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Antidepressant Activity of *Nigella Sativa* Plant Extract Using a Suitable Animal Model

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Abstract

The present study was designed to evaluate the antidepressant and antioxidant potential of *Nigella sativa* extract in reserpine-induced depressive rodent models. Behavioural assessments, including the Forced Swim Test (FST), were conducted to assess depressive-like behaviour, locomotor activity, and exploratory behaviour. Biochemical parameters, including liver enzymes (ALT, AST, ALP), lipid profile (cholesterol, triglycerides, HDL, LDL), glucose levels, and oxidative stress markers (MDA, SOD, catalase, GSH), were analysed to evaluate metabolic, hepatic, and antioxidant effects. Reserpine administration induced significant depressive-like behaviour, hepatic stress, dyslipidemia, hyperglycemia, and oxidative stress. Treatment with *Nigella sativa* extract significantly reduced immobility time in the FST, normalized liver enzyme and lipid/glucose levels, and restored antioxidant status in a dose-dependent manner, with the 200 mg/kg dose showing the most pronounced effects. These findings suggest that *Nigella sativa* extract possesses antidepressant, hepatoprotective, and antioxidant properties, highlighting its potential as a natural therapeutic agent for managing depression.

Keywords

Nigella sativa; Antidepressant activity; Liver enzymes; Lipid profile; Reserpine-induced depression.

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1. INTRODUCTION

1.1 Depression

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) classifies depressive disorders into disruptive mood dysregulation disorder, major depressive disorder, persistent depressive disorder (dysthymia), premenstrual dysphoric disorder, and depressive disorder due to another medical condition. The common features of all depressive disorders are sadness, emptiness, or irritable mood, accompanied by somatic and cognitive changes that significantly affect an individual's capacity to function. Because of false perceptions and social stigma, nearly 60% of people with depression do not seek medical help, even though most antidepressants are effective, with individual response varying.

Types of Depression: Major depression involves a depressed mood or loss of interest for most of the

day, nearly every day, for at least two weeks, interfering with daily activities. Persistent depressive disorder (dysthymia) consists of less severe symptoms that last much longer, usually at least two years. Other forms include seasonal affective disorder (which follows a seasonal pattern), depression with psychotic symptoms (delusions or hallucinations), and bipolar disorder, which involves depressive episodes alternating with manic or hypomanic episodes.

1.2 Etiology and Epidemiology

The etiology of major depressive disorder is multifactorial, involving both genetic and environmental factors. First-degree relatives of depressed individuals are about three times as likely to develop depression as the general population. Neurodegenerative diseases, stroke, chronic pain, and traumatic life events such as bereavement, financial problems, or interpersonal conflict are known triggers. The twelve-month prevalence of major depressive disorder is approximately 7%, with young adults (18-29 years) affected roughly threefold more than those over 60, and females experiencing 1.5- to 3-fold higher rates than males from early adolescence onward.

1.3 Symptoms

Common signs and symptoms of depression include persistent sad, anxious, or empty mood; feelings of hopelessness, guilt, or worthlessness; loss of interest in previously enjoyed activities; fatigue and low energy; difficulty concentrating or making decisions; changes in sleep and appetite; and, in severe cases, thoughts of death or suicide. Diagnosis under DSM-5 requires at least five of nine characteristic symptoms - including depressed mood, anhedonia, sleep disturbance, guilt, fatigue, poor concentration, appetite change, psychomotor disturbance, and suicidal ideation - to be present for a meaningful diagnosis.

Fig. 1: Symptoms of Depression

1.4 Treatment / Management

Medication alone, brief psychotherapy (cognitive-behavioural therapy or interpersonal therapy) alone, and combination therapy have all been shown to relieve depressive symptoms, with combination approaches associated with higher rates of improvement and better treatment compliance. Electroconvulsive therapy (ECT) is reserved for patients who respond poorly to medication or who are acutely suicidal.

