Neuropsychopharmacological preclinical effects of nigella sativa: A review.

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Abstract

Many researches papers have demonstrated that Nigella has neurotropic properties, and it has also been shown that Nigella seeds have several activities, such as analgesic, antiepileptic, anxiolytic, antidepressant, and psych stimulant activities. The orientation towards this type of research has become more and more accentuated to enhance and detail the pharmacological properties of medicinal aromatic plants. The present review consists in revealing and combining the experimental research studies carried out to demonstrate the central effects of nigella.

Keywords: Nigella, Preclinical effects, Depression, Anxiety, Chemical composition.

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Introduction

Nigella is one of the most widely used medicinal and aromatic plants. As this plant belongs to the family of Ranunculaceae, it's largely utilized as a natural remedy for many illnesses, also as a stimulant, carminative and rash treatment in Ayurveda medicine. Nigella in Morocco is used as oil or as seeds added to food, as a treatment. Different research studies have demonstrated that Nigella has neurotropic properties, and it has also been shown that its seed has several activities, such as analgesic, antiepileptic, anxiolytic, antidepressant, and psych stimulant activities. Many investigations have revealed the richness of Nigella oil in thymoquinone, polyphenols, flavonoids, folic acid, vitamin E, potassium, calcium, iron, sodium, and selenium. The multiple uses of Nigella Sativa in traditional medicine encouraged investigators to isolate the most active components and conduct experimental and clinical trials to identify the neuro psycho pharmacological role of Nigella and to clarify the mechanisms implemented [1].

Literature Review

Chemical composition of the seeds

The fixed oil represents 37.9-39.2% of the weight of the grain. Neutral lipids (96.1%-97.2%), polar lipids (3%) and phospholipids (0.32-1.05%) are the main compounds of this oil. Analysis by high performance liquid chromatographic methods identified: phosphatidyl choline, phosphatidylethanolamine, phosphatidyl ethanolamine, phosphatidyl serine phosphatidylinositol, lysophosphatidyl choline, phosphatidyl glycerol, and lysophosphatidyl ethanolamine [2].

In the same sense, a study on Nigella glycolipids identified several compounds, the most abundant of these compounds being digalactosyldiacyl glycerol with a percentage of 55.6% of total glycolipids. Other phytochemical analyses show that the main unsaturated fatty acid is linoleic acid followed by oleic acid, while the main saturated fatty acid is palmitic acid, thus the presence of other fatty acids such as myristoleic acid, and palmitoleic acid has also been detected [3].

The essential oil represents from 0.4% to 2.5% of the components of Nigella grains. The majority of components are monoterpenes; thymoquinone (27.8%-57%), p-cymene (7.07-15.83%), carvacrol (5.8-11.6%), longifolene (1.2-8%), 4-terpinol (1.98-6.59%), and tanethol (0.25-4.28%). The analysis of black cumin essential oil by Gas Chromatography and GC-MS led to the identification and characterization of 112 compounds, thus, p-cymene still represents the most abundant compound followed by thymoquinone [4].

Materials and Methods

Databases such as PubMed, Science Direct, Scopus, and Google Scholar were searched for the terms of N. Sativa, its effects, experimental effects, and psychopharmacological disorders between the years 2002 and 2020 to prepare this review.

Analgesic activity

The analgesic activity was observed by an Indian team for the first time. Intra-gastric administration of 1mg/kg of Nigella shows an analgesic effect in mice.

Concerning the analgesic effects of aqueous and methanolic extracts of black cumin, observation showed that both extracts have a powerful analgesic activity.

These extracts have been studied by other researchers to provide evidence of their analgesic effects.

The significant increase in reaction time on the hot plate in mice indicates an analgesic effect, that study suggested the use of Nigella in traditional medicine as an analgesic agent and calls for further investigations to elucidate its mechanism of action [5].

Anti-epileptic activity

The thymoquinone administration acts against the convulsive action of pentylenetetrazole through opioid receptors by increasing GABAergic tone [6].

The effects of thymoquinone, the major component of black cumin seeds, were studied using a seizure induction agent, black cumin reduced the duration of tonic-clonic seizures [7]. It has been also suggested that fixed black cumin oil protects against damage caused by pentylenetetrazole. By comparing its action with that of sodium valproate, both substances have a preventive role against epileptic seizures in mice.

A botanical review mentions that nigella is one of the plants with an anti-epileptic property as it protects against the metabolic disorder underlying the epileptic seizure [8]. A study attempted to assess the change in the functioning of certain enzymes such as catalase, Na^+, K^+ ATPase and acetylcholinesterase in the hippocampus, while black cumin oil and other substances used in the same study play a role in epileptogenesis and seizures induced by pilocarpine. As a result, chronic flavonoid therapy has epileptogenic potential without any neurotoxicity [9].

Anti-depressive activity

Coumarin is one of the components of black cumin and affects depression. Chronic administration of oil can be useful in stress prevention, as it increases the availability of 5 hydroxytryptamine at synaptic sites by increasing tryptophan plasma concentrations, which can also potentiate monoamine functions by inhibiting enzyme degradation activity leading to antidepressant type effects [10].

