

BRIEF REPORT



Artemisinin: a promising neuroprotective agent enhancing neuronal cell viability in vitro

Maria Petrova

Department of Microbiology, University of Agricultural Sciences and Veterinary Medicine of Cluj-Napoca, Cluj-Napoca, Romania

ABSTRACT

Artemisinin, a natural compound derived from *Artemisia annua*, is renowned for its potent antimalarial properties. Recent studies have revealed its potential neuroprotective effects, suggesting it may enhance neuronal cell viability and promote recovery in various neurodegenerative conditions. This paper explores the neuroprotective properties of artemisinin in vitro, focusing on its ability to mitigate cellular stress, reduce apoptosis, and improve neuronal function. We examine the molecular mechanisms underlying its effects, including modulation of oxidative stress, inflammatory pathways, and mitochondrial health. Our findings suggest that artemisinin holds promise as a therapeutic agent for neurodegenerative diseases, offering a novel approach to enhancing neuronal survival and function. Further research is warranted to validate its efficacy and safety in preclinical models and clinical settings. Studies investigating its impact on neuronal cell viability have revealed promising results, suggesting that artemisinin may offer novel avenues for treating neurodegenerative diseases and other neurological disorders. This article delves into the mechanisms through which artemisinin stimulates neuronal cell viability and its potential as a neuroprotective agent.

KEYWORDS

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Novel therapeutic strategies; Artemisinin;
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Introduction

Neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS), are characterized by progressive neuronal loss, impaired cell signaling, and chronic inflammation. These conditions are associated with oxidative stress, mitochondrial dysfunction, and apoptosis, contributing to the decline in neuronal viability [1]. Current treatments primarily focus on symptom management, with limited success in halting disease progression. Therefore, there is a critical need for novel therapeutic strategies that can protect neurons, enhance their viability, and potentially slow or reverse disease progression [2].

Artemisinin, a sesquiterpene lactone compound derived from the *Artemisia annua* plant, has garnered attention for its diverse biological activities, most notably its antimalarial and anticancer properties. However, emerging evidence suggests that artemisinin also exerts significant neuroprotective effects. In vitro studies have demonstrated that artemisinin can mitigate oxidative stress, promote neuronal survival, and reduce inflammation, making it a compelling candidate for the treatment of neurodegenerative diseases [3]. This paper aims to review the current understanding of artemisinin's neuroprotective mechanisms, its effects on neuronal cell viability, and its potential as a therapeutic agent for neurodegenerative disorders. Through a deeper understanding of its molecular actions, artemisinin may emerge as a promising candidate for future neuroprotective therapies.

Artemisinin: beyond malaria treatment

Artemisinin is best known for its use in combating malaria, a life-threatening disease caused by the *Plasmodium* parasite. The

compound is derived from the sweet wormwood plant (*Artemisia annua*), and it is a potent anti-malarial agent. Artemisinin-based combination therapies (ACTs) have revolutionized the treatment of malaria, providing a highly effective method for tackling the disease [3].

However, emerging research has suggested that artemisinin possesses broader pharmacological properties beyond its anti-malarial activity. Recent studies have shown that artemisinin and its derivatives exhibit anti-inflammatory, anti-cancer, and anti-viral effects. Moreover, scientists have begun to investigate its potential to protect against neurological damage, a property that could be beneficial in treating neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's disease [4].

Neuroprotective effects of artemisinin

The neuroprotective properties of artemisinin have gained attention due to the compound's potential to counteract neuronal damage, oxidative stress, and inflammation—all of which are key factors in the progression of neurodegenerative diseases [5].

Cell viability in neuronal cultures

In vitro studies using neuronal cell cultures have demonstrated that artemisinin can stimulate neuronal cell viability. These studies often involve exposing cultured neurons to various stressors such as oxidative agents or inflammatory cytokines, which induce cell death and mimic conditions associated with neurodegeneration [6]. Researchers have found that artemisinin treatment significantly increases neuronal survival by preventing or reducing the extent of damage caused by these stressors.

*Correspondence: Dr. Maria Petrova, Department of Microbiology, University of Agricultural Sciences and Veterinary Medicine of Cluj-Napoca, Cluj-Napoca, Romania, 400372.
e-mail: p.maria@usamvcluj.ro

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The ability of artemisinin to enhance neuronal viability is believed to be related to its antioxidant properties. Oxidative stress is a common feature in many neurological diseases, leading to the accumulation of free radicals that damage cellular structures, including lipids, proteins, and DNA. Artemisinin has been shown to possess antioxidant activity, which helps neutralize free radicals and protect neurons from oxidative damage [7].

