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A review : The Pharmacological activity for chemical constituents of "*NIGELLA SATIVA* "

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Abstract:

Nigella sativa, also known as Black Seed, is a plant with seeds that have been used as a spice for a long time. People also call it by various names like Kalonji, Black caraway, and Black cumin. Recently, there's been a growing interest in natural remedies, like Nigella sativa, because they have fewer side effects compared to pharmaceutical drugs.These seeds are packed with nutrients. The oil in the seeds is full of healthy fats, and the essential oil has antioxidants like thymoquinone and carvacrol. While it expands globally, its main growth regions are Eastern Europe, the Middle East, and Western Asia . It is grown commercially in several Indian states, including West Bengal, Punjab, Jharkhand, Himachal Pradesh, Bihar, and Assam. Also involved in small-scale farming are the states of Tamil Nadu, Rajasthan, Madhya Pradesh, and Uttar Pradesh They also contain proteins, alkaloids, and saponins, which are good for health.People use Nigella sativa and its components to improve health and treat various conditions like jaundice, fever, digestion problems, paralysis, piles, and skin diseases.This review focuses on how the chemicals in Nigella sativa work in the body to provide these health benefit.

Key words: Black cumin , Thymoquinone, Bioactive, Paralysis, Neutraceutical.

Introduction:

Black Seed (scientific name Nigella sativa) is derived from the Latin word "Niger" (black) (1). A popular spice is Nigella Sativa, according to its botanical name. It's also known by the names Black cumin, Black caraway, Black seed, Roman coriander, Kalonji, nutmeg bloom, and fennel flower (2). While it expands globally, its main growth regions are Eastern Europe, the Middle East, and Western Asia (3, 4).It is grown commercially in several Indian states, including West Bengal, Punjab, Jharkhand, Himachal Pradesh, Bihar, and Assam. Also involved in small-scale farming are the states of Tamil Nadu, Rajasthan, Madhya Pradesh, and Uttar Pradesh (3).Its seeds contain more than a hundred essential components, including fatty acids, volatile oils, proteins, carbohydrates, saponins, alkaloids, tannins, flavonoids, sterols, and trace minerals (5,6).There have been described activity related to hepatoprotection, renal protection, gastroprotection, analgesic, antibacterial, anti-inflammatory, spasmolytic, bronchodilator, antioxidant, antidiabetic, anticancer, and immunomodulator (7).The seeds of this plant are

commonly called “black cumin” in English, “habbat us sauda” in the Middle East, and “Kalonji” in southern Asia (8).In traditional medicine, the seed of this plant was used to cure a wide range of conditions, including back pain, asthma, fever, bronchitis, cough, chest congestion, dizziness,Ji paralysis, chronic headache, inflammation, infertility, and various gastrointestinal disorders like dyspepsia, flatulence, diarrhea, and dysentery.(9).

Common names: Kalonji seeds are commonly known as black seed, black cumin, or nigella seeds,Fennel flower, Black caraway,Roman coriander (2,10)

Botanical Description (11-15)

Black cumin :The hardy annual plants known as black cumin grow to a height of 20 to 60 cm (8 to 24 inches). Leaves and roots Fine, finely divided leaves adorn the branched stems, and the plant boasts a well developed taproot. Flowers: The flowers are pale blue or white, with five petals, many stamens, and five or six long fused carpels. Seeds-The dark, triangular or pyramid shaped seeds are carried in a capsule Consisting of five or six segments, each of which ends in an extended protrusion.

Taxomical classification of *Nigella Sativa* (9,16)

Kingdom	Plantae
Subkingdom	Tracheobionata
Supervision	Spermatophyte
Order	Ranunculales
Family	Ranunculaceae
Clade	Angiosperms, Eudicots
Species	N.Sativa
Genus	Nigella

Chemical composition (17-21)

- Thymoquinone
- Linoelic acid
- Dithymoquinone
- Oleic acid
- Thymohydroquinone.
- Eicosadienoic acid
- P-Cymene
- Dihomolinoleic acid
- Thymol.
- A -Pinene
- Thymoquinone
- carvacrol
- 4-terpineol
- t. -anethol
- Sesquiterpene longifolene
- Thymohydroquinone, dithymoquinone,
- p-cymene