Pharmacological classes commonly used include selective serotonin reuptake inhibitors (SSRIs such as fluoxetine, sertraline, and escitalopram), serotonin/norepinephrine reuptake inhibitors (SNRIs such as venlafaxine and duloxetine), atypical antidepressants (bupropion, mirtazapine), serotonin-dopamine activity modulators (SDAMs), tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs). Psychotherapeutic approaches such as cognitive-behavioural therapy (CBT), mindfulness-based cognitive therapy (MBCT), and interpersonal therapy (IPT) are also evidence-based options, particularly valuable for relapse prevention.

2. Plant Profile: Nigella sativa

Nigella sativa is an annual flowering plant of the family Ranunculaceae, native to western Asia and eastern Europe, and naturalized across parts of Europe, northern Africa, and as far east as Myanmar. It is widely used as a spice in food preparation and,

traditionally, as a medicinal herb. Common names include black cumin, fennel flower, nutmeg flower, black seed, black caraway, kalonji, and kalojeera.

Fig. 2: Nigella sativa plant (left) and fruit capsules (right)

Table 1: Taxonomical classification

Rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales
Family	Ranunculaceae
Genus	Nigella
Species	N. sativa

Morphology: *N. sativa* grows to 20-95 cm in height, with finely divided, linear leaves. The delicate flowers are white, pale blue, yellow, pink, or purple, with four to ten petals. The fruit is a large, inflated capsule composed of three to eight united follicles, each containing numerous small, black, angular seeds with a slightly aromatic odour and bitter taste.

Chemistry:

Oils constitute 32-40% of the total composition of *N. sativa* seeds, containing linoleic acid, oleic acid, palmitic acid, and trans-anethole, along with minor alkaloids such as nigellicine, nigellidine, and nigellimine. Aromatic constituents include thymoquinone - the principal bioactive compound responsible for the plant's antioxidant, anti-inflammatory, anti-hypertensive, hepatoprotective, hypoglycemic, and lipid-lowering properties - along with di-hydro thymo quinone, p-cymene, carvacrol, thymol, and other terpenes.

History and traditional use:

Archaeological evidence traces cultivation of *N. sativa* back three millennia, with seeds recovered from ancient Egyptian sites, including the Tomb of Tutankhamun. The Persian physician Avicenna described its use for dyspnea in *The Canon of Medicine*, and the plant has long been employed as a traditional medicine and culinary spice across the Middle East, the Indian subcontinent, and parts of Europe. The U.S. FDA classifies *N. sativa* as Generally Recognized as Safe (GRAS) for use as a spice and flavouring.

3. MATERIALS AND METHODS

3.1 Collection, Identification and Extraction of Plant Material

Dried *Nigella sativa* seeds were procured from an herbal market in Hyderabad, Telangana, India, and authenticated by the Department of Pharmacognosy, Nalanda College of Pharmacy, Nalgonda. The seeds were washed, air-dried, homogenized to a fine powder, and stored in airtight containers. One gram of powdered seed was macerated with 20 mL of solvent (hexane and methanol, in separate conical flasks) at room temperature for 4 hours. The extract was then centrifuged at 4000 rpm at 4 degrees C for 10 minutes and filtered to obtain the working extract, which was used for phytochemical screening and subsequent pharmacological evaluation.

Fig. 3: Nigella sativa powder, maceration setup, and the resulting plant extract (left to right)

3.2 Acute Oral Toxicity Study

An acute oral toxicity study was conducted following OECD Guideline 423 (Acute Toxic Class Method) to evaluate the safety of the *Nigella sativa* extract. Healthy, overnight-fasted adult female Swiss albino mice were dosed orally, starting at 300 mg/kg body weight, with stepwise dose escalation up to 2000 mg/kg in additional groups where no mortality or severe toxicity was observed. Animals were monitored closely for 4 hours post-administration and then daily for 14 days for behavioural changes, tremors, convulsions, salivation, lethargy, weight loss, or mortality. No significant toxic signs or deaths were observed at any dose tested, and the LD50 was considered greater than 2000 mg/kg, indicating a wide margin of safety for further pharmacological evaluation.

