RESEARCH ARTICLE

Oral *Nigella sativa* Oil Modulates Interleukin-1β and Interleukin-10, Improves Neurological Function, and Reduces Neuronal Necrosis after Traumatic Brain Injury in Rats

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Abstract

BACKGROUND: Current management of traumatic brain injury (TBI) is primarily directed toward preventing secondary brain injury, while specific pharmacological therapies targeting post-traumatic neuroinflammation remain limited. Bioactive constituents of *Nigella sativa*, particularly thymoquinone, have demonstrated anti-inflammatory and antioxidant properties that may modulate mechanisms involved in secondary brain injury. This study was conducted to evaluate the effects of oral *N. sativa* oil on serum interleukin (IL)-1β and IL-10 levels as inflammatory parameters, neurological function and necrosis in a rat model of TBI.

METHODS: Sixteen male Wistar rats underwent Marmarou weight-drop TBI and were randomly assigned into two groups given either oral *N. sativa* oil or distilled water (n=8/group) for 7 days. Serum IL-1β and IL-10 concentrations were measured using rat-specific enzyme-linked immunosorbent assays (ELISA), and neurological function was assessed using the modified Neurological Severity Score (mNSS) at post-injury baseline and on treatment day-1, -3, and -7. After day-7, brain tissue was examined using hematoxylin–eosin (H&E) staining, and necrotic-cell count was assessed.

RESULTS: IL-1β concentrations were significantly lower in the *N. sativa* group from day-1 onward, whereas IL-10 concentrations were significantly higher and mNSS scores were significantly lower from day-3 onward. By day-3, all three outcomes differed significantly: lower IL-1β (56.38±10.21 *vs.* 111.98±47.64 pg/mL; p=0.013), higher IL-10 (102.38±33.42 *vs.* 40.20±6.02 pg/mL; p=0.001), and lower mNSS (median: 4 (3-5) *vs.* 5 (5-6); p=0.003) than placebo group. These differences persisted through day-7, which also supported by lower necrotic-cell counts in the *N. sativa* group (3164.13±771.38 *vs.* 4028.38±204.58; p=0.008).

CONCLUSION: Administration of oral *N. sativa* oil shifted the circulating cytokine profile toward an anti-inflammatory pattern and was accompanied by better neurological function and fewer neuronal necrosis after TBI. These findings suggest that *N. sativa* oil may have beneficial effect on neuroinflammation after TBI.

KEYWORDS: *Nigella sativa*, traumatic brain injury, interleukin-1 beta, interleukin-10, neuroinflammation, modified Neurological Severity Score

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Introduction

Traumatic brain injury (TBI) initiates an immediate mechanical insult followed by secondary injury processes that can evolve over hours to days. Blood-brain barrier disruption, excitotoxicity, mitochondrial dysfunction, oxidative stress, and neuroinflammation contribute to delayed neuronal loss and functional impairment.(1–4) Unlike the primary injury, these secondary mechanisms offer a potential therapeutic window.

Interleukin (IL)-1β and IL-10 are established inflammatory mediators commonly used to characterize opposing components of the inflammatory response. (5) IL-1β is a key proinflammatory cytokine produced by activated microglia and other immune cells and contributes to inflammatory amplification and secondary neuronal injury after TBI.(6,7) In contrast, IL-10 is an anti-inflammatory and immunoregulatory cytokine that suppresses proinflammatory cytokine production and contributes to the resolution of inflammation and tissue repair.(7–10) Although neither cytokine is specific to TBI, they were selected as mechanistically complementary markers rather than disease-specific biomarkers. Their opposing biological functions provide a useful framework for simultaneously evaluating proinflammatory activation and counter-regulatory responses during secondary brain injury. Assessing both cytokines may therefore provide greater mechanistic insight into treatment-associated immunomodulation than evaluating either mediator alone.

Current management of TBI is primarily directed toward preventing and treating secondary physiological insults through supportive care, intracranial pressure management, optimization of cerebral perfusion, and surgical intervention when indicated. However, pharmacological therapies that specifically and reliably attenuate the complex neuroinflammatory component of secondary brain injury remain limited. This challenge may partly reflect the multifactorial nature of secondary injury, in which inflammation interacts with oxidative stress, mitochondrial dysfunction, excitotoxicity, and cell-death pathways.(1–4) Consequently, there remains a need to investigate adjunctive agents capable of modulating multiple components of the secondary injury cascade. Natural compounds with combined anti-inflammatory, antioxidant, and neuroprotective properties have therefore attracted interest as potential experimental therapeutic candidates, including *Nigella sativa* (black seed).

