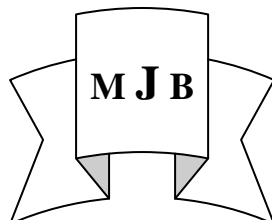


Spectacular Black Seeds (*Nigella sativa*) : Medical Importance Review

Zainab Hadi Kamil

Basic Science Department, College of Dentistry, University of Babylon, Hilla, Iraq.

Review Article



Received 15 August 2013

Accepted 28 August 2013

Introduction

Medical plants have been a major source of therapeutic agent since ancient times to cure human disease. The World Health Organization (WHO) estimated that up to 80% of people still rely on herbal remedies for their health care [1,2].

The *Nigella sativa* is an annual flowering plant, native to south west Asia and cultivated in countries like middle eastern Mediterranean region, South Europe, Syria, Turkey, Saudi Arabia, Pakistan, India [3]. In the religion of Islam, the plant has been

given a great importance because of its number of usage. Depend on the religion it is one of the greatest healing plants. 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 [4,5]. Of all the plant organs it is only the seeds which attracted most of the researchers [6].



Nigella sativa flower



Nigella sativa seeds

Composition

Physical constants

Foreign matter 2% w/w, total ash 6% w/w, acid insoluble ash 0.2% w/w, alcohol soluble extractive 15% w/w, total fixed oil 25-32% w/w, volatile oil 0.42% w/w organic matter, 3.91% w/w loss on drying 4% w/w [4].

The seeds are very rich and diverse in chemical composition. They contain amino acids, proteins, carbohydrates, fixed and volatile oils [3]. Many of the pharmacological activities mentioned above have been attributed to quinone constituents in the seed. Thymoquinone is the main active constituent of the volatile oil of the black seed. [7]

Active materials that extracted by cold water and ethyl alcohol for the black seeds (*Nigella sativa*) contain flavonoids, alkaloids, thymoquinone and tannins.[8] Hot water and ethanol extracts of *Nigella sativa* contain alkaloids, saponins, flavonoids, tannins, glycosides, terpins and steroids [9].

Nigellon is the carbonyl polymer of thymoquinone and has a medicinal property that includes antimicrobial, antitumor, antiviral, anti-inflammatory, reduction blood sugar, muscle relaxation and anti oxidation [10].

Traditional Uses

Black seeds are used as a carminative, aromatic, stimulant, diuretic, anthelmintic, galactagogue and diaphoretic, they are used as a condiment in curries. A tincture prepared from the seeds is useful in indigestion, loss of appetite, diarrhoea, dropsy, amenorrhoea, dysmenorrhoea and in the treatment of worms and skin eruptions. Externally the oil is used as an antiseptic, to arrest vomiting, seeds are roasted and given internally [11].

Therapeutic Uses

Nigella sativa seeds have been frequently used in folk medicine for treatment of various diseases. [5]

Antibacterial Effect

The isolated saponin compounds from *N. sativa* (seeds) showed significant inhibiting effect on the growth of some bacteria, which include: *Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Proteus vulgaris* and *Pseudomonas aeruginosa* [12].

In a project considered as an explorer study for the inhibitory effect of *N. sativa* L. seeds extract against *Streptococcus mutans* and *Streptococcus mitis*, the highest inhibition zone was observed with ethanol fraction and it inhibited the growth of two cariogenic bacteria [13].

N. sativa oil have a good antibacterial activity on the isolated bacteria causing wound infection. The oil gave good inhibitory effects on *Staph. aureus* and *Streptococcus* spp. [14].

In experiment was conducted to test *in vitro* the effect of active materials that extracted by cold water and Ethyl Alcohol for the black seeds (*N. sativa*) on inhibition growth of *Escherichia coli*, *S. aureus*, *Pseudomonas aureoginosa*, *Enterobacter*, *Proteus*, *klebsiella* for its clinical importance due to the cause of neumerous disease. The experiment proved the extracts of *Nigella sativa*; contain Flavonids, alkaloids, thymoquinone and tannins, showed effective inhibiton growth of these microorganisms and the highest inhibition effect was against the growth of *Enterobacter* [8].

Thymoquinone and thymohydroquinone have antibacterial activity and their activity could be potentiated by antibiotics especially in case of *S. aureus* [15].

