



Research Article

Astropharmacology of Antiepileptic terpenoids of *Nigella Sativa*

Luv Kush*

Department of Pharmaceutical Sciences and Applied Chemistry, Sardar Bhagwan Singh Post Graduate Institute of Biomedical Sciences and Research, Balawala, Dehradun-248161, Uttarakhand, India

ABSTRACT

The ethnopharmacology of natural products^[1-5] have reputable history *Nigella sativa* is a potent medicinal plant of family Ranunculaceae. Traditionally the seeds of this plant are known as kalonji or shoneez, having multiple bioactivities for the treatments of various ailments. The chemotherapeutic, pharmacodynamical, nutraceutical and dermatological bioactivities of seeds have validated by several modern publications. The antipetital activity of terpenoids was rationalized astropharmacologically by cosmobiological planetary attributions.

Key words: *Nigella sativa*, Bioactivity, Terpenoids, Astropharmacology, Ancient remedies, Antipetital.

Corresponding Author: Dr. Luv Kush, Department of Pharmaceutical Sciences and Applied Chemistry, Academic Advisor, Sardar Bhagwan Singh Post Graduate Institute of Biomedical Sciences and Research, Balawala, Dehradun-248161, Uttarakhand, India.

Email ID-luvdevraj@gmail.com.

Article Info: Date received: 22 Sept. 2018

Date accepted (for revision): 23 Sept. 2018

Cite this Article: Luv Kush., Astropharmacology of Antiepileptic terpenoids of *Nigella Sativa*. Int. J. of Pharmacy Res., 2018; 9(2): 1-6.

INTRODUCTION

Nigella sativa is a herb of family Ranunculaceae. The seeds of this plant are known as kalonji or shoneez which are extensively used in Unani medicine [6-8], originated in Greece and advanced by Arabs. This system authenticated that kalonji treats almost all the ailments of the human body. The medicinal part of this plant is harvested in north India (Punjab, Bihar, Himachal and Assam) [9]. It is a potent medicinal plant of ancient remedies useful in Chinese, Ayurveda and Unani systems [10]. The scientific literature and reviews revealed multiple bioactivities of this plant [11-14]. The chemotherapeutic [15-17] [anti-microbial, anti-fungal, anti-parasitic, anti-helminth, anti-viral and anti-tumor], pharmacodynamical [18,23] [anti-asthmatic, anti-diabetic, anti-hypertensive, anti-inflammatory, anti-anxiety, anti-spasmodic,

anti-urolithic, anti-nociceptive, anti-epileptic, anti-hyperlipidemic, gastroprotective, hepatoprotective, neuroprotective, pulmonary protective and nephro-protective] nutraceutical [12]. [anti-aging and immuno-modulatory] and dermatological [13] [anti-psoriasis, anti-acne, anti- vitiligo, anti-vulgaris and radioprotective] have attracted phytopharmacologists for the extensive research. The chief chemical constituents [24,30] of this herb are thymoquinone, thymohydroquinone, dihydrothymoquinone, thymol, nigellimine, nigellin, etc.

The multiplicity of the bioactivities [30] posed a problem that how come terpenoidal bioactive chemical structure can be therapeutically so diversified. The astropharmacological [31,33]

perspective was attempted for the innovative look at bioactivity profile. The antipetitm activity of terpenoidal structures [34,36] was selected for this study.

Epilepsy [37] is malfunctioning of nerves in the brain. It is common neurological disorder, characterized by seizures and behavioral spell in which neurons signal abnormally. Physiologically neurons generated electrochemical impulses that act on glands, muscles and other neurons to trigger normal human behavior, thoughts and actions. This normal pattern is disturbed in epilepsy, causing behavioral erraticness, convulsions, muscle spasms and loss of consciousness. The recurrent seizures involve cholinergic, gabaergic and glutamatergic neurotransmitters of the central nervous system. The release of extcitary amino acids [38] e.g. glutamic acid and aspartic acid cause hypersynchnous neuronal activity, whereas inhibitory amino acids eg. glycine and GABA modulate antiepileptic action. The monoterpenoids and phenylproponoids act as anticonvulants by enhancing action of GABA [39].

