

AN OVERVIEW ON NIGELLA SATIVA (BLACK CUMIN): A SUPERNATURAL HERBAL DRUG

Miss. Aaliya Asif Mulla¹, Mr. Ganesh Gophane²

^{1,2}Lokmangal College Pharmacy, Wadala, India.

ABSTRACT

It is annual flowering plant cultivated in southern, Europe, North Africa, southeast Asia.

N.sativa miraculous medicinal plant. It is well received medicine in Unani, Ayurveda, and Siddha system. The seed and oil extract broadly shows its pharmacological effects.

It is believed as universal remedy for all disease in Islamic culture. N.sativa seeds have been used traditionally in middle eastern folk medicine. The main phytoconstituent of N.sativa are thymoquinone, thymo hydroquinone, Di thymoquinone, thymol, carvacrol, α -hederin. Different studies by research here explored that N.sativa have anticancer, antidiabetic, antioxidant, antimicrobial, cardioprotective, immunomodulatory, neuroprotective action. The therapeutic component may show interaction with modern drugs. It shows toxic effect when consumed for long period of time. In future more research should be done to determine the pharmacokinetic and pharmacodynamic studied of N.sativa.

Keywords: N.sativa seed, seed oil, thymoquinone, folk remedies, drug nigella interaction, antioxidant, anticancer, antidiabetic

1. INTRODUCTION

Nowadays, medicinal plant are used in formulation of herbal medicinal because they are more safer than the aliphatic medicine. One of the copious medicinal plant. Nigella sativa is marvelous herb with its comprehensive pharmacological aptitude. Spice, Nigella sativa is food preservative and it act as flavouring agent in breads and pickles. Since it has pretty low level toxicity. N.sativa is native to southern Europe, north Africa and south west Asia and cultivated in multiple countries viz. (5) and also from Saudi Arabia, India, Syria, turkey, Pakistan, Egypt, Iran, Greece. It is commonly known as black seed. It is very popular in Unani, Tibbs, Ayurveda and siddha system of medicine. (2) There is Islamic belief that N.sativa is universal remedy for all diseases except cannot prevent ageing or death in one of the prophetic hadith. (1&8) It is suggest to use it on regular routine in Tibb-e-Nabwi (prophetic medicine). (5) The Holy Bible says that N.sativa is curative black cumin and is narrated as malathion by Hippocrates and Discords and as faith by Pliny. (1) The major active constituents are thymoquinone, thymohydroquinone, dithymoquinone, carvacrol, sesquiterpene longifolene. (6) The N.sativa has broad spectrum activities viz as diuretic, antidiabetic, antihypertensive, anticancer, immunomodulatory analgesic, anti-inflammatory, spasmolytic, bronchodilator, gastroprotective, hepatoprotective, renal protective, antioxidant properties. (5) The seeds are used to treat various disease like asthma, diarrhea, rheumatism, skin disorders. Also used as liver tonic, digestive, antidiarrhea, appetite stimulant, emmenagogue, to increase milk production in nursing mother to tight parasite infection and support immune system. Anti-obesity, hypolipemic, neuroprotective, fertility and reproduction. (2) Pungent, deodorant, carminative, purgatives, expectorant, febrifuge, antiepileptic, dyslipidemia, testicular protective, antidepressant. (6)

Traditional use of folk remedies:

N.sativa seeds have been used traditionally in Middle Eastern folk medicine as a treatment for various diseases for more than 2000 years ago. (4) Avicenna a well known physician of 10th century famous for his book "*The canon of medicine*" has recommended use of Nigella seeds for enhancement of body's energy and also support during recovery from fatigue and dispiritedness. (3) The seeds were used as stimulants, emmenagogue, appetizer, pungent, astringent, anthelmintic, pungent, deodorant, carminative, purgative, expectorant, febrifuge etc. (6) A tincture prepared from seeds is useful in indigestion, loss of appetite, diarrhea, dropsy, amenorrhea, and in treatment of worms and skin eruption. Extremely oil is used as on antiseptic and local anesthetic. Roasted black seeds are given internally to stop the vomiting. Black seeds and their oil have a long history of folivore usage in Indian and Arabic civilization as food and medicine. (5) Herbal medicine to treat many disease such as skin disorder, jaundice, gastrointestinal problem, anorexia, conjunctives, dyspepsia, diabetes, hypertension, paralysis, amenorrhea, cough, asthma, bronchitis, headache, back pain, fever influence. (4) The ancient Egyptian civilization used black seed as a perspective in the process of mummifications probably due to its antibacterial action. (2)

➤ Pharmacognosy characteristics:

COMMON NAMES

1. ENGLISH: black cumin, black seed, fennel flower, nutmeg flower, black caraway
2. USA ENGLISH : roman coriander, damascene, wild onion seed, devil in the bush

3. PERSIAN: Shanaiz
4. BANGALI: kalajira
5. HINDI OR URDU: kalonji
6. SANSKRIT: charanushkha
7. ARABIC : habbat -ul-barakh or habbat -ul-sauda



Fig no. 1 :- NS Plant



Fig no.2:- NS Seeds

TAXONOMIC CLASSIFICATION

kingdom	Plantae
subkingdom	Trophobiont
superdivison	Spermatophyte
phylum	Magnoliophyte
class	Magnoliopsida
order	Ranunculales
family	Ranunculaceae
genus	Nigella
species	N.sativa

morphology of the plant

N.sativa is an annual flowering plant that shoot up at 20-90cm tall with finely divided leaves, the leaf segment narrowly linear to thread like. The flower are fragile and usually colored white, yellow, pink, blue or purple. They having 3-7 petals. The fruit is large and inflated capsule formed of 3-7 united follicles. Each having lots of seeds. (5)

Seed characteristics

Seeds are dicotyledonous, angular small, trigonous, regulus tubercular. The seeds are black on the outside and white on the interior. They having bitter taste and gentle aromatic odour. (5) Transverse section show monolayered epidermis of 2-4 layers thick parenchyma cells and coated by papillae cuticle. (6)

PHYTOCONSTITUENTS:

CHEMICAL NAME	ACTION
1. Arachidonic	Precursor for synthesis of prostaglandin & leukotrienes
2. Steric Acid	Used in soap, detergents & several cosmetics
3. Myristic Acid	As a flow agent & emulsifier in food & beverages
4. Cycloartenol	Anti-inflammatory , antitumor, antioxidant, anti-alzheimer's
5. Nigellone	Asthma
6. Thymoquinone	In asthma, Hypertension, diabetics, inflammation, cough & skin diseases
7. Thymohydroquinone	Anticancer
8. Di thymoquinone	Skin, Anticancer
9. Thymol	Expectorant, anti-inflammatory, anti viral, antibacterial, antiseptic agents
10. Carvacrol	Food Flavoring , Additives & preservatives
11. p-cymene	Flavoring Agent ,cough syrup

12. T-anethole	Antibacterial, antifungal
13. 4-terpineol	Fragrance, Cosmetics, Shampoo
14. α -hederin	Anticancer
15. Sesquiterpene longifolene	Cosmetic, Soap, Fragrance
16. Camp sterol	Cardioprotective, reduce cholesterol, anti inflammatory, improve blood sugar level
17. Hederagenin	Neuroprotective, Antidiabetic, Anti cancer, anti viral , antidepressant
18. Melanthine	Provide pigmentation to skin, hair & eyes
19. Stigmasterol	Anti diabetic
20. α -pipne	Treatment of bladder, kidney & urinary stone
21. Qurcetin	Cardioprotective & Cancer
22. t-anethole	Food industry, Cosmetics, perfume & pharmaceutical
23. Terpenes	Anti insect, anti herbivore
24. α -copaene	Pesticides
25. Tocopherol	Anticancer, Atherosclerosis
26. Polyphenol	Improve digestion, Cardioprotective, Anti coagulant
27. P-coumaric acid	Anti oxidant, antimicrobial, anticancer, antiulcer
28. Fisetin	Antioxidant
29. Niacin	Reduces cholesterol, multivitamin

PHARMACOLOGICAL ACTION:

ANTI-CANCER ACTIVITY:

Thymoquinone have antioxidant, anticarcinogenic, and antimutagenic properties. It shows anticancer activity by causing death of cancer cell or by preventing genetic changes in normal cell. There profiler activity of antioxidant enzymes ,since oxidative stress has effective role in building of cancer types. (1) α -hederine a triterpene induce significant tumor inhibition rate. But the particular mechanism is not known yet. (10) Human breast cancer, colon cancer, ovary, prostate hepatic, lung, head and neck squamous cell.

ANTI-DIABETIC ACTIVITY:

Mechanism:

- Modulation of oxidative status
- Attenuation of inflammation
- Improvement of lipid profile
- Increase good cholesterol (HDL-C)
- Decrease bad cholesterol (LDL-C TC AND TG)
- Decrease or increase body weight (3)

N. sativa and TQ proven clinically useful in treatment of diabetic and oxidative stress. N.sativa oil accounted to effective as an add -on therapy in insulin.(5) Plant extract mixture may used as therapeutic agent in treatment on non-insulin diabetic Meletus.(10)

ANTI-MALERIAL ACTIVITY:

Various extract of N.sativa reveals anti plasmodial activity against plasmodia infection. In manifest 100% inhibition of parasite growth at concentration 50ug/ml and it have dose dependent activity against parasite.(10)

ANTI-OBESITY:

A experiment on hyperlipidemic rats revealed that dietary supplementation of black cumin seed extract surpasses, hyperlipidemia by promoting high density lipoprotein (HDL) and reducing cholesterol, triglycerides and low density lipoprotein (LDL).