Antifungal Effect

It was found that methanolic extract of black seeds exhibits potent inhibition of fungus growth against *Candida Parapsilosis*, and *Issatchenkia Orientalis* with IC₅₀ Value 4.846 µg/ml, and 6.795µg/ml, respectively and

ethanolic extract also shows significant anti-fungal activity against fungus strain *Issatchenkia Orientali* with IC₅₀ value 5.805 µg/ml [16]. Thymoquinone isolated from black seed extract was evaluated for antifungal activity [17].

Antiparasitic Effect

It was revealed that the water extract of *N. sativa L.* seeds effect against trophozoites isolated from chronic and acute cases of *Entamoeba histolytica* in Baquba General Hospital, Diyala.[18] Similar results have been showed that black seeds oil extract was very effective factor on trophozoites stage of *Entamoeba histolytica* in patients from Al-Hammar marsh, Al-Nassiriyah, Iraq [19]. As well as black seeds oil showed prophylactic and therapeutic effects on murine toxoplasmosis (*Toxoplasma gondii*) [20].

A promising effect of using *N. sativa* aqueous extract in treating *Trichomonas vaginalis* infection. It remarkably inhibited the motility of the trophozoites [21].

Intraperitoneal and oral administrations of ethanol, chloroform and aqueous seed extracts (50, 100, 200 and 400 µL kg) of *N. sativa*, showed suppression activities were for their anti-malarial properties against *Plasmodium berghei* in mice [22]. The provision of *N. sativa* may reduce the number of malaria parasites [23]. The alcoholic extract of *N. sativa* Showed a significant anti-cutaneous leishmanial activity [24].

The anthelmintic potential of essential oil of *N. sativa* Linn. Was evaluated against earthworms, tapeworms hookworms and nodular worms and exhibited fairly good activity against earthworms and tapeworms. The activity against hookworms and nodular worms was comparable with that of hexyl resorcinol. The main active principles of *N. sativa* are thymoquinone,

dithymoquinone cymene and α-pinene.[25]

Experimental studies indicated that *N. sativa* seeds had an efficiency against various parasitic infections. A study evaluated the *in vivo* efficiency of *N. sativa* aqueous seeds extract against hydatidosis found that mice treated with aqueous seeds extract had lower number and diameter of cysts and higher cyst reduction percentage. Histological sections of the liver from mice treated with aqueous seeds showed degeneration and necrosis of hydatid cysts . An elevation of adenosine deaminase (ADA) and dropping in alkaline phosphatase (ALP) activities was recorded in treated mice especially with 25 mg [26].

Anticancer Effect

N. sativa seed, its oil and extracts and some of its active principles, particularly thymoquinone and alpha-hederin, possess remarkable *in vitro* and *in vivo* activities against a large variety of cancers. The antioxidant and anti-inflammatory activities of *N. sativa* can contribute to the prevention and the reduction of the complications of neoplasms. Appropriate modifications in the molecular structure of thymoquinone and alpha-hederin could lead to more effective and safer drugs for the treatment of neoplastic tumors. Moreover, *N. sativa* seed, its oil, thymoquinone, alpha-hederin or their analogs could be used in suitable combinations with already established as chemotherapeutic agents [27].

Anti- hepatotoxicity

The role of *N. sativa* was investigated in the prevention of carbon tetrachloride (CCl₄)-induced liver toxicity, their results indicated that its' oil decreased significantly the elevated serum levels of liver enzymes and improve the state of oxidative stress induced by CCl₄.In conclusion, NS oil protects rats against CCl₄-inducedhepatotoxicity [28].

Alcoholic extract of *N. sativa* appears to be a potent candidate to ameliorate the oxidative stress and hepatotoxicity associated with naphthalene in rats and change in some biological markers related to liver disease [29].

Similar study confirm the protective role of vitamin E and flavonoids of *N. sativa* seed against hepatic dysfunction caused by sodium nitrate manifested by structural and functional change [30]. Another study confirmed that the black seeds have protective effect of against $AlCl_3$ induced toxicity in rabbits [31].