THEORETICAL METHODOLOGY

The organic structures of the natural products are under the umbrella of royal planets-Sun and Moon. They represent hydrogen and carbon respectively. The heteroatoms oxygen and nitrogen account for acidic and basic natures of phytochemicals and biomolecules [40,41].

Vedic medicine[40] accounts the epilepsy due to tridosha related to food habits gleaned from 2nd and 6th houses where moon's adversity occurs through configurational aspects and interactions with other planets.The astrological attributes participate in epileptogenesis [42,43] are briefed below:

Aries (Zodiacal sign) rules the brain. Sun, Mars Mercury and Saturn and Rahu are medically related to healthiness of CNS. Their malefic astro

aspects cause CNS disorders. The horoscopol combinations implicated in etiology of epilepsy are:

- Moon, Sun, Mars in Ist or 8th houses aspected malefic (Saturn or Rahu)
 - Rahu in ascendant and moon in sixth house
 - Mercury and venus in 6th house associated with Rahu or Ketu.
 - Sun and venus in ascendant opposing Saturn.
 - Afflicterd moon and mercury.
 - Moon, Mars and Saturn in 8th house.
 - Moon in malefic house with Rahu, Ketu, Saturn or Mars.
- Moon is the significator of emotions and consciousness Moon in 6th, 8th and 12th with evil influence of Rahu toxify emotions and consciousness which promote disorders of mind and consciousness, related to epilepsy. The chemical pharmacology of antipetitm terpenoids[44,48] is summarized in table-1.

Table-1: Antipetitm profile of Monoterpenoids

| Terpenoids | Molecular formula | Antipetitm Activity Dose (mg/kg) | Molecular Weights |
|----------------|--|----------------------------------|-------------------|
| Thymoquinone | C ₁₀ H ₁₂ O ₂ | 40 | 164 |
| Thymol | C ₁₀ H ₁₄ O | 25 | 150 |
| Benzoquinone | C ₆ H ₄ O ₂ | 80 | 180 |
| α-Terpineol | C ₁₀ H ₁₈ O | 100-400 | 154 |
| Terpinen-4-ol | C ₁₀ H ₁₈ O | 25-200 | 154 |
| (-) Isopulegol | C ₁₀ H ₁₈ O | 100-400 | 154 |
| Limonene | C ₁₀ H ₁₆ | 200 | 136 |

The transformation of chemical pharmacology of monoterpenoids into astropharmacology^[41] in given in table-2.

DISCUSSION AND RESULT

CNS depressant biomolecules should cross blood barrier to reach at site of action. Amazingly hydrogen is the key element in governance of aqueous (hydrophilic) and non-aqueous

(hydrophobic) behaviors of biomolecules. Astrologically hydrogen is ruled by Leo sign (Sun vibrations) is non aqueous, as alkyl, aryl, and acyclic groups have solar dominance. The carbon ruled by (moon vibrations) reduces solar influence by bonding with oxygen and nitrogen. It imparts ionic nature of acid- base behavior promoting (hydrophilic) property. The solar and lunar ranges of terpenoids have hydrogens between 12 to 18 and carbons between 8 to 12 respectively. Pharmacokinetically they are significant because the solar prominence of hydrogens enhance hydrophobicity, absorption and bioavailability.

Thymoquinone has methyl and isopropyl groups which characterize solar imparted hydrophobicity to cross blood-brain-barrier to reach at the site of action in CNS. The antiepileptic dose 40mg/kg proves that increase beyond twelve hydrogens or odd atomic numbers except thymol decrease potency. The absence of grandmal and psychomotor epilepsy in the monoterpenoidal structures is due to lack of aryl group of pharmacophoric nature. It has almost equal solar and lunar ratio. The biological polymorphism of single bioactive natural product cannot be rationalized purely by scientific validations. The versatile bioactivities of biomolecule implied that chemical similarity does not mean biological similarity in vivo. An astropharmacological concept combines cosmological synergism with clinical diversity of bioactive chemical conformation. The possible occult explanation

may be based on astropharmacological bioactive shape, composed of Sun-Moon=Solar-lunar=leo-cancer signs contents. Possibly It assumes the multidimensional changes at conformational level in vivo at different tissues.