Inhibition of inflammatory pathways

Another key mechanism by which artemisinin exerts its neuroprotective effects is through its anti-inflammatory properties. Neuroinflammation plays a central role in the progression of many neurodegenerative diseases. Chronic inflammation in the brain can lead to the activation of microglia (the resident immune cells of the central nervous system) and the release of pro-inflammatory cytokines, which contribute to neuronal injury.

Research has indicated that artemisinin may suppress the activation of inflammatory pathways in the brain. Specifically, it appears to inhibit the production of pro-inflammatory cytokines such as TNF- α and IL-6, which are implicated in neuroinflammation. By modulating these pathways, artemisinin may help reduce neuroinflammatory responses, thus protecting neurons from inflammatory-induced damage [8].

Regulation of apoptosis

Apoptosis, or programmed cell death, is a process that is tightly regulated in healthy cells but can become dysregulated in disease states, leading to excessive neuronal loss. Artemisinin has been shown to modulate apoptotic pathways, preventing excessive neuronal death under stress conditions. Studies suggest that artemisinin may exert its effects by altering the expression of apoptotic regulators such as Bax, Bcl-2, and caspases, which are involved in the execution of cell death [9]. By preventing apoptosis, artemisinin contributes to the preservation of neuronal cells, promoting their survival and maintaining proper brain function. This property is particularly important in the context of neurodegenerative diseases, where preventing neuronal loss is a key therapeutic goal [10].

Molecular mechanisms involved

The precise molecular mechanisms underlying artemisinin's neuroprotective effects are still being explored, but several potential pathways have been identified. Some of these include:

Activation of the Nrf2 pathway

Nrf2 (Nuclear factor erythroid 2-related factor 2) is a transcription factor that regulates the expression of antioxidant enzymes. Artemisinin has been shown to activate the Nrf2 pathway, which enhances the cell's ability to combat oxidative stress and protect against neurodegeneration [11].

Modulation of the MAPK pathway

The mitogen-activated protein kinase (MAPK) pathway is involved in cell signalling related to stress responses, survival, and inflammation. Artemisinin may influence this pathway to reduce inflammation and promote cell survival [12].

Regulation of mitochondrial function

Mitochondria are critical for energy production and cellular

function, and mitochondrial dysfunction is a hallmark of many neurological disorders. Artemisinin has been shown to exert positive effects on mitochondrial function, potentially contributing to its neuroprotective role.

Artemisinin and neurodegenerative diseases

Given the promising findings from in vitro studies, there is growing interest in exploring the potential of artemisinin for the treatment of neurodegenerative diseases. Alzheimer's disease, Parkinson's disease, and other conditions are characterized by the progressive loss of neurons, often due to a combination of oxidative stress, inflammation, and impaired cell signaling [13].

Artemisinin's ability to enhance neuronal viability, reduce inflammation, and prevent apoptosis positions it as a potential therapeutic agent for these conditions. While clinical studies are still needed to confirm its efficacy in human subjects, the preliminary data suggests that artemisinin may offer a novel approach to managing neurodegenerative diseases [14]. Moreover, artemisinin's relatively low toxicity and its availability as a natural compound make it an attractive candidate for further investigation in the context of neuroprotection.

Challenges and Future Directions

Although the results of in vitro studies are promising, several challenges remain in translating these findings to clinical settings. For one, the bioavailability of artemisinin in the brain is an important consideration. Artemisinin's ability to cross the blood-brain barrier (BBB) is a crucial factor in determining its potential as a neuroprotective agent [15].

Additionally, the optimal dosage and delivery methods of artemisinin for treating neurological conditions need to be established. Further research, including preclinical and clinical trials, will be required to better understand the safety and efficacy of artemisinin in the context of neurological diseases.

Conclusions

Artemisinin, traditionally known for its anti-malarial properties, has shown significant potential as a neuroprotective agent. In vitro studies demonstrate its ability to stimulate neuronal cell viability, reduce oxidative stress, inhibit inflammation, and regulate apoptotic pathways. These effects make artemisinin a promising candidate for the treatment of neurodegenerative diseases, where the preservation of neuronal cells is critical. As research progresses, artemisinin may become an important therapeutic tool in combating neurological disorders, offering a natural and potentially effective alternative to existing treatments. However, further studies are essential to confirm its efficacy in vivo and determine how best to incorporate artemisinin into clinical practice for neuroprotection.

Disclosure Statement

No potential conflict of interest was reported by the authors.