They also show cardioprotective and anti-hypertension effect.A preliminary treatment of black cumin ethanoic extract have a encouraging cardioprotective response antagonist toward isoproterenol persuade myocardial infraction by boosting cardiac biomarker and anti-oxidant status. (2) N.sativa and thymoquinone mitigates the blood pressure and reduces hypertension via blocking ,diuretic, and hypotensive (soothing heart beat) function. (1)

IMMUNOMODULATORY EFFECT

Black cumin extract stimulant phagocytic activities of 3 types of macrophages. NSO extract alters subset of T-lymphocytes and validates immunomodulatory effect in case of rheumatoid arthritis. It also have immunomodulatory effect against asthma, H9N2 a vain influenza virus, beta-thalassemia.(2)

ANTI-OXIDANT:

Black cumin lowers reactive oxygen species level and boost antioxidant enzyme. Supplementation of N.sativa rising SOD level without affecting MDA level and total anti-oxidant capacity.(2)

MDA:- malondialdehyde

SOD:- superoxide dismutase

Essential oil, TQ, carvacrol, anethole, 4-terpinol, thymol, Di thymoquinone (10)

ANTI-MICROBIAL:

ANTI-BACTERIAL:

The mechanism is not known. The activity is because of TQ various extract shows activity against various Gram +ve and Gram -ve species. (4)

ANTI-FUNGAL:

Essential oil having moderate activity against yeast, dermatophyte, and non-dermatophyte . TQ and thymo hydroquinone and thymol shows potent antifungal effect towards dermatophyte, modules, yeasts.(3)

ANTI-PARASITIC:

Seed have schistosomicidal properties. Methanolic extract shows admiring parasite clearance.(3)

ANTI-VIRAL:

Anti- oxidant inhibit apoptosis caused by viruses and also inhibit viral replication in target cell. Mostly the oil extract is used.(4)

NEUROPHARMACOLOGICAL ACTIVITIES:

A Potent central nervous system and analgesic activities are shown by the aqueous and methanol extract N.sativa seeds.N.sativa and its constituent TQ has a therapeutic effect against a wide range of neurological conditions such as neurodegenerative disorders (Alzheimer's disease and Parkinson's disease), anxiety, depression, ischemic stroke, schizophrenia, acute brain injury, epilepsy, etc. (1)

EFFECT ON FERTILITY AND REPRODUCTION:

Depending on the type of extract N.sativa shows both +ve and -ve effects on fertility and reproduction.The extracted N.sativa oil when taken orally for 45days improves the semen parameter, seminal vesical development in rats while 2.5ml of N.sativa oil twice daily.They improve the semen quality (e.g. volume and pH), sperms concentration, in Iranian infertile men.In some observational study it is investigated that oral administration of black cumin powder taken 1600mg/day for 12weeks reduces the menopausal symptoms in Iranian women.It also observed that the combination of black cumin tablet (500mg) and mefenamic acid tablet (250mg) lowers the post partum pain within 2 hour of delivery.(2)

DRUG -NIGELLA INTERACTION :

ACTIVE COMPOUND/EXTRACT	INTERACTING DRUG	EFFECT
Thymoquinone (TQ)	Cyclosporin A (CsA)	Bioavailability, oral CsA reduced by 32% but IP CsA was not affected chronic CsA (increase fasting glucose and marked kidney alteration) was reversed by TQ (2)
	Warfarin Glibenclamide (GBC)	Competitive inhibition warfarin-7-hydroxylase activity Plasma concentration of GBC increases by 13.4% & 21.8% with TQ synergistic effect on glucose level
Ethanolic extract	Phenobarbitone	Antagonist (7)
Oil	Gliclazide	Improve the sensitivity to insulin in insulin resistant rats (4)
Black cumin (Methanol & hexane)	Amoxicillin Carbamazepine (CBZ)	Boost Amoxicillin availability in both in vivo & in vitro Concurrent uses of Lepidium sativum but not black cumin alters the pharmacokinetics of CBZ

2. TOXICOLOGICAL STUDIES

The toxicity of TQ can be occurred by dose size, route of administration or health condition of animal used for this study.