N. sativa contains several bioactive constituents, particularly thymoquinone, with anti-inflammatory, antioxidant, and neuroprotective properties.(11–13) These multimodal effects may have relevancy to TBI since secondary brain injury is also involving inflammatory and oxidative pathways. Experimental studies have previously demonstrated neuroprotective effects of thymoquinone after TBI, including preservation of neuronal tissue and reductions in edema, ischemic changes, and cellular injury. In addition, *N. sativa* seed extract has shown favorable histopathological effects in experimental TBI. (11) Mechanistically, *N. sativa* and thymoquinone have been reported to modulate nuclear factor-kappa B (NF-κB) and inflammasome-related signaling and to influence nuclear factor erythroid 2-related factor 2 (Nrf2)-mediated antioxidant responses.(12,13) However, to date, the effects of oral *N. sativa* oil on the temporal balance between proinflammatory and anti-inflammatory cytokines, along with neurological function and necrosis after TBI, remain insufficiently reported. Therefore, this study was conducted to evaluate whether 7 days oral N. sativa oil treatment could improve these parameters in male Wistar rats subjected to weight-drop TBI.

Methods

Experimental Animals and Husbandry

Sixteen healthy male albino Wistar rats (*Rattus norvegicus*), aged 3–4 months and weighing 150–200 g, were obtained from the Animal Laboratory, Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia. Animals were acclimatized for 14 days and housed five per cage (40×20×20 cm) with wood-shaving bedding under controlled environmental conditions (temperature 28±2°C and a 12-hour light/dark cycle). Standard AD2 laboratory pellets and water were provided *ad libitum* throughout the study. Animals were maintained under conventional laboratory conditions, with no specific environmental enrichment provided. No animals died or were excluded because of illness or unexpected adverse events during the acclimatization or experimental period.

Animal Grouping and TBI Induction

After the 14-day acclimatization period, rats were randomly allocated in a 1:1 ratio to the *N. sativa* treatment group or placebo group (n=8 per group) using simple random allocation. A resource-equation approach had indicated an acceptable range of 7-11 animals per group.

The TBI was induced using the Marmarou weight-drop model. After intraperitoneal anesthesia with a 0.2 mL/50 g body weight (BW) ketamine-based anesthetic mixture, the physiological parameters, including oxygen saturation, heart rate, and respiratory rate, were monitored. The rats' scalp was shaved, disinfected with 10% povidone-iodine, infiltrated with 2% lidocaine, and opened through a midline incision under aseptic conditions. A metal disc was positioned on the skull between the bregma and lambda, and a 30-g weight was dropped from a height of 80 cm through a transparent tube with a 12-mm internal diameter onto the metal disc. The scalp was subsequently closed with interrupted 5-0 nylon sutures, and body temperature was maintained at approximately 37°C throughout the procedure.(14)

Intervention and Experimental Timeline

One hour after TBI induction, a tail-vein blood sample was collected, and neurological function was assessed using the mNSS. These measurements were designated as day-0 (post-injury, pretreatment baseline). The treatment group subsequently received 200 mg/kg BW/day Habbasyifa® Black Seed Oil (100% *N. sativa* oil; CV. Syifa Natural, Bogor, Indonesia by oral gavage for 7 consecutive days. The oil was diluted in distilled water to a final volume of 1 mL to facilitate oral administration. Meanwhile, the placebo group received 1 mL of distilled water by the same route and according to the same schedule. Serum cytokine measurements and mNSS assessments were measured repeatedly on treatment day-1, -3, and -7. After completion of the day-7 assessments and intervention period, the animals underwent terminal tissue collection for histopathological evaluation. The details of the experimental design, timeline and animal random grouping of the study were represented in Figure 1. All the intervention and report were prepared with reference to the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE) 2.0 recommendations, and according to the ethically approved study protocol.