Fig.1
Kalonji seeds

Fig.2
Flower

Fig.3
Whole plant of "NIGELLA SATIVA"

Pharmacological activity of "*NIGELLA SATIVA*" :

1.Anti diabetic activity:

Globally, 8.3% of people suffer from diabetes mellitus (DM), a chronic metabolic disease. Secondary disorders such as retinopathy, cataract, neuropathy, and heart issues can arise from improper therapy of this disease. Patients with type 2 diabetes have reportedly shown reductions in postprandial glucose levels, fasting blood glucose levels, insulin resistance, and glycosylated hemoglobin when treated with a daily dose of N. sativa seeds for a period of three months. (22,23).

2.Immunomodulatory activity :

Among the most beneficial characteristics of Nigella sativa are its immunomodulatory actions. Through T cells and NK cells, the active ingredients in N. sativa enhance the immunomodulatory qualities (El-Kadi and Kandil, 1986). While suppressive activity on immunity mediated by B cells has been observed by other ingredients, N. sativa oil has a potentiating effect on cellular immunity mediated by T cells. N. sativa The type of immune response and its stimulatory characteristics on cellular immunity are related(24,25).

3. Gastroprotective activity :

N. sativa oil lowers the amount of histamine in the gastric mucosa while raising mucin and glutathione levels in the stomach. As a result, it can be quite helpful in healing stomach ulcers brought on by ethanol and indomethacin. After being liberated from stomach cells, the pepsinnogen proenzyme of pepsin combines with the hydrochloric acid in gastric juice to become pepsin. TQ has a preventive effect against stomach ulcers by stimulating pepsinogen, which activates pepsin in gastric juice (26,27).

4.Antioxidant effect:

The plant separated the phytochemicals. The compounds' potent antioxidant activity and ability to scavenge radicals have been demonstrated by thin-layer chromatography (28).

5.Bronchodilator effect:

Nigella sativa has the capacity to suppress the histamine H1 and is useful as a bronchodilator. Additionally, it triggers the inhibitory portion of the non-adrenergic, non-cholinergic nervous system (NANC), which obstructs the stimulatory portion of the NANC. Potassium channel opening and phosphodiesterase inhibition may be substitute methods for the bronchodilator action and, most crucially, calcium blocking. The bronchial muscles are also relaxed by the calcium inhibitory effect (29).

6.Antibacterial activity :

These qualities have been known for centuries, despite attempts as far back as the early 1900s to demonstrate the antibacterial effects of herbal plants and their extracts in a laboratory setting. The pathogen's current resistance to several widely used antibiotics is driving research into the development of novel antimicrobial agents in an attempt to address the problems of resistance and adverse drug reactions linked to the antimicrobial drugs that are currently

on the market.Melanin and TQ specifically may be in charge of this characteristic, even if the precise process behind the antibacterial activity of N. sativa seeds has not yet been identified (30,31).

7.Anticancer activity :

Cancer is growing in importance as a global public health concern (32). Thymoquinone from Nigella sativa exhibits promising anti-mutagenic, anti-carcinogenic, anti-neoplastic, and anti-proliferative qualities against many tumor cell types (33). In order to decrease the negative effects of treatment, it is also utilized as a chemopreventive agent in combination with other therapeutic medications (34).

8.Antidepressant:

N. sativa exhibits antidepressant properties through modifying neuroendocrine factors and regulating neurotransmitter levels. By changing the delicate chemical balance in the brain, the plant helps regulate mood and may be used to treat depression disorders (35, 36).

9.Antimicrobial Activity:

The antibacterial properties of Nigella sativa have been shown to be effective against a wide variety of pathogens, including bacteria, viruses, and fungi. In a study conducted by Blunden and Ali, an important oil derived from Nigella sativa seeds demonstrated strong antibacterial action against a range of pathogens, suggesting that it may find use in treating infectious disorders (37).