- Acute Toxicity:-

To study the acute toxicity, 2-3 gm/kg of TQ is given orally to the mice. Within the 3 hours of drug administration mice shows hypoactivity malaise, problem in breathing and decrease in weight of heart, liver & kidney. Another studies shows that low doses (less than 6mg/kg/day for 2 weeks) does not show any toxic effects whether high dose (8mg/kg/day) shows the toxic effect. The several studies evaluate that at the second trimester of pregnancy the dose of 35mg/kg and 50mg/kg of TQ affect the maternal health and embryo fetal development. (2)

- Chronic Toxicity:-

At 500mg/kg/dose of TQ the death of mice is occurred. (2)

- Sub-chronic Toxicity:-

At 30, 60 & 90 mg/kg/day dose of TQ for 90 days dose not show any toxic effect as well as the death of mice. But shows the decrease in fasting plasma glucose level. (2)

3. CONCLUSION

N.sativa is widely used herbal medicine. It is the folk medicine used for treatment of various disease for more than 2000 years ago. There are various active component, mainly TQ shows various therapeutic effect. Having antidiabetic, antimicrobial, anticancer, cardioprotective, neuroprotective actions.

4. FUTURE PERSPECTIVE

Chemical modification in the SAR of main constituent of NS i.e. TQ, α -hederin & other constituent leads to produce most safest & effective drugs which are used for various diseases in the future. Chemical modification also increases the bioavailability. In future by combination with others compounds or natural product we can enhance the biological activity of NS and also we can synergizes the effect of NS. In future to minimize the toxicity of NS we can reduce the size dose of NS. In future by using nanoparticle of TQ /NS drug can easily cross BBB, which makes the barrier for the drugs in the treatment of the brain tumor. By animal study it is confirmed that NS can be used for treatment of various chronic non infectious diseases (neurological disorder, hypertension, dyslipidemia, inflammatory disorder, cancer etc.) & infectious diseases (bacterial, fungal, viral, parasitic) But for the safety of humans, chemical studies should be assessed.

5. ABBREVIATION

NS=Nigella Sativa

TQ= Thymoquinone

C_sA= cyclosporine A

HDL= High Density Lipoprotein

LDL= Low Density Lipoprotein

BBB= Blood Brain Barrier

SAR= Structural Activity Relationship

GBC=Glibenclamide

CBZ= Carbamazepine

6. REFERENCES

- [1] Alyaa majid*. The Chemical Constituents And Pharmacological Effect Of Nigella Sativa- A Review
- [2] Hannam M.A, Rahman M.A, Sohag A.A.M, Uddin M.J, Dash R, Sikder M.H, Rahman M.S, Timalsina B, Munni Y.A, Sarker P. P, et al. Black Cumin (Nigella Sativa L.): A Comprehensive Review on Phytochemistry, Health Benefits, Molecular Pharmacology, and Safety. *Nutrients* 2021, 13, 1784. <https://doi.org/10.3390/nu13061784>
- [3] Ebrahim M. Yimer, Kald Beshir Tuem, Aman Karim, Najeeb Ur-Rehman, and Farooq Anwar. Nigella Sativa L. (Black Cumin): A Promising Natural Remedy for Wide Range of Illness.
- [4] Fatemeh Forouzanfar, Bibi Sedigheh Fazyl Bazzaz, and Hosseinzadeh*. Black Cumin (Nigella sativa) and its constituent (thymoquinone): a review on antimicrobial effect.
- [5] Aftab Ahmad*, Asif Husain, Mohd Mujeib, Shah Alam Khan, Abul Kalam Najmi, Nasir Ali Siddique, Zoheir A. Damanhour, and Firoz anwar. A review on therapeutic potential of Nigella sativa: A miracle herb.
- [6] Prashant Tiwari*, Susmita Jena, Swaroop Satpathy, Pratap Kumar Sahu. Nigella Sativa: Phytochemistry, Pharmacology and its Therapeutic Potential.

-
- [7] Lovelyn Joseph, Rejeesh Edavan Puthallath, Sudarshanram Narayan Rao. Drug interaction analysis-Nigella Sativa L. seed (Black Cumin) ethanolic extract on anti-seizure activity of Phenobarbitone Sodium.
- [8] Jeffry Adiwidjaja, Lucy Sasongko. Effect Of Nigella Sativa oil on pharmacokinetic and pharmacodynamic of gliclazide in rats. #
- [9] Zhen Wang, Zhe Wang, Xiaoyu Wang, Xin Lv, Hang Yin, Lili Jiang, Yanguliu Xia, Wei Li, Wenli Li, Young Liu. Potential Food-Drug interaction risk of thymoquinone with warfarin. #
- [10] S.V. Tembhurne, S. Feroz, B.H. More, and D.M. Sakarkar. A review on therapeutic potential of Nigella Sativa (Kalongi) seeds.