Anti-Diabetic

N. sativa seeds were used as an adjuvant therapy in patients with diabetes mellitus type two added to their anti-diabetic medications. A dose of 2 gm/day of *N. sativa* might be a beneficial adjuvant to oral hypoglycemic agents (reductions in fasting blood glucose [FBG], , blood glucose level two hours postprandially [2hPG], and glycosylated hemoglobin [HbA1]) in type 2 diabetic patients [32].

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 [11]. Oral administration of *N. Sativa* seeds crude alkaloid and administration of *N. Sativa* seeds volatile oil to male rabbits caused a significant decline in blood glucose concentration [33]. Similar study confirmed that oral administration of volatile oils of black seeds into Balb / c male mice at dose (2 mg/ g BW) revealed a significant decrease in blood glucose concentration [34].

Hypocholesterolemic and antiatherogenic cardioprotective properties

N. sativa produces antiatherogenic effect by decreasing low density lipoprotein cholesterol level significantly [35,36]. Serum

triglycerides, total and LDL cholesterol decreased significantly after treatment with 750 mg of powdered grains of *N. sativa* enclosed in a capsule twice daily for 28 days, While HDL cholesterol increased significantly [37]. Similar results revealed that *N. sativa* oil decreased he levels of total cholesterol , triglycerides, phospholipids , LDL cholesterol and uric acid [38].

N. sativa either in powder or oil forms was shown to significantly reduce total cholesterol (TC) and low-density lipoprotein cholesterol (LDL) levels and enhance high-density lipoprotein cholesterol (HDL) levels after treatment for 2, 4, 6 and 8 weeks compared to the positive control group [39].

3-2-8. Effects on Reproduction

The administration of 1ml/kg/day of *N.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 [40].

In a study to evaluate the probable effect of *N. 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.[41]

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 *N. sativa* as compare with control and group . 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 *N. sativa* , in contrast to control group [42].

Alcoholic extract of black seed caused significant increase in body weight gain, reproductive parameters (seminiferous tubules thickness and diameters, account of spermatogonia,

primary and secondary spermatocytes, spermatids, free spermatozoa, account of sertoli and Leydig cells, diameter of Leydig cells and the height of epithelial cells entirely covered epididymal caudal) and hormones (testosterone and follicle stimulating hormone) [43].

N. sativa oil possess an antioxidative actions to counter act the impairment in the epididymal sperm characters caused by hydrogen peroxide (H₂O₂) treatment [44].

It was found that the treatment of adult rats treated with lead acetate with (100 mg/kg B.W) of *N. sativa* caused a significant enhancement of its reproductive function including increase in ovarian weight to body weight ratio, FSH, numbers and diameters of graffian follicles [45].

Effect on immunity

Treatment of typhoid-antigen-challenged rat with the volatile oil revealed an immunosuppressant action as evidenced by the significant decreases in the antibody titer and the splenocytes and neutrophils counts [6].

Albino mice were administered orally with 0.1 of the extract at dose of 100 mg/kg, body weight the results showed high level of white blood cell ,total and differential count of WBC, phagocytosis index, mitotic index, Arthus and delayed type hypersensitivity [9].

In a study investigate the role of *N. sativa* aquatic extracted in stimulation of the immunity response in white mice, the thymus index and the delayed hypersensitivity significant increase at the concentration of (300, 500) mg/kg body weight from the aquatic extract of *N. sativa* seeds,. The ability of macrophages to phagocyte and the activity of macrophages revealed significant increase at all concentration (200, 300, and 500) mg/kg body weight but the best was at 500 mg/kg [46].

A study revealed that treatment of blood samples with herbal extraction

results in highly significant elevation of Neutrophils' count with time passing particularly the aqueous one and after six hrs. incubation period. In conclusion *N. sativa* aqueous extract can be used against bacterial infections which required recruitment of Neutrophils [47].

Acne treatment

The *N. sativa* oil lotion has proved its efficacy as a topical therapy for acne vulgaris. This is a new natural plant extract, which lacks any side effects [48]. Hadi and Ashor (2010) found that *N. sativa* oil lotion 20% is more effective and safe than benzoyl peroxide lotion 5% in the treatment of mild to moderate acne vulgaris [49].

Wound and Ulcer healing

A study indicated that the black seed oil was enhanced wound healing in rabbits, and that may be due to its therapeutic and nutritional activities [50]. Other study concluded that *N. sativa* oil has an obvious effect on the rate of healing process of oral ulcer [51].