ELISA Analysis for IL-1β and IL-10

Tail-vein blood (approximately 1 mL per sampling) was collected at day-0 and on treatment day-1, -3, and -7. Serum IL-1β and IL-10 concentrations were quantified using rat-specific enzyme-linked immunosorbent assays (ELISA) kits according to the manufacturer's instructions. Serum IL-1β concentrations were measured using Rat IL-1β (Interleukin 1 Beta) ELISA Kit (Cat. No. ELK1272, Lot No. 56310370; ELK Biotechnology, Wuhan, China) with detection range of 15.63–1,000 pg/mL and sensitivity of 5.9 pg/mL, while and serum IL-10 was measured using Rat IL-10 (Interleukin 10) ELISA Kit (Cat. No. ELK1144, Lot No. 56310170; ELK Biotechnology, Wuhan, China) with detection range of 7.82–

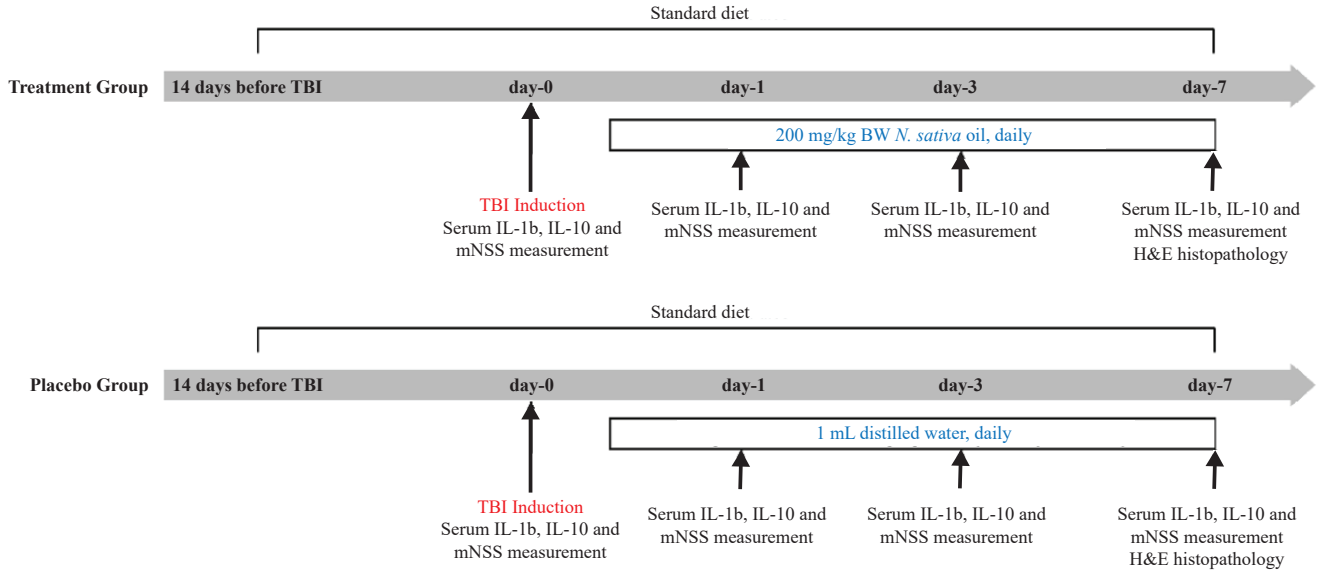

Figure 1. Schematic diagram of the study design and experimental timeline. Following 14 days of acclimatization period, sixteen male Wistar rats were randomly allocated into two groups to either the placebo group or the *N. sativa* treatment group (n=8 per group). TBI was induced on day-0 using the Marmarou weight-drop model. Baseline blood samples were collected after TBI induction before treatment initiation (day-0). Animals then received either oral *N. sativa* oil (200 mg/kg BW/day) or distilled water (1 mL/day) by gavage for seven consecutive days. Serum IL-1β, serum IL-10, and mNSS were evaluated on day-0, -1, -3, and -7. Within 24 hours after the final intervention, animals were euthanized, and brain tissues were collected for hematoxylin-eosin (H&E) histopathological examination and necrotic cell quantification.

