effects.

Precautions and Adverse Reactions ^[59]

No health hazards or side effects are known with the proper administration of designated therapeutic dosages.

Black seed dosing:

The appropriate dose of black seed depends on several factors such as the user's age, health, and several other conditions. At this time there is not enough scientific

information to determine an appropriate range of doses for black seed. Keep in mind that natural products are not always necessarily safe and dosages can be important ^[60]. Be sure to follow relevant directions on product labels and consult your pharmacist or physician or other healthcare professional before using.

CONCLUSION:

Nature gives us very valuable gifts in forms of plants, trees, herbs, shrubs etc. There are a lot of plants and their products are very useful for human beings. We use plants in many ways such as as for medicinal use. Herbs are the natural drugs used to regain the alterations made in normal physiological system by foreign organisms or by any malfunctioning of the body. The WHO has already recognized the contribution of traditional health care in tribal communities. It is very essential to have a proper documentation of medicinal plants and to know their potential for the improvement of health and hygiene through an eco friendly system. It is very essential to know about a detailed and systematic study is required for identification, cataloguing and documentation of plants, which may provide a meaningful way for the promotion of the traditional knowledge of the herbal medicinal plants. The present review shows that black seeds have a lot of medicinal properties and these medicinal properties are used for treating many diseases. For the improvement of human beings. Scientists, researchers should works to know more its other medicinal use in different diseases. They should carry their research for develops its suitable formulation. Which can be beneficial for humans as well as animals.

REFERENCES:

- **1.** Zohary, Daniel, Hopf, Mari. Domestication of plants in the Old World Oxford University Press. 2000.
- Ali BH, Blunden G. Pharmacological and toxicological properties of Nigella sativa, Phytother Res.2003; 17(4): 299.
- 3. New_International_Encyclopedia
- **4.** Domestication of plants in the Old World (4 ed.). Oxford University Press. 2000.
- **5.** Andrews, F.W. The Flowering Plants of Anglo-Egyptian Sudan; Arbroath, Scotland: 1952.
- **6.** Buckingham, J. (edit). Dictionary of Natural Products, 1994; 7: 683.
- **7.** Department of Biomedical Sciences, Zyed Complex for Herbal Research and Traditional Medicine, Unpublished results.2004.
- 8. Department of Pharmacognostic Sciences, Zyed Complex for Herbal Research and Traditional Medicine, Unpublished results.2002.

- **9.** Amin G.Popular Medicinal Plants of Iran. cytes and membrane lipid peroxidation. Planta Med. Research Deputy of Health Ministry, Tehran, 1991; 61(1): 118-119.
- **10.** Mozaffarian V. A Dictionary of Iranian PlantsNames. Farhang Moaser Publishers, Tehran, 1998; 6:365.
- **11.** Zargari A. Medicinal Plants, Vol. 1. Tehran University Press, Tehran, 1990; 1: 43-44.
- 12. http://www.naturalnews.com/026868_nigella_sativa _migraine_seeds.html.(acesseson26/12 /2013)
- 13. http://www.naturalnews.com/038644_black_cumin_ oil_immune_system_NK_cells.htm. (accesses on 12/ 01/2014)
- 14. Randhawa MA and Al-Ghamdi MJ. A review of pharmacotherapeutic effects of Nigella sativa, Pak J Med Res. 2002; 41(2):77-83.
- **15.** Ghazanfar,S.A. Handbook of Arabian Medicinal Plants. Library of Congress.1994
- **16.** Hanafy MS, Hatem ME. Studies on the antimicrobial activity of Nigella sativa seed (black cumin. J Ethnopharmacol. 1991; 34(2-3):275-8.
- **17.** National Committee for Clinical Laboratory Standards, Performance standards for antimicrobial disc susceptibility testing; Twelfth information supplement (M100-S12). Wayne, PA: NCCLS, 2002.
- **18.** Kotb, T. F. Medicinal Plants in Libya. Arab Encyclopedia House.Tripoli-Libya.1985.
- **19.** Warrier, P.K. Nambiar, V.P.K. & Ramankutty C., Vaidya, Sala A. Indian Medicinal Plants Orient Longman, Kottakal, India. 1961;1:163-72.
- 20. Rathee P.S, Mishra S.-H, and Kaushal R.Anti microbial activity of essential oil, fixed oil and unsaponifiable matter of *Nigella sativa* L. Indian J. Pharm Sci.1982; 44, 8-10.
- **21.** Aqel M. Effects of *Nigella sativa* seeds on intestinal smooth muscle. Int. J. Pharmacogn.1993; 31:55-60.
- **22.** http://theblessedseed.blogspot.com/2012/01/forenergy-and-improved-immune-system.html
- **23.** Toama MA, Taha S El-Alfy and El-Fatatry HM, Antimicrobial Activity of the Volatile Oil of *Nigella sativa* Linneaus Seeds. Antimicrob Agents Chemother, 1974; 6(2): 225-226.
- **24.** Al-Hader A., Aqel M., and Hasan Z. Hypoglycemic effects of the volatile oil of Nigella sativa. Int. J. Pharmacogn.193; 31: 96-100.
- **25.** Hanafy M.S. and Hatem M.E. Studies on the antimicrobial activity of *Nigella sativa* seed (black cumin). J. Ethnopharmacol.1991; 34: 275-278.
- 26. Department of Microbiology, Zayed Complex for Herbal Research and Traditional Medicine, Unpublished results.