3.3 Reserpine-Induced Depression Model

Depression was induced by administering reserpine intraperitoneally at 0.5 mg/kg once daily for three consecutive days, a well-established model that produces depressive-like behaviour, hepatic stress, dyslipidemia, hyperglycemia, and oxidative stress through monoamine depletion. Treatment with the plant extract or the standard drug began immediately after the first reserpine dose and continued daily for 14 days, after which behavioural assessments were performed to evaluate antidepressant activity.

3.4 Experimental Design and Grouping

Group	Treatment	Dose
Group I	Normal saline (control)	10 mL
Group II	Reserpine + Nigella sativa extract	100 mg/kg, oral
Group III	Reserpine + Nigella sativa extract	200 mg/kg, oral
Group IV	Reserpine + Standard drug (Imipramine)	10 mg/kg, oral

Healthy male mice weighing 25-30 g were acclimatized under standard laboratory conditions for one week before the study and randomly divided into four groups of six animals each (n = 6). All experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC) and conducted in accordance with CPCSEA guidelines. Data obtained were statistically analysed using one-way ANOVA followed by Dunnett's / Tukey's post-hoc test, with significance set at $p < 0.05$.

Fig. 4: Albino mice used in the study

4. Parameters

4.1 Forced Swim Test (FST)

The Forced Swim Test is a widely used behavioural assay to assess depressive-like states and the antidepressant potential of test substances in rodents. Each animal was placed in a cylindrical container filled with water at 23-25 degrees C, deep enough to prevent escape or the animal touching the bottom. The test lasted 6 minutes in total: the first 2 minutes allowed the animal to acclimate, while the

final 4 minutes were used for scoring. The time the animal spent immobile - floating without making escape-directed movements - was recorded, as immobility reflects behavioural despair. Antidepressant treatments are considered effective when they significantly reduce immobility time by promoting active behaviours such as swimming or climbing. After testing, animals were dried and kept warm to prevent hypothermia.

Fig. 5: Forced Swim Test set-up

5. RESULTS AND DISCUSSION

5.1 Qualitative Phytochemical Analysis

Preliminary phytochemical screening of the ethanolic extract of *Nigella sativa* revealed the presence of glycosides, tannins and phenolics, saponins, flavonoids, carbohydrates, proteins and amino acids, and terpenoids, while alkaloids gave mixed results across tests (positive by Hager's test, negative by Dragendorff's and Mayer's tests) and gums/mucilage were absent. These findings indicate a phytochemically rich extract with several classes of compounds known to contribute to antioxidant and neuroprotective activity.

Table 2: Qualitative phytochemical analysis of Nigella sativa (ethanolic extract)

Phytochemical	Test	Result
Alkaloids	Dragendorff's test	-
	Hager's test	+
	Mayer's test	-
Glycosides	General test	+
Tannins & Phenolics	Ferric chloride test	+
Saponins	Foam test	+
Flavonoids	Shinoda test	+
Carbohydrates	Fehling's test	+
	Molisch test	+
Proteins & Amino acids	Million's test	+
	Biuret test	+
	Salkowski test	+
Gum & Mucilage	Ruthenium red test	-
Terpenoids	Liebermann-Burchard test	+

5.2 Forced Swim Test Results

Reserpine administration significantly increased immobility time in the control group, confirming induction of depressive-like behaviour. Treatment with *Nigella sativa* extract reduced immobility time in a dose-dependent manner, and the standard drug imipramine produced the greatest reduction.