N. Sativa and thymoquinone could protect gastric mucosa against the injurious effect of absolute alcohol and promote ulcer healing as evidenced from the ulcer index (UI) values NS prevented alcohol-induced increase in thiobarbituric acid-reactive substances (TBARS), an index of lipid peroxidation. Its' also increased gastric glutathione content (GSH), enzymatic activities of gastric superoxide dismutase (SOD) and glutathione-Stransferase (GST), likewise, thymoquinone protected against the ulcerating effect of alcohol and mitigated most of the biochemical adverse effects induced by alcohol in gastric mucosa, but to a lesser extent than *N. sativa*, neither *N. sativa* nor thymoquinone affected catalase activity in gastric tissue [52].

Psychiatric treatment

A study is concluded that a drug containing 500mg *N. sativa* is effective in long term management of opioid dependence. It not merely cures the opioid dependence but also cures the infections and weakness from which majority of addicts suffer, it is suggested that further long-term follow up studies are needed to evaluate the benefit of this drug in maintaining the patients opioid free [53].

Others

Black seeds act as analgesic, anti-inflammatory action, anti-asthmatic, antihistaminic, anti-allergic, antihypertensive, antihypertensive and anti-oxidant [5,6,54,55].

Safety

Although several studies have reported the safety of consuming *N. sativa* seeds, a recent comprehensive investigation has shown that the plant is relatively unsafe if consumed for prolonged periods of time, it is worth mentioning that thymoquinone is both an irritant and a potent elicitor of allergic contact dermatitis [7].

Volatile oil from *N. sativa* was preformed and show a presence of considerable amount of sex hormones estradiol, progesterone, prolactin, testosterone, FSH and LH ; the hormones that controlled menstrual cycle by altering the bodies natural hormonal balance, thus inhibiting ovulation, preventing implantation of the egg and making the cervical mucus hostile to sperm [56].

Acute and chronic toxicity studies have recently confirmed the safety of *N. sativa* oil and its most abundant active component, thymoquinone, particularly when given orally [27].

Conclusion

Evidence indicates that *N. sativa* seeds have a potential medicinal value and are relatively safe to consume. Future research should focus on the

mechanisms by which *N. sativa* seeds medically effected and understand its mechanism of bioactivity and diagnostic the active components that have medicinal effectiveness.

References

- 1- Asgary, S.; Najafi, S.; Ghannadim A. ana Dashti, G. (2012). Efficiency of black cumin seeds on hematological factors in normal and hypercholesterolemic rabbits. ARYA Atherosclerosis Journal. 7(4) 146-150
- 2- Al-Attar, A.M. and Al-Taisan, W.A. (2010). Prevention Effect of Black seed (*Nigella sativa*) Extract on Sprague Dawely Rats Exposed to Diazinon. Australian Journal of Basic and Applied Science, 4(5): 957-968
- 3- Rajsekhar, S. and Kuldeep, B.(2011). Pharmacognosy And Pharmacology of *Nigella sativa* -A Review. International Research Journal of Pharmacy. 2(11): 36-39
- 4- Paarakh, P.M. (2010). *Nigella sativa* Linn.- A comprehensive review. Indian Journal of Natural Products and Resources. 1(4): 409-429
- 5- Naz, H. (2011). *Nigella sativa*: the miraculous herb. Pak. J. Biochem. Mol. Biol. 44 (1): 44-48
- 6- El-Tahir, K.E.H. and Bakeet, D.M. (2006). The black seed *Nigella sativa* Linnaeus – A mine for Multi Cures: A Plea for Urgent Clinical Evaluation of its Volatile Oil. J T U Med Sc, 1(1): 1-19
- 7- Gali-Muhtasib, H.; El-Najjar, N. and Schneider-Stock, R.(2006). The medicinal potential of black seed (*Nigella sativa*) and its components. *Lead Molecules from Natural Products* :133-153
- 8- Mohsen, Z.A., Ghani, S.W. and Hussein, J.M.(2009). Study of the effect of black seed extract in some bacteria that cause urinary tract infection. journal of kerbala university, 7(1): 156-160 [in Arabic]