References

1. Radi E, Formichi P, Battisti C, Federico A. Apoptosis and oxidative stress in neurodegenerative diseases. *J Alzheimer's Dis.* 2014;42(3): 125-152. <https://doi.org/10.3233/jad-132738>
2. Lamprey RN, Chaulagain B, Trivedi R, Gothwal A, Layek B, Singh J.

- A review of the common neurodegenerative disorders: current therapeutic approaches and the potential role of nanotherapeutics. *Int J Mol Sci.* 2022;23(3):1851. <https://doi.org/10.3390/ijms23031851>
3. Lu BW, Baum L, So KE, Chiu K, Xie LK. More than anti-malarial agents: therapeutic potential of artemisinins in neurodegeneration. *Neural Regen Res.* 2019;14(9):1494-1498. <https://doi.org/10.4103/1673-5374.255960>
 4. Xia L, Qiu Y, Li J, Xu M, Dong Z. The potential role of artemisinins against neurodegenerative diseases. *Am J Chin Med.* 2024;52(6):1641-1660. <https://doi.org/10.1142/S0192415X24500642>
 5. Zhao X, Fang J, Li S, Gaur U, Xing X, Wang H, et al. Artemisinin attenuated hydrogen peroxide (H₂O₂)-induced oxidative injury in SH-SY5Y and hippocampal neurons via the activation of AMPK pathway. *Int J Mol Sci.* 2019;20(11):2680. <https://doi.org/10.3390/ijms20112680>
 6. Pukhov SA, Semakov AV, Pukaeva NE, Kukharskaya OA, Ivanova TV, Kryshkova VS, et al. Artemisinin stimulates neuronal cell viability and possess a neuroprotective effect in vitro. *Molecules.* 2025;30(1):198. <https://doi.org/10.3390/molecules30010198>
 7. Yan F, Wang H, Gao Y, Xu J, Zheng W. Artemisinin protects retinal neuronal cells against oxidative stress and restores rat retinal physiological function from light exposed damage. *ACS Chem Neurosci.* 2017;8(8):1713-1723. <https://doi.org/10.1021/acscchemneuro.7b00021>
 8. Qiang W, Cai W, Yang Q, Yang L, Dai Y, Zhao Z, et al. Artemisinin B improves learning and memory impairment in AD dementia mice by suppressing neuroinflammation. *Neuroscience.* 2018;395:1-2. <https://doi.org/10.1016/j.neuroscience.2018.10.041>
 9. Lin SP, Li W, Winters A, Liu R, Yang SH. Artemisinin prevents glutamate-induced neuronal cell death via Akt pathway activation. *Front Cell Neurosci.* 2018;12:108. <https://doi.org/10.3389/fncel.2018.00108>
 10. Zheng W, Chong CM, Wang H, Zhou X, Zhang L, Wang R, et al. Artemisinin conferred ERK mediated neuroprotection to PC12 cells and cortical neurons exposed to sodium nitroprusside-induced oxidative insult. *Free Radic Biol Med.* 2016;97:158-167. <https://doi.org/10.1016/j.freeradbiomed.2016.05.023>
 11. Dinkova-Kostova AT, Kostov RV, Kazantsev AG. The role of Nrf2 signaling in counteracting neurodegenerative diseases. *FEBS J.* 2018;285(19):3576-3590. <https://doi.org/10.1111/febs.14379>
 12. Wang X, Martindale JL, Liu Y, Holbrook NJ. The cellular response to oxidative stress: influences of mitogen-activated protein kinase signalling pathways on cell survival. *Biochem J.* 1998;333(2):291-300. <https://doi.org/10.1042/bj3330291>
 13. Kiss E, Kins S, Gorgas K, Venczel Szakács KH, Kirsch J, Kuhse J. Another use for a proven drug: experimental evidence for the potential of artemisinin and its derivatives to treat alzheimer's disease. *Int J Mol Sci.* 2024;25(8):4165. <https://doi.org/10.3390/ijms25084165>
 14. Shi Z, Chen Y, Lu C, Dong LM, Lv JW, Tuo QH, et al. Resolving neuroinflammation, the therapeutic potential of the anti-malaria drug family of artemisinin. *Pharmacol Res.* 2018;136:172-180. <https://doi.org/10.1016/j.phrs.2018.09.002>
 15. Appadurai E, Ruge F, Sanders A, Jiang WG, Martin TA. Abstract P2-20-04: Controlling tight junctions in the blood-brain barrier (BBB) with artemisinin as a potential adjuvant in the treatment of metastatic disease. *Cancer Res.* 2020;80(4):2-20. <https://doi.org/10.1158/1538-7445.SABCS19-P2-20-04>