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Neuroprotective Effects of Antioxidants in Alzheimer's Dementia: A Literature Review

Komang Trisna Sumadewi*, Saktivi Harkitasari, Ni Putu Diah Witari, Fransiscus Fiano Anthony
Universitas Warmadewa, Indonesia
Email: trisna.sumadewi@warmadewa.ac.id*, saktiviharkitasari085@gmsil.com, diahkishori@gmail.com, fianokerans@warmadewa.ac.id

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Abstract

This research aims to analyze the neuroprotective effects of antioxidants in Alzheimer's disease (AD) by examining their roles in mitigating oxidative stress and related pathological mechanisms. The research employs a qualitative design with a descriptive approach through a literature review, utilizing secondary data from peer-reviewed scientific articles and relevant academic sources. Data were collected through systematic literature searching and analyzed using thematic qualitative methods, including data reduction, categorization, and inductive interpretation. The findings indicate that oxidative stress plays a central role in AD pathogenesis by interacting with amyloid-beta accumulation, tau hyperphosphorylation, mitochondrial dysfunction, neuroinflammation, and metabolic dysregulation. Antioxidants, particularly mitochondria-targeted compounds and natural bioactive substances such as polyphenols and flavonoids, demonstrate significant neuroprotective potential through multi-target mechanisms. However, their clinical effectiveness is limited by factors such as low bioavailability and restricted blood–brain barrier penetration. These findings highlight the importance of developing multi-target therapeutic strategies and advanced drug delivery systems to enhance treatment efficacy. In conclusion, this study contributes to a deeper understanding of the role of antioxidants in AD and supports the shift toward integrative and system-based approaches in neurodegenerative disease management.

INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the leading cause of dementia worldwide, accounting for approximately 70% of all dementia cases and posing a substantial global health burden (Wang et al., 2025). The disease is characterized by a gradual decline in cognitive function, including memory impairment, language deterioration, and behavioral disturbances, which significantly affect patients' quality of life and increase dependency (Topalis et al., 2025). With the global population aging rapidly, the prevalence of AD is expected to rise dramatically, with projections estimating tens of millions of affected individuals in the coming decades, underscoring the urgent need for effective preventive and therapeutic strategies (Wang et al., 2025).

The pathophysiology of AD is highly complex and multifactorial, involving hallmark features such as amyloid-beta (Aβ) plaque accumulation and neurofibrillary tangles composed of hyperphosphorylated tau protein (Iliyasu et al., 2023). These pathological processes are closely associated with neuronal damage, synaptic dysfunction, and progressive cognitive decline. However, growing evidence suggests that these hallmark features are not isolated phenomena but are interconnected with other underlying mechanisms, including oxidative stress, neuroinflammation, and mitochondrial dysfunction (Kim and Moon, 2024).

Among these mechanisms, oxidative stress has emerged as a central contributor to AD pathogenesis (Bai et al., 2022). It results from an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense systems, leading to cellular and molecular damage (Kim and Moon, 2024). Excessive ROS production promotes lipid peroxidation, protein oxidation, and DNA damage, all of which contribute to neuronal degeneration and cognitive impairment (Martináková et al., 2026).

Recent studies further highlight oxidative stress as a key bridging mechanism linking neurodegenerative and vascular components in dementia, particularly in mixed dementia conditions (Beretti et al., 2025). ROS not only exacerbate Aβ aggregation and tau hyperphosphorylation but also disrupt the blood–brain barrier and induce endothelial dysfunction, creating a vicious cycle that accelerates disease progression. This reinforces the notion that targeting oxidative stress may provide a comprehensive therapeutic approach.

Mitochondrial dysfunction plays a crucial role in amplifying oxidative stress in AD. Impaired mitochondrial dynamics, reduced energy production, and abnormal mitophagy contribute to increased ROS generation and neuronal vulnerability (Wang et al., 2025). Since mitochondria are the primary source of cellular energy and ROS production, their dysfunction is considered a key driver of neurodegeneration and a promising therapeutic target.

In addition to mitochondrial impairment, metabolic dysregulation has also been implicated in AD progression. Alterations in glucose metabolism, insulin resistance, and lipid dysregulation are frequently observed in AD patients, further exacerbating oxidative stress and neuronal damage (Barnwal et al., 2025). These metabolic abnormalities highlight the systemic nature of AD and emphasize the need for multi-targeted therapeutic strategies.

Another important aspect of AD pathology is the interaction between oxidative stress and neuroinflammation. Chronic activation of microglia and astrocytes leads to the release of pro-inflammatory cytokines, which, in turn, increase oxidative stress and neuronal injury (Topalis et al., 2025). This bidirectional relationship creates a self-perpetuating cycle that accelerates disease progression and complicates therapeutic interventions.

Given the central role of oxidative stress in AD, antioxidants have gained significant attention as potential neuroprotective agents. Antioxidants can neutralize ROS, reduce oxidative damage, and modulate signaling pathways involved in neuronal survival (Squillace et al., 2026). Both natural and synthetic antioxidants have been investigated for their ability to mitigate AD-related pathology and improve cognitive outcomes.