10.Acne Vulgaris :

One of the most common illnesses impacting people today, acne vulgaris, is believed to be an infectious disease. Numerous research investigations examined the efficacy of Nigella sativa oil in the management of acne vulgaris. Hadi and Ashor (2010) found that the traditional therapy of 5% benzoyl peroxide lotion for mild to moderate acne vulgaris was less effective and more harmful than using 20% N. sativa oil extract.(38)

11.Hepatic Cancer:

One of the most common malignant diseases, hepatocellular carcinoma, has witnessed a sharp rise in cases worldwide in recent years. Human hepatoma HepG2 cell lines were cultivated with varying amounts of N. sativa extract for a whole day, and this demonstrated the cytotoxicity of N. sativa seeds (39). Oral TQ therapy has been shown to enhance the activities of quinine reductase and glutathione transferase, and it may be utilised as a preventative measure against hepatic cancer toxicity and chemical carcinogenesis (40).

12.Anti viral activity:

Apoptosis brought on by viral infections causes the host cell's lymphocyte count to decrease. The antiviral and antioxidant activities are connected because antioxidants can stop both virus-induced apoptosis and viral multiplication in target cells (41, 42). Natural killer (NK), suPressor T (T8), and T helper (T4) cells are reportedly activated in healthy volunteers by N. sativa. N. sativa extract inhibits the human immune deficiency virus's protease in addition to increasing immunity. In one study, 450 mg of N. sativa oil capsules were given to hepatitis C patients three times a day for three months. Overall, total protein, albumin, platelets, and red blood cells were found to be greatly enhanced, whereas oxidative stress, viral load, and sig-NOT were found to be significantly decreased. Two advantages of the higher red blood cell count include decreased membrane lipid peroxide levels and a lower risk of hemolysis.(43, 44, 45, 46). N. sativa demonstrates antiviral properties by impeding viral development and enhancing immune responses. Because of these characteristics, the plant can be used as a home remedy to strengthen the body's natural defences against viral infections (47, 48).

Pharmacological activity of chemical constituents:

1.Thymoquinone -

1.Antioxidant:

Numerous academic publications have documented the anti-oxidant qualities of TQ in relation to mitigating oxidative stress. Nitric oxides (NO•), hydroxyl radicals (OH−•), hydrogen peroxide (H2O2), superoxide anion (O2−•), and other oxidative enzymes (e.g., catalase, superoxide dismutase, etc.) are signs of oxidative stress, which

starts the molecular level degradation of cells by changing different metabolic processes (49, 50).In this case, TQ stimulates the synthesis of cytoprotective enzymes, which aid in averting oxidative stress-related cell damage.Glutathione peroxidase (GPX) scavenges the highly reactive oxygen (52) when TQ-based cytoprotective enzymes such lipid peroxidation (51)H2O2 [24] are induced through overexpression of mRNA.

2.Anti-inflammatory effects:

TQ has been shown in numerous research to have anti-inflammatory properties (30–50). The anti-inflammatory properties of TQ are due to enhanced production of heme-oxygenase 1 (HO-1) in human keratinocytes (HaCaT)(53). This is accomplished via phosphorylating cyclic AMP-activated protein kinase-alpha (AMPKalpha) and protein kinase B (PKB/Akt) in order to activate nuclear factor (NF)-erythroid2-(E2)-related factor-2 (Nrf2). It has been observed that TQ prevented liver fibrosis caused by thioacetamide (TAA). Lower levels of collagen-I, tissue inhibitor of toll-like receptor 4 (TLR4), pro-inflammatory cytokine levels, and the protein and mRNA expression of α-smooth muscle actin (α-SMA) were observed in conjunction with this. Furthermore, it lowered the phosphorylation of phosphatidylinositol 3-kinase and raised that of liver kinase B (LKB) and adenosine monophosphate-activated protein kinase (AMPK) (54).

3.Anti-cancer and antitumor activity:

Natural compounds with anti-cancer properties have gained increasing attention because they can be acquired in an easily absorbed form and are presumably harmless for healthy cells. Most scientists concur that TQ shows encouraging anti-cancer properties. Several research have provided evidence in favour of the chemopreventive or chemotherapeutic activity. Consequently, it can be advantageous to take it as a dietary supplement to increase the efficacy of anti-cancer drugs.Studies indicate that TQ induces apoptosis that is p53-independent by activating caspase-8, caspase 9, and caspase 3 in the caspase cascade. Activation of caspase-8 facilitates the release of cytochrome c from mitochondria into the cytoplasm. Furthermore, it alters the Bax/Bcl2 ratio in p53-deficient HL-60 cells by upregulating proapoptotic Bax and downregulating antiapoptotic Bcl2 proteins throughout the apoptotic process (55).