- 9- Al-Zendi,S.K.J.; Jasim,A.N. and AL-Mousawi,A.H.(2009). The effect of hot water and ethanol extract of *Nigella sativa* in immune system of Albino Mice. Um Salamah Journal for Science 6(2):235-243 [in Arabic]
- 10- Janfaza, S.and Janfaza, E.(2012). The study of pharmacologic and medicinal valuation of thymoquinone of oil of *Nigella sativa* in the treatment of diseases. Annals of Biological Research, 3 (4):1953-1957
- 11- Sharma, N. K.; Ahirwar, D.; Jhade, D. and Gupta, S.(2009). Medicinal and Phamacological Potential of *Nigella sativa* : A Review. *Ethnobotanical Review* 13: 946-55
- 12- Mohammed, M.J.(2009). Biological Effect of Saponins Isolated from *Nigella sativa* (seeds) on Growth of Some Bacteria. Tikrit Journal of Pure Science, 14(2):30-33
- 13- Mohammed, N.A.(2012). Effect of *Nigella Sativa* L. extracts against *Streptococcus mutans* and *Streptococcus mitis* in Vitro. Journal of Baghdad college of dentistry, 24(3): 154-157.
- 14- Khuder, S.I.(2012). The effect of *Nigella sativa* oil and some antibiotics on bacteria isolated from wound infection in hospitals. College of Basic Education Researches Journal, 12(1): 707-715
- 15- Halawani, E.(2009). Antibacterial Activity of Thymoquinone and Thymohydroquinone of *Nigella sativa* L. and Their Interaction with Some Antibiotics. Advances in Biological Research 3 (5-6): 148-152
- 16- Raval, B.P.; Shah, T.G.; Suthar, M.P. and Ganure, A.L.(2010). Screening of *Nigella Sativa* Seeds for antifungal activity. Annals of Biological Research, 1(1): 164-1
- 17- Suthar M. P, Patel, P. N., Shah T. G. and Patel, R. K.(2010). *In vitro* Screening of *Nigella sativa* Seeds for Antifungal Activity. International Journal of Pharmaceutical and Applied Sciences 1 (2):84-91
- 18- Hassan, A.S.; Mawlood, N.A. and Alwan, D.I.(2009).Effect of Aqueous Extract of Black Seeds *Nigella Sativa* L. In The Vitality of The Parasite *Entamoeba Histolytica* In Laboratory. Journal of Kerbala university , 7 (3) : 26-34 [in Arabic]
- 19- Shariff, H.A.; Ajmi, R.N. and Jasim,A.(2011). Effect of Plant extract of *Nigilla Sativa* on the effectiveness of the Parasite *Entamoeba histolytica* in Patients from Al-Hammar Marsh Iraq, Al-Nasiriyah. AJPS 9(1):105-112
- 20- Rayan, H. Z.; Wagih, H.M. and M.M. Atwa.(2011). Efficacy of Black seed oil from *Nigella sativa* against Murine Infection with Cysts of Me49 Strain of *Toxoplasma gondii*. PUJ, 4(2): 165-176
- 21- Tonkal, A.M.D.(2009). *In Vitro* Antitrichomonal Effect of *Nigella Sativa* Aqueous Extract and Wheat Germ Agglutinin. JKAU: Med. Sci.,16 (2): 17-34
- 22- Abdulelah, H.A.A. and Zainal-Abidin, B. A. H (2007). *In Vivo* Antimalarial Tests of *Nigella sativa* (Black Seed) Different Extracts. American Journal of Pharmacology and Toxicology 2 (2): 46-50
- 23- Sosiawan, T. I.; Linda,W. and Etty, W.(2012). Anti-Malaria Study of *Nigella sativa* L. Seed Water Extract in *Mus musculus* Mice Balb C Strain *In Vivo*. Makara Journal of Science 16(3) 192-196
- 24- Bafghi,A.F.; Vahidi, A.R.; Anvari, M.H.; Barzigar, A. and Ghafourzadeh, M.(2011).the in vivo antileishmanial activity of alcoholic extract from *Nigella sativa* seeds. African journal of Microbiology Research, 5(12):1504-1510
- 25- Mali, R.G. and Mehta, A.A.(2008). A Review on Anthelmintic Plants. Natural Product Radiance,7(5):466-475
- 26- Al-Mayah,K.Sh.; Al-Bashir, N.M. and Al-Azzawi, B.M.(2012). *In Vivo*