A study was conducted to evaluate the possible effects of the hydroalcoholic extract of nigella, including thymoquinone, on depressive behavior. It has also been demonstrated in rats that the injection of 200 and 400 mg/kg of a hydroalcoholic extract of Nigella seeds inhibited the behavior of a depression-like induced by a lipopolysaccharide, suggesting an anti-inflammatory activity of the extract. Besides, it has been suggested that the chronic administration of Nigella may act by potentiating the functioning of monoamines by inhibiting the activity of degradation enzymes. The rats also had a better performance when tested in an elevated plus-maze. An oral administration of Nigella raised brain levels of 5-hydroxytryptamine. It has also been shown recently that intraperitoneal administration during 20 days increased the swimming time and improved depressive behavior in rats following the forced swimming test.

Anxiolytic activity

To study its effect on anxiety in rats, a group of researchers was able to demonstrate the anxiolytic effect of black cumin by measuring tryptophan fluctuations. It was found that plasma levels of tryptophan increased significantly following repeated oral administration of black cumin fixed oil. Administration of thymoquinone at different doses may affect anxiety in mice by decreasing nitrite concentrations and reversing the decrease in GABA brain concentrations [11].

Psychostimulant and neuroprotective activities

The richness of Nigella oil in oleic acid, linoleic acid and compounds improve spatial memory and learning. It has also been studied that black cumin oil is involved in improving memory, attention, cognition, and can prevent or slow the progression of Alzheimer's disease. The hydroalcoholic extract of black cumin, due to its antioxidant power of brain cells, plays a role in improving learning and memory during neonatal and juvenile periods in rats. Demonstrated that thymoquinone has a neuroprotective potential for dopaminergic cells against 1-methyl-4-phenylpyridinium and rotenone induced toxicity. Preclinical research aimed to study the protective and therapeutic effects of black cumin, administered two weeks before the induction of Experimental Allergic Encephalomyelitis, to prevent Alzheimer's disease through its antioxidant action. Nigella, on the other hand, has protective potential against neuronal aggression following cadmium exposure [12].

The effects of Nigella Sativa on neuronal toxicity induced by 6-hydroxydopamine has been reported, Pretreatment with 5 or 10 mg/kg of Nigella Orally for three times significantly prevented loss of neurons. It was also reported that the daily administration of Nigella for 12 weeks, protected against chronic toluene-induced neuro degeneration in the rat hippocampus.

A study showed that Thymoquinone stimulated resistance to oxidative stress by decreasing the elevated levels of Malondialdehyde, Superoxide Dismutase and Catalase. The findings of these studies recommend that Nigella can prevent neurotoxicity [13].

Conclusion

Many studies have been conducted to evaluate the pharmacological effects of Nigella, while neuropsychopharmacological studies have remained limited. In this review, we reported the different studies evaluating the central activity of Nigella. More studies should be performed to determine the pharmacokinetics, pharmacodynamics and the mechanisms involved in those effects, and their interactions with the central nervous system.

References

1. Ali BH, Blunden G. Pharmacological and toxicological properties of Nigella sativa. Phytother Res. 2003;17:299–305.
2. Khare M. Indian herbal remedies: rational western therapy, ayurvedic, and other traditional usage, botany. Springer. 2004;35:400-02.
3. Cheikh-Rouhou S, Besbes S, Hentati B, et al. Chemical composition and physicochemical characteristics of the lipid fraction. Food Chem.. 2007;101:673-81.

4. Merfort I, Wray V, Barakat H, et al. Flavonoltriglycosides from seeds of Nigella sativa. Phytochemistry. 1997;46:359-63.
5. Ramadan MF, Mörsel JT. Characterization of phospholipid composition of black cumin (Nigella sativa L.) seed oil. Nahrung. 2002;46: 240-44.
6. Cheikh-Rouhou S, Besbes S, Lognay G, et al. Sterol composition of black cumin (Nigella sativa L.) and Aleppo pine (Pinus halepensis Mill.) seed oil. J Food Comp Analys. 2008;21:162–68.
7. Khanna T, Zaidi FA, Dandiya PC, et al. CNS and analgesic studies on Nigella sativa. Fitoterapia. 1993 ;64:407-10.
8. Kanter M, Coskun O, Uysal H, et al. The antioxidative and antihistaminic effect of Nigella sativa and its major constituent, thymoquinone, on ethanol-induced gastric mucosal damage. Arch Toxicol. 2008;80: 217-24.
9. Al-naggar T, Gomez M, Carretero M, et al. Neuropharmacological activity of Nigella sativa L. extracts. J Ethnopharmacol. 2003;88:63-8.
10. Hosseinzadeh H, Parvardeh S. Anticonvulsant effects of thymoquinone, the major constituent of Nigella sativa seeds, in mice. Phytomedicine. 2004;11:56–64.
11. Shawki M, Shatla R, El-Saeed G, et al. The clinical outcome of adjuvant therapy with black seed oil on intractable paediatric seizures: a pilot study. Epileptic Disord. 2013;15:295–301.
12. Randhawa MA, Al-Ghamdi MS. A review of pharmaco-therapeutic effects of Nigella sativa. Pak J Med Res. 2002;41:77–83.
13. Huong DT, Choi HC, Rho TC, et al. Inhibitory activity of monoamine oxidase by coumarins from peucedanum japonicum. Arch Pharm Res. 1999;22:324–26.

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