2.Linoelic acid (50-60%) -.

1.Obesity and LA:

Over 43% of individuals in the US who are 20 years of age and older are fat, accounting for 74% of overweight or obese adults. Despite the alarming nature of these figures, the American Obesity Association predicts that 50% of Americans may be obese by 2025. Predictions indicate that the percentage will most likely rise to 60% by 2030. A growing body of evidence suggests that polyunsaturated fatty acids (PUFAs), such as those found in vegetable oils, may contribute to the obesity epidemic. Most of this evidence comes from studies conducted on animals. (56,57)

2.Cardiovascular Disease and LA:

In the 19th century, there were just nine articles that documented the ailment in the literature, making a diagnosis of cardiovascular illness rare. Furthermore, the first American heart attack was recorded in 1912; nevertheless, due to the rising incidence of this condition, the American Heart Association (AHA) was not established until 1920.One of the initial changes in atherosclerosis, the condition that precedes cardiovascular disease, is the remodelling of macrophages. Foam cells, which are essentially macrophages coated with fat and cholesterol, are the result of atherosclerotic macrophages. Atherosclerotic plaque is therefore composed of dead macrophages and other cell types that have accumulated fat and cholesterol.(59,58)

3.Cancer and LA:

In addition to cardiovascular disease, drinking excessive amounts of LA and the ensuing OXLAMs might cause various diseases. Oxidised metabolites also have a major impact on cancer, the second largest cause of mortality in the United States. The usage of seed oil is associated with an increased risk of cancer, based on animal studies. Once an animal's diet accounts for 4% to 10% of its energy, cancer typically hits . (60,61)

3.Oleic Acid

1.HEALING OF CUTANEOUS WOUNDS :

Tissue wounds also set off a series of inflammatory-based biological processes, such as angiogenesis, re-epithelialization, extracellular matrix deposition, and cell migration (62). To control these diverse activities, a range of biological mediators are therefore needed. One such mediator is nitric oxide (NO), which affects the actions of fibroblasts, macrophages, and keratinocytes throughout the healing process, thereby contributing significantly to the healing of skin wounds (63). Decreased NO generation leads to the production of specific mediators by fibroblasts and inflammatory cells, which decreases the quantity of collagen deposited at the wound site (64).

2.EFFECTS OF OLEIC ACID ON CANCER :

Several epidemiological studies revealed that the Mediterranean region was less likely than the US, the UK, or Scandinavia to experience cancer, especially when it comes to malignancies of the skin, intestines, endometrium, prostate, and breast (65).One of the most important inferences made from these data was related to Mediterranean eating habits, specifically the high consumption of fruits, vegetables, and olive oil—rich in omega-3 fatty acids—and limited consumption of meat (66). Additionally, diets high in linoleic acid, or saturated fatty acid, and total fat were associated with an increased risk of developing cancer; however, a high consumption of olive oil and OA was already linked to a reduction in the risk of developing cancer, mainly colorectal, prostate, and breast cancer (67,68).

4. Thymol

1.Mosquito repellent activity:

Thymol is widely used in commercial formulations due to its ability to repel mosquitoes. Specifically, it has been shown that thymol repels Culex pipiens pallens (69) and is toxic to the larvae (70). Thymol has been shown in another investigation to have both insecticidal and genotoxic effects on Drosophila melanogaster (71). Thus, thymol might be useful in the search for cutting-edge natural insecticides. The aforementioned aromatic herbs and thymol, the main component of its essential oil, have been used for their medicinal properties as well as in the food industry and as a repellent since ancient times.