Table 3: Effect of Nigella sativa extract on antidepressant activity in mice (Forced Swim Test; Mean ± SEM, n = 6)

Group	Treatment	Dose	FST Immobility Time (sec)	% Decrease vs Control
Group 1	Normal saline	10 mL	175.2 ± 4.8	2%
Group 2	Nigella sativa extract	100 mg/kg	150.6 ± 5.1	15.1%
Group 3	Nigella sativa extract	200 mg/kg	129.4 ± 4.3	27.1%
Group 4	Standard (Imipramine)	10 mg/kg	112.2 ± 3.9	36.6%

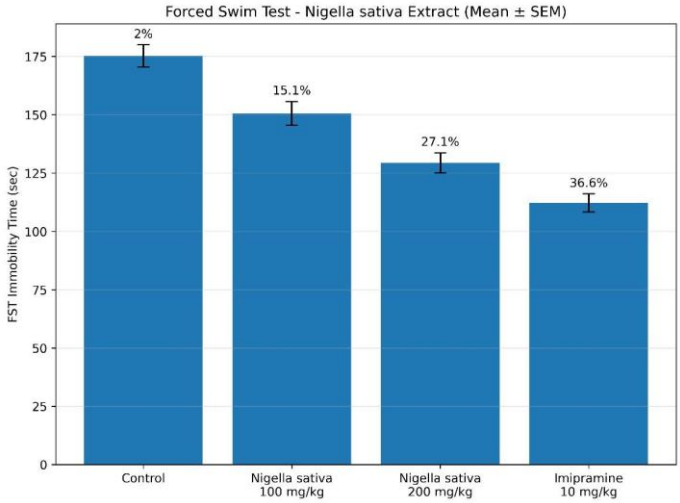

Fig. 6: Forced Swim Test - immobility time across treatment groups (Mean ± SEM)

5.3 DISCUSSION

The present study evaluated the antidepressant potential of *Nigella sativa* extract using behavioural, biochemical, and oxidative stress parameters in reserpine-induced depressive rodent models. The FST demonstrated that reserpine effectively induced depressive-like behaviour, evidenced by increased immobility time. Treatment with *Nigella sativa* extract significantly reduced immobility time and improved exploratory behaviour in a dose-dependent manner, with the 200 mg/kg dose showing more pronounced effects, although the standard drug (imipramine) exhibited slightly superior efficacy.

Biochemical parameters supported these behavioural findings. Reserpine administration elevated serum ALT, AST, and ALP (indicating hepatic stress), along with dyslipidemia (increased cholesterol, triglycerides, and LDL, and decreased HDL) and hyperglycemia, reflecting metabolic disturbances associated with depression and stress. *Nigella sativa* extract improved liver enzyme levels, normalized lipid profiles, and restored glucose levels toward normal, particularly at the higher dose, suggesting hepatoprotective and metabolic regulatory effects.

Oxidative stress markers further corroborated the antidepressant-like activity. Reserpine induced significant oxidative stress, shown by increased malondialdehyde (MDA) and decreased superoxide dismutase (SOD), catalase, and glutathione (GSH). Treatment with *Nigella sativa* extract attenuated lipid peroxidation and enhanced enzymatic and non-enzymatic antioxidant defences in a dose-dependent manner, indicating that its neuroprotective and antidepressant effects may be mediated, at least in part, through antioxidant mechanisms.

6. CONCLUSION

This study demonstrates that *Nigella sativa* extract possesses significant antidepressant-like activity in reserpine-induced depressive rodent models. Behavioural assessment using the Forced Swim Test revealed that the extract reduces immobility time and improves locomotor and exploratory activity in a dose-dependent manner, with the 200 mg/kg dose showing the most pronounced effects. Biochemical analyses showed that the extract ameliorates reserpine-induced hepatic stress, dyslipidemia, and hyperglycemia, indicating hepatoprotective and metabolic regulatory effects. Furthermore, oxidative stress markers revealed that the extract reduces lipid peroxidation and enhances antioxidant defences by increasing SOD, catalase, and GSH levels, suggesting a strong neuroprotective mechanism. Compared with the standard drug imipramine, the 200 mg/kg dose of the plant extract showed a favourable antidepressant response, supporting its potential as a natural therapeutic agent for managing depression. Further studies evaluating other phytochemical constituents and additional pharmacological activities are warranted.