Page /

- **27.** http://www.prweb.com/releases/TMJ_relief/migrain e_prevention/prweb10440184.htm
- **28.** http://www.drweil.com/drw/u/ART03106/Migraine-Headaches.html
- **29.** http://health.howstuffworks.com/diseasesconditions /headache/migraine3.htm
- **30.** Halwani R, Habbal MZ and Abdelnoor AM, The antibacterial effect of some constituents of *Nigella sativa* oil, *Arab J Pharm Sci*, 1999;1(1): 87-96.
- **31.** Domestication of plants in the Old World (3 ed.). Oxford University Press. 2000.
- **32.** Varghese E. SVD "Applied Ethnobotany- A case study among the Kharias of Central India", Deep Publications, New Delhi. 1996
- 33. Adams R.-P. (1995), Identification of Essential Oil Components by Gas Chromatography /Mass Spectroscopy. Allured Publishing Co., Carol Stream.1995
- **34.** Chakravarty N. Inhibition of histamine release from mast cells by nigellone. Ann Allergy 1993; 70:237-42.
- **35.** Daba MH, Abdel-Rahman MS. Hepatoprotective activity of thymoquinone in isolated rat hepatocytes. Toxicol Lett 1998; 95:23-9.
- **36.** Mutabagani A. and El-Mahdy S.A.Study of the antiinflammatory activity of *Nigella sativa* L., and thymoquinine in rats. Saudi Pharm. J.1997; **5**: 110-113.
- Dehkordi FR, Kamkhah AF. Antihypertensive effect of Nigella sativa seed extract in patients with mild hypertension. Fundam Clin Pharmacol 2008; 22:447-52.
- **38.** Dwivedi S et.*al.*, Relivance of medicinal herbs used in traditional system of medicine, Farmavita. Net, 2007.
- **39.** Kurion, J.C. "Plants that heals", 5th ed. Pune, Oriental watchman publishing house, 2003.
- **40.** Nagi MN, Alam K, Badary OA, et al. Thymoquinone protects against carbon tetrachloride hepatotoxicity in mice via an antioxidant mechanism. Biochem Mol Biol Int 1999; 47:153-9.
- **41.** Salomi NJ, Nair SC, Jayawardhanan KK, et al. Antitumour principles from Black seed seeds. Cancer Lett 1992; 63:41-6.
- **42.** Worthen DR, Ghosheh OA, Crooks PA. The in vitro anti-tumor activity of some crude and purified components of blackseed, Black seed L. Anticancer Res 1998; 18(3A):1527-32.
- **43.** Salomi NJ, Nair SC, Jayawardhanan KK, et al. Antitumour principles from Black seed seeds. Cancer Lett 1992; 63:41-6.

- **44.** Agel M. The relaxing effects of the volatile oil of *Nigella sativa* seeds on vascular smooth muscles.1995
- 45. Rittel & Reichstein, ibid., 1954;37: 1361
- **46.** Pendse & Dutt, Bull. Acad. Sci. Unit. Prov., 1933; 34(3): 209.
- 47. http://www.divineremedies.com
- 48. http://www.unigraz.at/~katzer/engl/generic_frame.html?Nige_sat.ht ml.
- **49.** Dwivedi, Sumeet, Shrivastava, Satyaendra, Dubey, Dar shan; Kapoor, Shweta & Jain, Sanjay "Status and conservation strategies of herbal oral contraceptives", Planta Indica, 2007; 3(1): 5-7.
- **50.** Dwivedi SN, Herbal remedies among tribals of sidhi district of Madhya Pradesh, *J. Econ.Tax.* 2004; 28(3) 675-686.
- 51. Akhtar MS, Riffat S. Field trial of Saussurea lappa roots against nematodes and Nigella sativa seeds against cestodes in children. J Pak Med Assoc 1991;41:185-7.
- **52.** A.G. and Peter A.C. (1998), *The in vitro* antitumor activity of some crude and purified components of black seed. *Nigella sativa*. Anticancer.1998;18:1527-1532.
- **53.** Houghton PJ, Zarka R, de las Heras B, Hoult JR. Fixed oil of Black seed and derived thymoquinone inhibit eicosanoid generation in leukocytes and membrane lipid peroxidation. Planta Med 1995; 61:33-6.
- 54. Salem, M. L. and M. S. Hossain (2000). Protective effect of black seed oilfrom *Nigella sativa* against murine cytomegalovirus infection. International Journal of Immunopharmacology.2000
- **55.** Salomi, N. J., S. C. Nair, et al. Antitumour principles from *Nigella sativa* seeds. Cancer Letters1992; 63(1): 41-46.
- **56.** Khanna, T., F. A. Zaidi. CNS and analgesic studies on *Nigella sativa*. Fitoterapia 1993; 64(5): 407-410.
- **57.** Kotb, T. F. Medicinal Plants in Libya. Arab Encyclopedia House.Tripoli-Libya.1985
- 58. El, Dakhahny M. M. M., G. A. M. Abdel, (1997). Prevention of skin tumors induced by 7,12dimethylbenz anthracene in mice by black seed oil.Oncology Reports,1997; 4(1): 139-141.
- **59.** El-Dakhakhny M, Mady N, Lembert N, Ammon HP.The hypoglycemic effect of *Nigella sativa* oil is mediated by extrapancreatic actions. Planta Med.2002; 68(5): 465-6.
- 60. http://www.webmed.com/vitamins-supplements/ ingredient mono-901-balck seed .aspx. (acessed on 2 may/2014)