- Efficacy of *Nigella Sativa* Aqueous Seed Extract Against Metacestode of *Echinococcus granulosus*. Medical Journal of Babylon 9 (1): 140-151
- 27- Randhawa, M., A. and Alghamdi, M.S. (2011). Anticancer Activity of *Nigella sativa* (Black Seed)-A Review. The American Journal of Chinese Medicine 39 (6):1075-1091
- 28- Ahmed, Z.A. (2010). Protective Effect of *Nigella sativa* oil against CCl₄-induced Hepatotoxicity in Rats. Al-Mustansiriyah Journal for Pharmaceutical Sciences, 8 (2): 46-55
- 29- Hamad, Z.M. (2012). Protective effect Ethanol extract of *Nigella sativa*. L on hepatic damage induced by naphthalene in male rats. journal of al-qadisiyah for pure science, 17 (2):1-10
- 30- AL-Okaily, B.N.; Mohammed, R.S.; Al-Mzain, K.A. and Khudair, K.K. (2012). Effect of Flavonoids Extracted from Black Cumin (*Nigella sativa*) and Vitamin E in Ameliorating Hepatic Damage Induced by Sodium Nitrate in adult male rats. The Iraqi Journal of Veterinary Medicine 36 (2):172-181
- 31- Mohammed, A.K. (2010). Ameliorative effect of black seed (*Nigella sativa* L) on the toxicity of aluminum in rabbits. The Iraqi Journal of Veterinary Medicine, 34 (2) :110-116
- 32- Bamosa, A.O.; Kaatabi, H.A.; Lebda, F.m.; AL Elq, A. and AL-Sultan, A.A. (2010). Effect Of *Nigella Sativa* Seeds on The Glycemic Control of Patients With Type 2 Diabetes Mellitus. Indian J Physiol Pharmacol 2010; 54 (4) : 344-354
- 33- ALAssadi, E.H. and Al-mzaïen, K.A. (2006). Effect of Glucose Specific lectins, Alkaloid and Volatile Oil Extracted From *Nigella Sativa* L Seeds in Blood Glucose Level In Normal Rabbits The Iraqi Journal of Veterinary Medicine 30 (2): 11-22
- 34- Al-Salman, H. K. Y. (2008). Effect of Volatile Oils of Some Medical Plants on the Blood Glucose and Cholesterol Levels in Mice. AL-ANBAR JOURNAL OF AGRICULTURAL SCIENCES 1: (6) : 284-295
- 35- Bhatti, I., Rehman, F.U., Aslam Khan, M. and Marwat, S.K. (2009). Effect of Prophetic Medicine *Kalonji* (*Nigella sativa* L.) on Lipid Profile of Human Beings: An *In Vivo* Approach. World Applied Sciences Journal 6 (8): 1053-1057
- 36- Huseein F.F. (2012). EFFECT OF OLIVE OIL , BLACK SEEDS , FLAX SEEDS AND BUTTER ON BLOOD LIPID PROFILE IN HEALTHY PERSONS. Mesopotamia Journal of Agriculture. 40 (2): 146-152
- 37- Qibi, N.M., Al-Hayali, R.M. A. and Mohammad, H.A. (2006). Effect of *Nigella Sativa* (Black seed) on the serum lipids of healthy individuals. Mustansiriya Medical Journal. 6(2):10-15
- 38- AL-Hindi, A.S., Abdulla, M.S. and Al-Janabi, J.M. (2006). Study of Therapeutic Effect of Black Seed Oil on Hyperlipoproteinemia. Tikret Journal of Pharmaceutical Sciences. 2:26-30
- 39- Al-Naqeep, G., Al-Zubairi, A.S., Ismail, M., Amom, Z.H. and Esa, N.M. (2011). Antiatherogenic Potential of *Nigella sativa* seeds and oil in Diet-Induced Hypercholesterolemia in Rabbits. Evidence-Based Complementary and Alternative Medicine. 2011, Article ID 213628, 8 pages
- 40- Juma F.T and Abdulrahman, H.M.A. (2011). The effects of *Nigella sativa* oil administration on some physiological and histological values of reproductive aspects of rats. The Iraqi Journal of Veterinary Medicine, 35 (2): 52-60
- 41- Al-Tae, A.A. (2008). Effect of black seed *Nigella sativa* (L.) seed extract on reproductive organs of male albino rats. journal of kerbala university, 6 (4) : 244-251
- 42- AL- Zuhairy, R.G.M. (2012). The Phytotherapeutic Effect of Traditional