5.Carvacrol -

1. Anti-oxidant property :

Carvacrol's hydroxyl group (OH) is primarily responsible for its capacity to scavenge radicals, including superoxide radicals, nitric oxide, and hydrogen peroxide. Hydrogen atoms are more readily contributed to unpaired electrons due to its mild acidity, which stabilises another radical produced by electron scattering at the molecular resonance structure (72). Carvacrol protects the kidneys, liver, and brain against damage brought on by oxidative stress. Studies have indicated that carvacrol has anti-oxidative and hepatoprotective properties. Numerous liver organ failures are brought on by acute pancreatitis (73).

2.Antimicrobial activity:

Carvacrol has strong antibacterial activity against a variety of bacteria, including Staphylococcus epidermis, Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia, Streptococcus pneumonia, Proteus mirabilis, Serratia spp., and Enterobacter spp. (74). shown that carvacrol and thymol together had antibacterial effects against S. aureus, Clostridium perfringens, and Pseudomonas aeruginosa. Carvacrol has antifungal effects on a variety of bacteria, including Aspergillus niger, Aspergillus flavus, Candida spp., Alternaria alternata, Trichoderma viride, Penicillium rubrum, and dermatophytes. Among the fungal plant diseases susceptible to carvacrol's antibacterial action are Colletotrichum acutatum, Colletotrichum fragariae, and Colletotrichum gloeosporioides (75).

Conclusion:

“In conclusion, Nigella sativa has shown promising health benefits in various studies. It has potential for improving conditions like inflammation, allergies, and digestive issues. However, more research is needed to fully understand

its effects and potential side effects. Overall, Nigella sativa could be a valuable natural remedy, but further investigation is required for its safe and effective use."

References

(1)Nasir, Irshad. 2022.Evaluation of the antimicrobial –Activity of aqueous, ethanolic and methanolic extractsOf Nigella sativa (kalonji) against gram positive andGram-negative bacterial isolates, Institute of BiochemIstry and Biotechnology.

(2) Chopra RN, Chopra SL, Handa KL, Kapur LD.1958. Indigenous Drugs of India, UNDhur and Sons Pvt Ltd, Calcutta.

(3) Padhyel S. et.al. 2008. From here to eternity the secret of pharaohs: potential of black cumin seeds and beyond, Cancer Ther, 6:495–510.

(4) Khare CP. 2004. Encyclopedia of Indian medicinal plants. NewYork: Springes-Verlag Berlin SHeidelberg.

(5) Shafiq H. et.al. 2014. Cardio-protective and anti-cancer therapeutic potential Of Nigella sativa, Iran J Basic Med Sci, 17(12):967–79.

(6) Butt MS.et.al. 2010. Nigella sativa: reduces the risk of various maladies, Crit Rev Food Sci Nutr ,50(7):654–65.

(7) Yimer E.M. et.al. 2019. Nigella sativa L. (Black Cumin): A Promising Natural Remedy for Wide Range of Illnesses, Evid. Based Complement. Altern. Med.

(8) Gilani A.-U. et.al. 2004. A review of medicinal uses and pharmacological activities of Nigella sativa, Pak. J. Biol. Sci,7(4):441–445.

(9).Darakhshan S., Pour A.B. et.al. 2015. Thymoquinone and its therapeutic potentials, Pharmacol. Res,95:138–158.

(10) Chevallier A. 1996. Encyclopedia of Medicinal Plants. New York, NY: DK Publishing. P. 237

(11) B.M. Razavi H. Hosseinzadeh. A review of the effects of Nigella sativa L. and its constituent, thymoquinone, in Metabolic syndrome.

(12) Asif Husain,Mohd Mujeeb, A review on therapeutic potential of Nigella sativa: A miracle herbAftab Ahmad

(13) Sharma Priya Vrat, Dravyaguna Vijnana, 2011. Varanasi, Chaukhambha Bharati Academy, Volume II, page no 596.

(14) Dr. J.L.N. SHASTRI and prof. k.c. chunekar. 2006. illustrated dravya gunavijnana, 2nd, Chaukhambha orientalia, Varanasi, 152.

(15) K.niteshwar & K.hemadri. 2013.chaukhamba publications,209.

(16) Sharma NK, Ahirwar D. et.al. 2009.Medicinal and Pharmacological Potential of Nigella Sativa: A Review. Ethnobotanical leaflets, 11.