500 pg/mL and sensitivity of 3.3 pg/mL. Both assays were based on a sandwich enzyme-linked immunosorbent assay (ELISA) principle, in which the target cytokine was captured by a specific immobilized capture antibody and subsequently detected using a second enzyme-linked detection antibody. Following substrate addition, the resulting colorimetric signal was measured spectrophotometrically, with the signal intensity proportional to the concentration of the target IL-1β and IL-10 in the serum samples. According to the manufacturer's quality-control specifications, the assays demonstrated an intra-assay coefficient of variation of <8% and a linear correlation coefficient of ≥0.990.

Neurological Function Assessment

Neurological function was evaluated using the modified Neurological Severity Score (mNSS) system, a composite assessment of motor function, sensory function, balance, and reflexes. The total score ranges from 0 to 18, with higher scores indicating greater neurological impairment. Scores of 1–6, 7–12, and 13–18 represent mild, moderate, and severe neurological deficits, respectively.

Histopathology Analysis of Neuronal Necrotic Cells

Within 24 hours after the final intervention, animals were euthanized under deep anesthesia induced by an intraperitoneal 0.2 mL/50 g BW ketamine-based anesthetic mixture, and brain tissues were collected. The cerebral cortex was processed for histopathological examination. Tissue sections (3–4 µm thick) were stained with Harris hematoxylin–eosin (H&E) and examined under a light microscope at 40× magnification. Five non-overlapping microscopic fields were randomly selected from each section for manual evaluation. Histological slides were labeled with coded identifiers before examination, and certified pathologist performing the assessment was blinded to treatment allocation. Necrotic-cell count was used as the quantitative histopathological outcome.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY, USA). Data normality was assessed using the Shapiro–Wilk test. Normally distributed continuous variables were presented as mean±standard deviation (SD), whereas non-normally distributed variables were presented as median (minimum–maximum). Between-group comparisons were performed using the independent-samples t-test or Mann–Whitney U test, as appropriate. Within-group paired comparisons were analyzed using the paired t-test or Wilcoxon signed-rank test. Longitudinal repeated measurements were analyzed using repeated-measures analysis of variance (ANOVA) for normally distributed data and the Friedman test for non-normally distributed data. Necrotic-cell counts were compared between groups using the independent-samples t-test. All statistical tests were two-sided, and $p<0.05$ was considered statistically significant.

Results

Baseline post-injury serum IL-1β, IL-10, and mNSS scores were similar between the treatment and placebo groups (all $p>0.05$) (Table 1, Table 2), indicating similar initial injury severity after TBI induction.

Lower Serum IL-1β in Treatment Group

The proinflammatory cytokine IL-1β concentrations increased during the first day after TBI in both groups, indicating that inflammation occurred after TBI, although the increase was less pronounced in rats treated with N. sativa. Thereafter, serum IL-1β levels progressively declined in the treatment group, whereas they remained elevated in the placebo group. From day-1 to day-3, IL-1β declined in both groups, indicating that the acute inflammatory peak had passed; nevertheless, concentrations significantly

Table 1. Serum IL-1β and IL-10 concentrations on day-0, -1, -3, and -7 after TBI.

Time	Mean±SD Serum IL-1β Concentrations				Mean±SD Serum IL-10 Concentrations			
	Treatment Group (pg/mL)	Placebo Group (pg/mL)	*p*-value[a]	∓(Δ)	Treatment Group (pg/mL)	Placebo Group (pg/mL)	*p*-value[a]	∓(Δ)
Day-0	58.29±7.69	57.27±5.72	0.766	1.03 pg/mL	35.56±4.68	37.79±6.68	0.453	2.23 pg/mL
Day-1	75.52±23.17	141.38±66.22	0.027*	65.87 pg/mL	38.64±3.74	39.75±4.59	0.605	1.11 pg/mL
Day-3	56.38±10.20	111.98±47.64	0.013*	55.60 pg/mL	102.38±33.42	40.20±6.01	0.001*	62.18 pg/mL
Day-7	43.34±6.48	102.95±42.50	0.005*	59.61 pg/mL	207.53±79.02	43.68±9.39	0.001*	163.86 pg/mL
p-value[b]	<0.001*	<0.001*			<0.001*	0.065		

∓Δ: Differences between treatment and placebo groups. [a]Comparison between treatment and placebo groups, tested with Independent-samples t-test. [b]Comparison within group, tested with Repeated-measures analysis of variance. *$p<0.05$ is considered significant.