- Crude Oil of *Nigella sativa* on Male Reproductive System of Albino Mice Treated with Low Toxic Dose of Paracetamol. Medical Journal of Babylon 9 (1):229-237
- 43- Al-Sa'aidi, J. A. A. ; Al-Khuzai, A. L. D. and Al-Zobaydi, N. F.H. (2009). Effect of alcoholic extract of *Nigella sativa* on fertility in male rats. Iraqi Journal of Veterinary Sciences, 23, Supplement II :123-128
- 44- Tawfeek, F.Kh.(2006). Effect of *Nigella sativa* oil Treatment on The Sex Organs and Sperm Charactors in Rats Exposed to Hydrogen Peroxide. Mesopotamia Journal of Agriculture, 34 (1): 2-8
- 45- Arak, J.K. and Assi, M.A.(2011). Effect of *Nigella sativa L.* seeds on ovaries function in adult Rats treated with Lead Acetate. Al- Anbar Medical Journal, 9 (1) : 59-70
- 46- Abdulkareem, I.Q.(2011). Study The Role of *Nigella sativa* Aquatic Extracted in Stimulation of The Immunity Response. journal of kerbala university 9 (1) : 44-49 [In Arabic]
- 47- Al-Haidary, B.A.(2008). Effect of *Nigella sativa* seeds' extract Treatment on Neutrophils count. Journal of the Faculty of Medicine , 50 (2) : 261-285
- 48- Al-Harchan N.A.H.(2010). Treatment of Acne Vulgaris With *Nigella sativa* Oil Lotion. Iraqi postgraduate Medical Journal. 9(2): 140-144
- 49- Hadi, N. A. and Ashor, A.W. (2010). *Nigella Sativa* Oil Lotion 20% vs. Benzoyl Peroxide Lotion 5% in the Treatment of Mild to Moderate Acne Vulgaris. THE IRAQI POSTGRADUATE MEDICAL JOURNAL 9(4):371-376
- 50- Al-Mutheffer ,E. A.(2010). The effect of local application black seed (*Nigella Sativa*) oil on wound healing in rabbits. Al-Anbar Journal of Veterinary Sciences_ 3 (1): 91-97
- 51- AL-Douri, A. S. and Al-kazaz , S. Gh.A. (2010). The Effect of *Nigella sativa* Oil (Black Seed) on the Healing of Chemically Induced Oral Ulcer in Rabbit (Experimental Study). Al-Rafidain Dental Journal, 11: 151-157
- 52- Kanter, M.; Demir, H.; Karakaya, C. and Ozbek H.(2005). Gastroprotective activity of *Nigella sativa L* oil and its constituent, thymoquinone against acute alcohol-induced gastric mucosal injury in rats. *World J Gastroenterol* 11(42):6662-6666
- 53- Sangi, S. Ahmed, S.P, Channa M.A., Ashfaq,A. and Mastoi, S.M. (2008). A New and Novel Treatment of Opioid Dependence: *Nigella sativa* 500 mg. J Ayub Med Coll Abbottabad ;20(2): 118-124
- 54- Randhawa, M. A. (2008). Black Seed, *Nigella sativa*, Deserve More Attention. J Ayub Med Coll Abbottabad, 20(2):1-2
- 55- Parvardeh, S. and Fatehi, M. (2003). Effects of Thymoquinone, the Major Constituent of *Nigella sativa* Seeds, on the Contractile Responses of Rat vas Deferens. *Pharmaceutical Biology* 41(8): 616–621
- 56- Abdulsamie H. Alta'ee, Ewadh, M. J and Zaidan, H.K.(2006). Hormonal Contents of Two Types of Black Seed (*Nigella sativa*) Oil: Comparative Study. Medical Journal of Babylon, 3 (1-2):17-21