(17) Begum S, Mannan A. 2020. A review on nigella sativa: a marvel herb. Journal of Drug Delivery and Therapeutics,15;10(2):213-9.

(18) Cheikh-Rouhou S, Besbes S. et.al. 2008. Sterol composition of Black cumin (Nigella sativa L.) and Aleppo pine (Pinus halpensis Mill.) seed oils. J Food Comp Anal,21(2):162–168.

(19) Bourgou S, Ksouri R. et.al. 2008.Phenolic composition and Biological activities of Tunisian Nigella sativa L. shoots and roots. C R Biol, 331(1):48–55.

(20) Al-Jassir MS. 1992. Chemical composition and microflora of black cumin (Nigella sativa L.) seeds Growing in Saudi Arabia. Food Chem, 45:239–242.

(21) Atta-Ur-Rahman. 1995. Nigellidine-a new indazole alkaloid from the seed of Nigella sativa. Tetrahedron Lett,36(12):1993–1994.

(22) Bamosa, A.O., Kaatabi. Et.al. 2010. Effect of Nigella Sativa seeds on the glycemic control of patients with type 2 diabetes mellitus. Indian J. Physiol. Pharmacol, 54 (4), 344–354.

(23) Heshmati, J., Namazi, N., 2015. Effects of black seed (Nigella sativa) on metabolic Parameters in diabetes mellitus: a systematic review. Complem. Ther. Med, 23 (2), 275–282.

(24) El-Kadi, A., Kandil, O., 1986. Effect of Nigella sativa (the black seed) on immunity, Proceeding of the 4th International Conference on Islamic Medicine, Kuwait. Bull Islamic Med, pp. 344–348.

(25).Salem, M.L., 2005. Immunomodulatory and therapeutic properties of the Nigella sativa L. seed. Int. Immunopharmacol, 5 (13–14), 1749–1770.

(26) El-Dakhakhny, M., 1965. Studies on the Egyptian Nigella sativa L. part IV: some Pharmacological properties of the seed's active principle in comparison to its Dihydro compound and its polymer. Arzneim. Forsch, 15, 1227–1229.

(27) Kanter, M., Coskun, O., Uysal, H., 2006. The antioxidative and antihistaminic effect of Nigella sativa and its major constituent, thymoquinone on ethanol-induced gastricMucosal damage. Arch. Toxicol, 80 (4), 217–224.

(28) Burits M, Bucar F. 2000.Anti-oxidant activity of Nigella sativa essential oil. Phyto Therapy Research,14, 323-328.

(29) Boskabady MH, Mohsenpoor N, Takaloo L.2010. Anti-asthmatic effect of Nigella sativa in Airways of asthmatic patients.Phytomedicine 17, 707-713.

(30) Morsi NM. 2000. Antimicrobial effect of crude extracts Of Nigella sativa on multiple antibiotics-resistant Bacteria. Acta Microbiol , 49:63-74.

(31) Hannan A, Saleem S. et.al. 2008.Anti-bacterial activity of Nigella sativaAgainst clinical isolates of methicillin resistant Staphylococcus aureus. J Ayub Med Coll Abbottabad ,20:72-74.

(32) Ahmad, M.F., 2020. Ganoderma lucidum: A rational pharmacological approach to Surmount the cancer. J. Ethnopharmacol., 113047.

(33) Shoieb, A.M., Elgayyar. Et.al. 2003. In vitro inhibition Of growth and induction of apoptosis in cancer cell lines by thymoquinone. Int. J. Oncol, 22 (1), 107–114.

(34) Khader, M., Eckl. 2007. Effects of aqueous extracts of medicinal plants on MNNG-treated rat hepatocytes in primary cultures. J. Ethnopharmacol. 112 (1), 199–202.

(35) .Perveen, T., Haider, S. et al. 2014. Increased 5-HT Levels Following Repeated Administration of Nigella sativa L. (Black Seed) Oil Produce Antidepressants Effects in Rats. Sci. Pharm, 82(1), 161-170.

(36). Akbar, A. 2022. Antidepressant and anti-nociceptive effects of Nigella sativa and its Main constituent, thymoquinone: A literature review. Asian pacific Journal of Tropical Biomedicine, 12(12), 495-503.