Table 2. mNSS scores and necrotic brain cell count on day-0, -1, -3, and -7 after TBI.

Outcome and Time	Treatment Group (n=8)	Placebo Group (n=8)	*p*-value
mNSS, median (min-max)			
Day-0	6 (5-7)	5 (5-7)	0.505[a]
Day-1	5 (5-7)	5 (5-7)	0.721[a]
Day-3	4 (3-5)	5 (5-6)	0.003[a,*]
Day-7	3.5 (3-4)	6 (4-6)	<0.001[a,*]
p- value	<0.001[b]	0.629[b]	
Necrotic-cell count			
mean±SD	3164.13±771.38	4028.38±204.58	0.008[c,*]

[a]Comparison between treatment and placebo groups, tested with Mann-Whitney U test. [b]Comparison within group, tested with Friedman test. [c]Comparison between treatment and placebo groups, tested with Independent-samples t-test. *$p<0.05$ is considered significant.

lower in the treatment group on day-3 (56.38±10.21 *vs.* 111.98±47.64 pg/mL; $p=0.013$) and persisted through day-7 (43.34±6.49 *vs.* 102.94±42.50 pg/mL; $p=0.005$) (Table 1, Figure 2A).

Higher Serum IL-10 in Treatment Group

No significant differences of serum IL-10 levels between groups immediately after injury and on day-1. On day-3, the treatment group demonstrated a marked increase in IL-10 concentrations, while only minimal changes were observed in the placebo group (102.38±33.42 *vs.* 40.20±6.02 pg/mL; $p=0.001$). Consequently, significantly higher IL-10 levels were also found in the treatment group on day-7 compared to the placebo group (207.53±79.02 *vs.* 43.68±9.39 pg/mL; $p=0.001$) (Table 1, Figure 2B). This indicated that *N. sativa* oil was able to increase anti-inflammatory cytokine IL-10.

Improved Neurological Function in Treatment Group

Baseline and day-1 mNSS scores were similar between groups. From day-3 onward, rats receiving *N. sativa* exhibited significantly lower mNSS scores than placebo-treated rats (median: 4 (3-5) *vs.* 5 (5-6); $p=0.003$), indicating improved neurological fuction. This difference became persisted on day-7, when the treatment group showed the lowest neurological deficit scores of 3.5 (3–4) compared to the placebo groups that had the highest neurological deficit scores of 6 (4–6) ($p<0.001$) (Table 2).

Lower Neuronal Necrotic Cells in Treatment Group

Histopathological examination demonstrated significantly fewer necrotic cells count in the *N. sativa*-treated group than in the placebo group (3164.13±771.38 *vs.* 4028.38±204.58; $p=0.008$), indicating reduced neuronal tissue damage following treatment of N. sativa oil (Table 2). Representative histological findings were presented in Figure 3.

Discussion

The principal finding was that a coordinated treatment-associated effect was already evident by whether 3 days or 7 days of oral *N. sativa* oil after experimental TBI altered both