CONCLUSION

The botanical diversity of natural kingdom has extraordinary biosynthetic variations in chemical structures. The therapeutical biomolecules of natural origin are composed of carbons, hydrogens, nitrogens and oxygens. Astrologically Sun (Leo) and Moon (Cancer) govern these elements. The Solar and lunar lights have profound effect on natural products. Antipetital activity explained by absence of aryl group in monoterpenoidal structures. In other words Sun (hydrogen) - Moon (carbon) contents are structurally diluted.

ACKNOWLEDGEMENT

The author expresses thankfulness to Shri S.P. Singh (Chairman) for suggesting this herb in order to offer an innovative look at multiple bioactivities of *Nigella stavia* Linn. The author expresses his gratefulness to Prof. Varsha Parcha head of Applied chemistry for supporting revitalization of ancient knowledge at multidisciplinary level. Dr. Yogita Dobhal Assistant Professor in pharmacology is greatly appreciated for providing the dose data for the antipetital terpenoid.

Table-2: Astropharmacological Elementenkresis of Antiepileptic Monoterpenoids

| Structural Standards | Number of Carbon Atoms | Number of Hydrogen Atoms | Number of Oxygen Atoms | Number of Even Atomic numbers | Number of Odd atomic number |
|----------------------|------------------------|--------------------------|------------------------|-------------------------------|-----------------------------|
| | Moon | Sun | Moon | | |
| Thymoquinone | 10 | 12 | 02 | 12 | 12 |
| Benzoquinone | 06 | 04 | 02 | 08 | 04 |
| Thymol | 10 | 14 | 01 | 11 | 14 |
| α -Terpineol | 10 | 18 | 01 | 11 | 18 |
| Terpinen-4-ol | 10 | 18 | 01 | 11 | 18 |

| | | | | | |
|-------------|----|----|----|----|----|
| Limonene | 10 | 16 | 0 | 10 | 18 |
| Iso pulegol | 10 | 18 | 01 | 10 | 18 |