(37). Ali, B.H., Blunden, G. 2003. Pharmacological and toxicological properties of Nigella Sativa. Phytotherapy Research, 17(4), 299-305.

(38)Ahmed Jawad H., Ibraheem Azhar Y. et.al. 2014. Evaluation of efficacy, safety and Antioxidant effect of Nigella sativa in patients with psoriasis: a randomized clinical trial. Journal of Clinical and Experimental Investigations,5(2):186–193.

(39).Thabrew, M.I., Mitry. Et.al. 2005. Cytotoxic effects of a Decoction of Nigella sativa, Hemidesmus indicus and Smilax glabra on human Hepatoma HepG2 cells. Life Sci, 77 (12), 1319–1330.

(40). Nagi, M.N., Almakki, H.A., 2009. Thymoquinone supplementation induces quinone Reductase and glutathione transferase in mice liver: possible role in protection Against chemical carcinogenesis and toxicity. Phytother, Res. 23 (9), 1295–1298.

(41) Peterhans E. 1997. Oxidants and antioxidants in viral Diseases: disease mechanisms and metabolic Regulation, J Nutr Ranian Journal of Basic Medical Sciences, 127: 962S- 965.

(42) Fatemah Forouzanfar , Bibi Sedigheh Fazly Bazzaz. Et.al. 2014. Black cumin (Nigella sativa) and its constituent (thymoquinone): a review on antimicrobial effects . Iranian Journal of Basic Medical Science,17:929-938.

(43)Aljabre, S.H., Alakloby. Et.al. 2015. Dermatological effects of Nigella Sativa. Jof Dermatol. Dermat. Surg, 19 (2), 92–98

(44) Barakat, E.M.F. et.al. 2013. Effects of Nigella sativa on outcome Of hepatitis C in Egypt. World J. Gastroenterol.: WJG ,19 (16), 2529.

(45) Forouzanfar, F., Bazzaz. Et.al. 2014. Black cumin (Nigella sativa) and Its constituent (thymoquinone): a review on antimicrobial effects. Iran. J. Basic Med. Sci, 17 (12), 929.

(46)Md Faruque Ahmad a, Fakhruddin Ali Ahmad b. et.al. 2021. An updated knowledge of Black seed (Nigella sativa Linn.): Review of Phytochemical constituents and pharmacological properties Journal of Herbal Medicine, 25:100404.

(47) Maideen, N.M.P., Balasubramanian. Et.al. 2023. Therapeutic Potentials of Black Seeds (Nigella sativa) in the Management of COVID-19 -A Review of Clinical and In-silico Studies. Anti-Infective Agents, 21(1).

(48) Usmani, H., Malik, S. et.al. 2023. Effects of Active Compounds of Nigella sativa In COVID-19: A Narrative Review. Recent Adv. Antiinfect Drug Discov.

(49)Y.K. Mahmoud, H.M. Abdelrazek 2019. Cancer: thymoquinone antioxidant/pro-oxidant effect as potential anticancer remedy Biomed. Pharmacother, 115 Article 108783.

(50) S. Banerjee, S. Padhye. Et.al. 2010. Review on molecular and therapeutic potential of thymoquinone in cancer Nutr. Cancer, 62 (7), pp. 938-946 .

(51)O.A. Badary, R.A. Taha. Et.al. 2003. Thymoquinone is a potent superoxide anion scavenger Drug Chem Toxicol, 26 (2) 87-98.

(52) M.M. Sayed-Ahmed, A.M. Aleisa. Et.al. 2010. Thymoquinone attenuates diethylnitrosamine induction of hepatic carcinogenesis through antioxidant signaling Oxidative Med. Cell Longev, 3 (4), pp. 254-261 .

(53).Kundu J, Kim DH. Et.al. 2014. Thymoquinone induces heme oxygenase-1 expression in HaCaT cells via Nrf2/ARE activation: Akt and AMPKalpha as upstream targets. Food Chem Toxicol,65:18–26.

(54).Bai T, Yang Y.et al. 2014. Thymoquinone alleviates thioacetamide-induced hepatic fibrosis and inflammation by activating LKB1-AMPK signaling pathway in mice. Int Immunopharmacol, 19:351–357.