REFERENCES

1. Chand SP, Arif H. Depression. StatPearls / National Library of Medicine, National Center for Biotechnology Information; July 17, 2023.
2. National Institutes of Health. Depression: Pathophysiology, Evaluation and Symptoms. NIH Publication No. 24-MH-8079, revised 2024, pp. 81-84.
3. Sharma D, Kosankar KV, Lanjewar AM. Nigella sativa plant profile. World Journal of Pharmaceutical Research. 2018;7(2):532-540.
4. Huchchannanavar S, Yogesh LN, Prashant S. Taxonomic classification of Nigella sativa.

International Journal of Chemical Studies. 2019;7(3):13-21.
5. Nasiri N, Ilaghi Nezhad M, Sharififar F, et al. Therapeutic effects of Nigella sativa on skin disease. Evidence-Based Complementary and Alternative Medicine. 2022; 2022:7993579.
6. Adam SH, Abu IF, Febriza A, et al. Potential health benefits of Nigella sativa on obesity and its associated complications. Plants (Basel). 2023;12(18):3210.
7. Derosa G, D'Angelo A, et al. The use of Nigella sativa in cardiometabolic diseases. Biomedicines. 2024;12(2):405.
8. Zielinska M, Deren K, Stepien AE, et al. The role of bioactive compounds of Nigella sativa in rheumatoid arthritis. Nutrients. 2021;13(10):3369.
9. Mohamed N, Mohamadi N, et al. Pharmacotherapeutic potentials of black seeds (Nigella sativa) in the management of monkeypox infection. Current Traditional Medicine. 2024;10(2):109.
10. Lobo DAR, Salish S, Shabaraya AR. An investigation on antidepressant activity of fresh fruit of Malus domestica in experimental animal models. International Journal of Pharmacy and Pharmaceutical Sciences. 2019;4(1):19-23.
11. Golla P, Tirupathi H. To evaluate and compare antidepressant activity of Centella asiatica in mice by using forced swimming test. IJBCP. 2016;5(5):2017-2020.
12. Chowdhury B, Bhattamisra SK, Das MC. Involvement of monoaminergic system in antidepressant like activity of Glycyrrhiza glabra root extract in rat. Pharmacology Online. 2011; 2:405-415.
13. Pemminati S, Gopalakrishna HN, Shenoy KA, et al. Antidepressant activity of aqueous extract of fruits of Emblica officinalis in mice. IJABPT. 2010;1(2):449-454.
14. Es-safi I, Mechchate H, Amaghnouje A, et al. Assessment of anti-depressant like, anxiolytic effects and impact on memory of Pimpinella anisum L. total extract on Swiss albino mice. 2021;10(8):1573.
15. Malviya MB, Patel MN, Tyagi C, Budholiya P. Phytochemical screening and antidepressant activity of leaves extract. Journal of Biomedical and Pharmaceutical Research. 2021;10(2):01-08.
16. Petit-Demouliere B, Chenu F, Bourin M. Forced swimming test in mice: a review of antidepressant activity. Psychopharmacology. 2005.
17. Bonda C, Pawar S, Lokhande J. Evaluation of antidepressant activity of tramadol in comparison with imipramine in Swiss albino mice. International Journal of Basic & Clinical Pharmacology. 2017;6(3):695-699.
18. Zaoui A, Cherrah Y, Mahassini N, Alaoui K, Amarouch H, Hassar M. Oral acute toxicity of Nigella sativa. Phytomedicine. 2002; 9:69-74.
19. Cryan JF, Mombereau C, Vassout A. The tail suspension test as a model for assessing antidepressant activity: review of pharmacological and genetic studies in mice. Neuroscience & Behavioral Reviews. 2005;29(4-5):571-625.