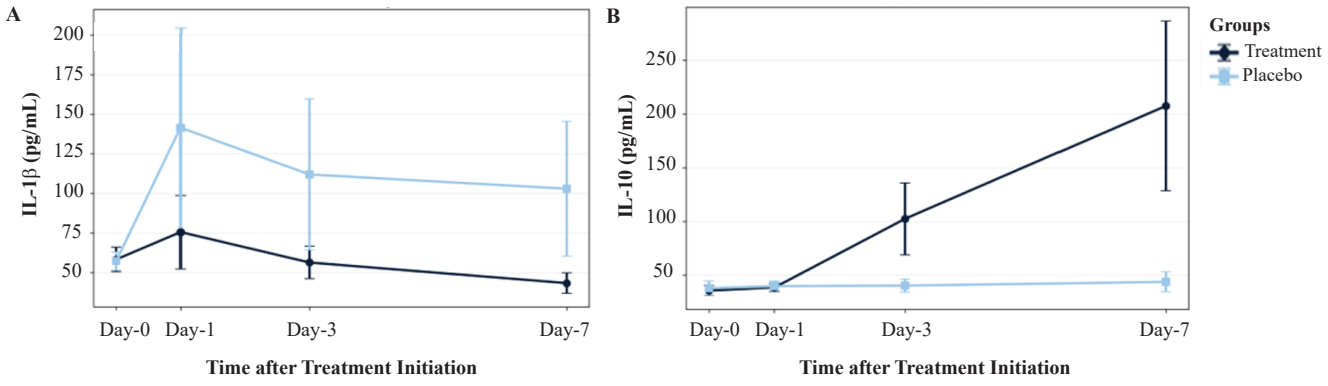

Figure 2. Serum inflammatory and anti-inflammatory cytokines of subjects on day-0, -1, -3, and -7 after TBI. Data are presented as mean±SD.

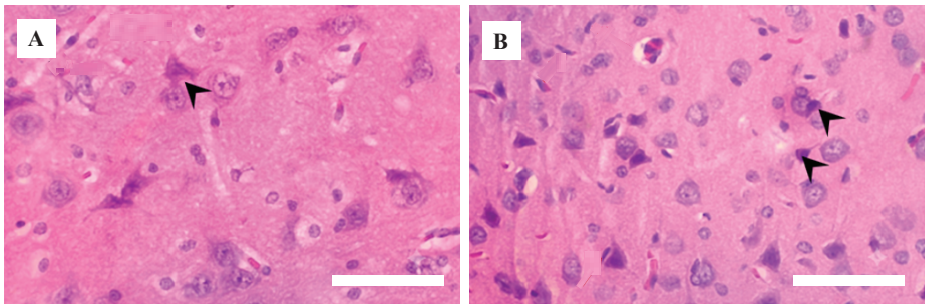

Figure 3. Representative H&E-stained brain sections obtained 7 days after TBI. A: Treatment group. B: Placebo group. Treatment group showing fewer neuronal necrosis cell-count compared to placebo group (black arrowhead: necrotic cell). White bar: 10 µm.

inflammatory and anti-inflammatory cytokine trajectories. Compared with placebo, treatment limited the post-injury rise in IL-1β, produced a marked increase in IL-10, improved mNSS, and reduced the number of necrotic cells from day-3 onward. These differences persisted through day-7, and the terminal convergence of biochemical, functional, and histopathological outcomes supports a biologically coherent treatment signal, although the small exploratory design requires cautious interpretation.

The secondary injury after TBI involves blood-brain barrier disruption, oxidative stress, excitotoxicity, and activation of microglia and infiltrating immune cells. (1–4,15) IL-1β is an early amplifier of this response and can promote leukocyte recruitment, microglial activation, and neuronal injury.(6) Experimental IL-1β antagonism or neutralization has improved neurological or cellular outcomes in TBI models, supporting this cytokine as a plausible treatment-associated marker.(16–18) In the present study, placebo-treated animals showed a large IL-1β rise on day-1 that remained above the baseline through 7 days of obeservation. *N. sativa* did not abolish the early response, but substantially attenuated it and produced a continuous decline by day-7.

IL-10 counter-regulates proinflammatory signaling and contributes to the resolution phase of post-traumatic inflammation.(8,9) The delayed separation between groups, which was shown by minimal level on day-1 but pronounced on day-3 and -7, suggests that *N. sativa* may first constrain acute inflammatory amplification and subsequently support immunoregulatory pathways. Studies in other inflammatory settings have reported increased IL-10 or broader immunomodulatory effects after N. sativa exposure.(19,20) The very large day-7 difference observed here should nevertheless be replicated using fully characterized assays and prespecified analytical procedures.

Thymoquinone and other constituents of *N. sativa* have been linked to suppression of NF-κB and inflammasome-related signaling and to activation of antioxidant pathways such as Nrf2.(10,11) These mechanisms could reduce IL-1β maturation while favoring an anti-inflammatory environment. However, thymoquinone content, NF-κB activity, NLR family pyrin domain containing 3 (NLRP3) activation, oxidative-stress markers, and microglial phenotypes were not measured in this experiment. The mechanistic explanation therefore remains a hypothesis rather than a directly demonstrated pathway.