(55). El-Mahdy MA, Zhu Q. et.al. 2005. Thymoquinone induces apoptosis through activation of caspase-8 and mitochondrial events in p53-null myeloblastic leukemia HL-60 cells. Int J Cancer, 117:409–417.

(56).Defining Adult Obesity Centers for Disease Control and Prevention. Updated 7 June 2021. [(accessed on 22 March 2023)]

(57)Global Oil & Fats Business Online North America: Vegetable Oil Consumption.

(58). White P.D. Perspectives. Prog. Cardiovascular. Dis. 1971;14:250–255.

(59) The American Heart Association History of the American Heart Association: Our Lifesaving History. [(accessed on 12 April 2023)].

(60).Centers for Disease Control and Prevention (CDC) National Center for Health Statistics: Leading Causes of Death. [(accessed on 12 April 2023)]

(61).Liput K.P., Lepczynski. Et.al. 2021. Pierzchała M. Effects of dietary n−3 and n−6 polyunsaturated fatty acids in inflammation and cancerogenesis. Int. J. Mol. Sci, 22:6965.

(62) Clark, M.E.; Rafferty, M. 1985. The sickness that won't heal. Health care For the nation's homeless. Health PAC Bull,16, 20-28.

(63) Frank, S.; Kampfer, H. et.al. 2002. Nitric oxide Drives skin repair: novel functions of an established mediator. Kidney Int, 61, 882-888.

(64) Schaffer, M.R.; Tantry, U. et.al. 1996. A.Nitric oxide regulates wound healing. J Surg Res, 63, 237-240.

(65) Trichopoulou, A.; Lagiou, P. et.al. 2000. Cancer And Mediterranean dietary traditions. Cancer Epidemiol Biomarkers Prev, 9, 869-873.

(66) Harwood, J.L., Yaqoob, P. 2002. Nutritional and health aspects of olive Oil. European Journal of Lipid and Science Technology, 104, 685-697.

(67) Trichopoulou, A.; Lagiou, P. 1997. Healthy traditional Mediterranean Diet: an expression of culture, history, and lifestyle. Nutr Rev., 55, 383-389.

(68) Binukumar, B.; Mathew, A. Dietary fat and risk of breast cancer. World J Surg Oncol., 2005, 3, 45.

(69)Park, B.-S., Choi. Et.al. 2005. Monoterpenes from thyme (Thymus Vulgaris) as potential mosquito repellents. Journal of the American Mosquito Control Association, 21(1), 80-83.

(70) Zahran, H. E.-D. M., & Abdelgaleil, S. A. 2011. Insecticidal and developmental inhibitory properties of Monoterpenes on Culex pipiens L.(Diptera: Culicidae). Journal of Asia-Pacific Entomology, 14(1), 46-51.

(71)Karpouhtsis, I., Pardali, E. et.al. 1998. Insecticidal and genotoxic activities of oregano essential oils. Journal of Agricultural and Food Chemistry, 46(3), 1111-1115.

(72) Cocolas, A. H. , Parks, E. L. et.al. 2019. Heterocyclic β-keto sulfide derivatives of carvacrol: Synthesis and copper (II) ion reducing capacity. Bioorganic & Medicinal Chemistry Letters, 29(19), 126636.

(73) Mir, M. , Permana, A. D. , Ahmed, N. et.al. 2020. Enhancement in site-specific delivery of carvacrol for potential treatment of infected wounds using infection responsive nanoparticles loaded into dissolving microneedles: A proof of concept study. European Journal of Pharmaceutics and Biopharmaceutics, 147, 57–68.

(74)Alagawany, M. , El-Hack. Et.al. 2015. Biological effects and modes of action of carvacrol in animal and poultry pro-duction and health-a review. Advances in Animal and Veterinary Sciences, 3(2s), 73–84.

(75) Rodriguez-Garcia, I. , Silva-Espinoza, B. 2016. Oregano essential oil as an antimicrobial and antioxidant additive in food products. Critical Reviews in Food Science and Nutrition, 56(10), 1717–1727.