REFERENCES

- The Ayurvedic Formulary of India, Part-I, Ministry of Health & Family Welfare, Govt. of India, New Delhi, 1978, pp.243-244.
- Medicinal Plants of India, Vol. II, ICMR, New Delhi, 1987 pp. 474-475.
- Warrier PK, Nambiar VPK, Ramankuty, Indian Medicinal Plants – A Compendium of 500 species, Vol. 4 Orient Longman Pvt. Ltd. Chennai, 2004, pp.139-142.
- Quality standards of Indian Medicinal Plants Ministry of Health Welfare, Government of India, New Delhi, 2005, 161-167.
- Sharma PC, Yelne MB and Dennis TJ. Database on Medicinal Plants used in Ayurveda, Vol. 6, CCRAS, New Delhi, 2005, pp. 420-440.
- Mohammad Yaheya, Mohammad Ismail. Therapeutic Role of Prophetic Medicine Habbat-al-Baraka (*Nigella sativa L.*) – A Review. *World Applied Sciences Journal* 2009; 7(9): 1203-1208.
- Bugdadi Ibne-Hubal, Kitabul Mukhtarat-fil-tibb (Urdu). Vol. 1. CCRUM AYUSH Ministry of Health and Family Welfare. Govt. of India; (2007). P. 268.
- Ali Safiuddin Syed, *Unani advia mufradah Urdu* Beurou, New Delhi, p. 230-231.
- Rastogi Ram P et al. *Compendium of Indian medicinal plant*” vol.5, 1990-1994, Central Drug Research Institute Lucknow Publications & Informations, Directorate, New Delhi, (1998): 483-484, 577-585.
- Raza A, Asif AR and Yasin G. Uses of *Nigella sativa*, (Ranunculaceae) A Traditional Medicine. *International Journal of Agriculture & Biology* 1560-8530/99/01-3-184-187.
- Randhawa, Mohammad Akram, Editorial Black Seed, *Nigella sativa* deserves more attention. *J. Ayub Med Coll* 2008; 20 2.
- Masood Sadiq Butt, Muammad Tauseef Sultan. *Nigella sativa*: Reduces the Risk of Various Maladies. *Food Science and Nutrition*, 2010; 50: 654-665.
- Padmaa M. Praarakh. *Nigella Sativa* Linn. – A comprehensive review. *In J Nat Pdts Resources* 2010; 4: 409-429
- Rabindra Kumar Singh, Kaml Nayan Jhunjhunwalla. Chemical composition of volatile oil of *Nigella Sativa* seeds. *Molecules* 2011; 16: 2726-2742.
- Swamy SMK and Tan BHH. Cytotoxic and immunopotentiating effects of ethanolic extract of *Nigella sativa*. *J Ethnopharmacol*, 2000; 70: 1-7.
- Kumara SS and Huat TK, Extraction, isolation and characterization of anti-tumor principle, α -hederin from seeds of *Nigella sativa*, *Planta Med*, 2001; 67: 29-32.
- Chehl N, Chipitsyna G, Gong Q, Yeo Cj and Arafat HA. Anti-inflammatory effects of the of *Nigella sativa* seed extract, thymoquinone, in pancreatic cancer cells. *HPB (Oxford)* 2009; 11 (5): 373-381.
- Freitas RM. Investigation of oxidative stress involvement in hippocampus in epilepsy model induced by pilocarpine. *Neurosci Lett* 2009; 462: 225-229.
- Farah N, Benghuzzi H, Tucci M and Cason Z. The effects of isolated antioxidants from black seed on the cellular metabolism of A549 cells. *Biomed Sci Intrum*, 2005; 41: 211-216.
- Meddah B, Duroc R, El-Abbes-Faouzi M, Eto B, Mahraoui L, Benhaddou-Andaloussi A, Martineau LC, Cherrah Y and Haddad PS. *Nigella sativa* inhibits intestinal glucose absorption and improves glucose tolerance in rats, *J Ethnopharmacol*, 2009; 21(3): 419-424.
- Dhaneshwar S, Patel V, Patil D, Meena, G. Studies on synthesis stability release and Pharmacodynamic profile of the noval diacerein- thymol prodrug. *Bioorg. Med Chem Lett* 2013; 23: 55-61.
- Kaleem M, Kirmani D, Asif M, Ahmed Q and Bano B. Biochemical effects of *Nigella sativa* L seeds in diabetic rats. *Indian J Exp Biol*, 2006; 44 (9): 745-748.
- Singh Sanjiv, Manvi FV, Basavraj Nanjwade, Rajesh Kumar Nema. Antihyperlipidemic Screening of Polyherbal Formulation of *Annona squamosa* and