The neurological function and necrosis cell count strengthen the inflammaroty and anti-inflammatory cytokine results. mNSS improved by day-3 and remained better on day-7 in treated animals, whereas placebo scores did not improve significantly over time. The lower necrotic-cell count is consistent with reduced secondary cellular injury. Because the mNSS encompasses motor, sensory, balance, and reflex domains, the observed change suggests functional relevance beyond a serum biomarker effect. Still, the study did not include an uninjured sham group, long-term behavioral testing, lesion-volume quantification, or region-specific neuronal markers, so the magnitude and durability of neuroprotection remain uncertain. Neuronal adaptation after injury, should also be assessed based on significant astrocyte adaptation.(21)

There are some restrictions of the generalizability and assessment for the longer-term effects of *N. sativa* oil effects since the sample size was small, only male rats were included, only a single dose of *N. sativa* was evaluated, and follow-up was limited to 7 day. The *N. sativa* oil preparation was also not chemically standardized for thymoquinone content, to confirm whether the beneficial effect of *N. sativa* oil was due to the thymoquinone content. The structural brain injury was also not histopathologically confirmed immediately after TBI induction and before treatment. Although post-injury, pretreatment mNSS deficits provided functional evidence of neurological impairment, the initial extent and consistency of structural brain injury were not independently verified. Future studies should incorporate an appropriate model-validation strategy with early

histopathological confirmation. Finally, circulating cytokine concentrations may not directly reflect the inflammatory environment within injured brain tissue. These findings might suggest that N. sativa oil might be beneficial for neuroinflammation therapy after TBI, but it warrant confirmatory studies with prospectively defined primary outcomes, concealed allocation, blinded neurological and histopathological assessments, sham and dose-response groups, inclusion of both sexes, standardized thymoquinone content, brain-tissue inflammatory markers, and longer neurological follow-up.

Conclusion

Oral *N. sativa* oil at 200 mg/kg BW/day was associated with reduced circulating IL-1β, increased IL-10, improved mNSS, and lowered neuronal necrotic-cell counts benefit by day-3, which persisted through day-7, compared with placebo after experimental TBI in male Wistar rats. These findings suggest that *N. sativa* oil may have beneficial effect on neuroinflammation after TBI.

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Authors Contribution

AHGH was involved in the conceptualization, investigation, data curation, and formal analysis. W, DW, JD, AA, and NM prepared the methodology and performed the validation. JD interpreted the data. W, DW, AAI, and NM supervised the study. W was involved in the project administration. AHGH prepared the visualization and wrote the original draft of the manuscript. W, DW, JH, AAI, and NM assissted in the manuscript review and editing. All authors have confirmed and gave final approval and accountability for the work before submission.

Ethical Statement

The study protocol was reviewed and approved by the Research Ethics Committee, Faculty of Medicine, Hasanuddin University-Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia (Approval No. 190/UN4.6.4.5.31/PP36/2026; Protocol No. UH26010134; approval date: 31 January 2026). All procedures were conducted in accordance with institutional regulations governing the ethical use and welfare of laboratory animals, and efforts were made to minimize animal suffering and reduce the number of animals used.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Khellaf A, DZ K, Helmy A. Recent advances in traumatic brain injury. J Neurol. 2019; 266(11): 2878-89.
2. Xiong Y, Mahmood A, Chopp M. Current understanding of neuroinflammation after traumatic brain injury and cell-based therapeutic opportunities. Chin J Traumatol. 2018; 21(3): 137-51.
3. Sulhan S, KA L, LA S, JH H. Neuroinflammation and blood-brain barrier disruption following traumatic brain injury: pathophysiology and potential therapeutic targets. J Neurosci Res. 2020; 98(1): 19-28.
4. Kalra S, Malik R, Singh G, Bhatia S, Al-Harrasi A, Mohan S, *et al.* Pathogenesis and management of traumatic brain injury (TBI): role of neuroinflammation and anti-inflammatory drugs. Inflammopharmacology. 2022; 30(4): 1153-66.
5. Febriza A, Ridwan, As'ad S, Kasim VN, Idrus HH. Adiponectin and its role in Inflammatory process of obesity. Mol Cell Biomed Sci. 2019; 3(2): 60-6.
6. Lindblad C, Rostami E, Helmy A. Interleukin-1 receptor antagonist as therapy for traumatic brain injury. Neurotherapeutics. 2023; 20(6): 1508-28.
7. Yunus Y, July J, Islam AA, Wahjoepramono EJ, Yusuf I. Dynamic pattern of interleukin-1beta and -10 in cerebrospinal fluid following aneurysmal subarachnoid hemorrhage. Indones Biomed J. 2014; 6(2): 97-100.
8. Niiranen TJU, Chiollaz AC, Takala RSK, Voutilainen M, Tenovuo O, Newcombe VFJ, *et al.* Trajectories of interleukin 10 and heart fatty acid-binding protein levels in traumatic brain injury patients with or without extracranial injuries. Front Neurol. 2023; 14: 1133764. doi: 10.3389/fneur.2023.1133764.
9. Denawati, Setiawan E, Priyantini S. Hypoxia-derived mesenchymal stem cell exosomes downregulate CXCL12 and upregulate IL-10 expression in a murine model of androgenic alopecia. Mol Cell Biomed Sci. 2026; 10(1): 32-41.
10. Bao W, Lin Y, Chen Z. The peripheral immune system and traumatic