- Nigella sativa*, *Int J Toxicol Pharmacol Res* (2010); 2(1): 1-5.
24. Khan M. Akram. Chemical composition and medicinal properties *Nigella sativa* Linn. *Inflammopharmacology* 1999; 7(1): 15-35.
25. Atta-Ur-Rahman Nigellidine a new indazole alkaloid from the seed of *Nigella sativa*, *Tetrahedron Lett* 1995; 36 (12): 1993-1994.
26. Ali Z, Ferreira D, Carvalho P, A very MA and Khan IA, Nigellidine-4-O-sulfite, the first sulfated indazole-type alkaloid from the seeds of *Nigella sativa*, *J Nat Prod*, 2008; 71 (6): 11111-11112.
27. Morikawa T, Xu F, Ninomiya K, Matsuda H and Yoshikawa M, Nigellamines A3, A4, A5 and C, dolebellane-type diterpene alkaloids, with lipid metabolism-promoting activities from the Egyptian medicinal food black cumin *Chem Pharm Bull*, 2004; 52 (4): 494-497.
28. Bourgou S, Ksouri R, Bellila A, Skandrani I, Falleh H and Marzouk B, Phenolic composition and biological activities of Tunisian *Nigella sativa* L. shoots and roots, *C R Biol*, 2008; 331 (1): 48-55.
29. Nickavar B, Mojab F, Javonia K and Amoli MA. Chemical composition of the fixed and volatile oils of *Nigella sativa* L. from Iran. *Z Naturforsch C* 2003; 58(9-10): 629-631.
30. Ali B H and Blunden G. Pharmacological and Toxicological Properties of *Nigella sativa* Phytotherapy Research *Phytother Res.* (2003). 17; 299-305.
31. Tucker. Dr. William. J *Astropharmacology* "Prescribing for the Vital Requirement of the Individual from the Evidence Offered in the Birth Cart reprinted Pythagorean publication, Sidcup Kent, 1969.
32. Jancky Robert Carl. Introduction of Holistic Medical Astrology American Federation of Astrologers. It Tempe. Arizona 1983.
33. Tucker, Dr. William. "Astromedical Research" Reprinted- Pythagorean publications Sidcup, Kent, 1965.
34. De souze et al. Anticonvulsant activity of thymoquinone and its structural analogues... <https://www.researchgate.net/...262464917,2011>.
35. Yuksel A, Cengiz M, Seven M et al. Changes in the antioxidant system in epileptic children receiving antiepileptic drugs: two year prospective studies. *J Child Neurol* 2001;16: 603-606.
36. Abdul Nasir et. el. Essential oil and Fixed Oil Content of *Nigella sativa* after A Traditional... www.researchtrend.net/...BFIJ%2018%20HAJIMEHDI%20POOR%20117, Reinaldo Nobrega da...and Damiao Pergentino de Souse 2011. Essential Oils and Their Constituents: Anticonvulsant Activity – MDPI.c www.mdpi.com/1420-3049/16/3/2726/pdf
37. Sander JW, Shorvon SD. Epidemiology of the epilepsies. *J. Neurol. Neurosurg. Psychiat.* 1996; 61: 433-443.
38. Tarek EI-Naggae et. Al. *Nigella Sativa* seed extract modulates Amino acids release in cultured neurons In Vitro 2010, *J. of biomedicine and biotechnology* 398312.
39. Rabindra et. al. potentiation of Valproate –induced Anticonvulsant Response by *Nigella Sativa* Seed constituents. The role of GABA Receptors. *World J of Pharmacy and Pharmaceutical Sci* 2014; 3 (10): 1588-1594.
40. Luvkush, Shivam K Singh, Ankit Devshali. Astropathological perspective of Ayurveda' Internat. J.innovat research & development 2016; 5(6): 58-61.
41. Luvkush, Vermaram, Yogita Dobbal, Shivam K.S., Fascinating innovation of Astropharmacology 2016; 5(6): 316-318
42. Bhasin JN. "Medical Astrology & Diagnosis" Reprinted-Sagar Publication, New Delhi, 2005
43. Khot, Major S.G. "Astrology & Diagnosis" Reprinted – Sagar Publication, New Delhi
44. Viana GS, do Vale TG, Silva CM, Matos FJ. Anticonvulsant activity of essential oils and active principles from chemotypes of *Lippia alba* (Mill.) N.E. Brown. *Biol Pharm Bull* 2000; 23:1314-7.
45. De Sousa DP, Nobrega FFF, Santos CCMP, and De Almediada RN, "Anticonvulsant activity of the linalool enantiomers and racemate: investigation of chiral influence," *Natural product Communications* 2010; 5(12): 1847-1851.
46. De Sousa DP, Quintans JL, Almedia RN. Evaluation of the Anticonvulsant Activity of alfa-Terpineol. *Pharm. Bio.* 2007; 45; 69-70.

47. Bhatia SP, McGinty D, Letizia CS, Api AM. Fragrance material review on isopulegol. *Foiod Chem Toxicol* 2008; 46: 185-189.
48. Damiao P de Sousa, Franklin FT Nobrega, Camila CM P Santos, Rubens B Bencdito, Ygor W Vieira, Marciana P Ulhana, Timothy J Brocksom, Reinaldo N de Almeida. Anticonvulsant activity of themoquinone and its structural analogues. *Brazilian Journal of Pharmacognosy* 2011: 21 (3): 427-431.