brain injury: insight into the role of T-helper cells. Int J Med Sci. 2021; 18(16): 3644-51.
11. Kulsum K, Syahrul S, Hasballah K, Balqis U. Propofol and Nigella sativa L seeds ethanol extract enhance neuroprotection: A histopathological study in rat models with traumatic brain injury. Indones Biomed J. 2024; 16(5): 450-8.
12. Ciesielska-Figlon K, Wojciechowicz K, Wardowska A, KA L. The immunomodulatory effect of Nigella sativa. Antioxidants. 2023; 12(7): 1340. doi: 10.3390/antiox12071340.
13. Sadeghi E, Imenshahidi M, Hosseinzadeh H. Molecular mechanisms and signaling pathways of black cumin (Nigella sativa) and its active constituent, thymoquinone: A review. Mol Biol Rep. 2023; 50(6): 5439-54.
14. BZ M, CC G, FM K. The nanotheranostic researcher's guide for use of animal models of traumatic brain injury. J Nanotheranostics. 2021; 2(4): 224-68.
15. Hasan D, Alzuabe M, Ismail Y, Al Tibi A, Abdelnour A. TNF-α, VEGF, and procalcitonin levels dynamic changes during severe traumatic brain injury. Indones Biomed J. 2022; 14(2): 180-5.
16. AE H, ER Y, Turkoglu E, Kertmen H, Horasanli B, Hayirli N, *et al.* Therapeutic evaluation of interleukin 1-beta antagonist anakinra against traumatic brain injury in rats. Ulus Travma Acil Cerrahi Derg. 2015; 21(1): 1-8. doi: 10.5505/tjtes.2015.57894.
17. Ozen I, Ruscher K, Nilsson R, Flygt J, Clausen F, Marklund N. Interleukin-1 beta neutralization attenuates traumatic brain injury-induced microglia activation and neuronal changes in the globus pallidus. Int J Mol Sci. 2020; 387. doi: 10.3390/ijms21020387.
18. PJ B. Treatment of traumatic brain injury with anti-inflammatory drugs. Exp Neurol. 2016; 275 Pt 3(Pt 3): 367-80.
19. Gholamnezhad Z, MH B, Hosseini M. Effect of Nigella sativa on immune response in treadmill exercised rat. BMC Complement Altern Med. 2014; 14: 437. doi: 10.1186/1472-6882-14-437.
20. Hadi V, Kheirouri S, Alizadeh M, Khabbazi A, Hosseini H. Effects of Nigella sativa oil extract on inflammatory cytokine response and oxidative stress status in patients with rheumatoid arthritis: a randomized, double-blind, placebo-controlled clinical trial. Avicenna J Phytomed. 2016; 6(1): 34-43.
21. Gonzalez D, Afadlal S, Lizal K, Hermanto Y, Miki T, Takeuchi Y, *et al.* Enucleation induces parvalbumin and glial fibrillary acidic protein, but not calbindin D28k protein expression in superior colliculus of Wistar rats. Mol Cell Biomed Sci. 2018; 2(1): 28-37.