Natural antioxidants, including vitamins and plant-derived compounds, have shown promising neuroprotective effects in preclinical studies. For example, vitamin-based antioxidants such as vitamins C and E have demonstrated the ability to reduce oxidative stress and improve cognitive performance, although their clinical efficacy remains inconsistent (Squillace et al., 2026). Similarly, polyphenols and flavonoids have been reported to exert antioxidant, anti-inflammatory, and anti-amyloidogenic effects (Grabska-Kobyłecka et al., 2023).

Recent advancements have also focused on mitochondria-targeted antioxidants, which aim to directly address mitochondrial dysfunction and ROS overproduction. These novel compounds, such as MitoQ and SkQ1, have shown more consistent neuroprotective effects in experimental models compared to conventional antioxidants (Squillace et al., 2026). This suggests that targeting specific cellular compartments may enhance therapeutic efficacy.

Moreover, endogenous antioxidant defense mechanisms, particularly those regulated by nuclear factor erythroid 2-related factor 2 (NRF2), play a critical role in maintaining redox homeostasis. Activation of NRF2 has been shown to reduce oxidative stress, inhibit Aβ accumulation, and attenuate neuroinflammation, highlighting its potential as a therapeutic target (Zheng et al., 2025).

Despite these promising findings, current antioxidant-based therapies face several limitations. Clinical trials have yielded inconsistent results, partly due to issues such as poor bioavailability, limited blood–brain barrier penetration, and the multifactorial nature of AD (Jiménez-Jiménez et al., 2023). These challenges indicate a significant gap between preclinical success and clinical application.

Furthermore, most existing treatments for AD primarily provide symptomatic relief without addressing the underlying disease mechanisms (H. S. and P. V., 2025). This highlights the urgent need for disease-modifying therapies that can target multiple pathological pathways simultaneously, including oxidative stress, mitochondrial dysfunction, and neuroinflammation.

Another critical gap lies in the lack of comprehensive understanding of how different antioxidants interact with various molecular pathways in AD. While numerous studies have investigated individual compounds, there is limited integration of findings to identify the most effective strategies for clinical translation (Zhou et al., 2025). Addressing this gap is essential for developing targeted and effective interventions.

The novelty of this study lies in its systematic and integrative synthesis of the multi-target neuroprotective mechanisms of antioxidants spanning mitochondrial dysfunction, metabolic dysregulation, and neuroinflammation within a single coherent framework, which has not been comprehensively addressed in previous literature reviews on Alzheimer's dementia. Unlike prior reviews that focus on isolated pathways or single compound classes, this study uniquely bridges the gap between molecular pathology and therapeutic strategy by comparing conventional, natural, and mitochondria-targeted antioxidants while identifying key translational barriers such as bioavailability and blood–brain barrier penetration.

Therefore, a comprehensive literature review focusing on the neuroprotective effects of antioxidants in Alzheimer's dementia is highly relevant and necessary. By synthesizing current evidence, it is possible to identify key mechanisms, evaluate therapeutic potential, and highlight areas requiring further investigation.

The primary objective of this article is to critically review and analyze the neuroprotective effects of antioxidants in Alzheimer's dementia, with a particular focus on their mechanisms of action, therapeutic efficacy, and translational challenges. This study aims to bridge existing knowledge gaps and provide a clearer understanding of the role of antioxidants in AD management.

The expected benefits of this article are both theoretical and practical. Theoretically, it contributes to the advancement of scientific knowledge regarding oxidative stress and neuroprotection in AD. Practically, it provides insights that may guide future research and support the development of more effective antioxidant-based therapies for Alzheimer's dementia.

METHODS

This research employed a qualitative research design with a descriptive approach through a literature review (library research). Qualitative research is particularly suitable for exploring complex phenomena, such as the neuroprotective effects of antioxidants in Alzheimer's dementia, by providing an in-depth understanding of theoretical and empirical findings from various scholarly sources. Recent developments in qualitative methodology emphasize systematic procedures, transparency, and analytical rigor to ensure credibility and trustworthiness of findings (Bingham, 2023; Pratt, 2025). The descriptive approach allows the researcher to comprehensively present and interpret existing knowledge without manipulating variables, making it appropriate for synthesizing scientific evidence related to oxidative stress and neuroprotection in Alzheimer's disease (Doyle et al., 2019).

The data sources used in this study consisted of secondary data obtained from credible academic materials, including peer-reviewed journal articles, scientific reviews, and relevant scholarly publications related to Alzheimer's disease, oxidative stress, and antioxidant therapy. These sources were selected to ensure scientific validity and relevance to the research topic. Literature such as recent reviews on mitochondrial dysfunction, oxidative stress mechanisms, and antioxidant interventions in Alzheimer's disease were prioritized to reflect current scientific trends and advancements (Squillace et al., 2026; Wang et al., 2025). Additionally, methodological references on qualitative research and library studies were incorporated to strengthen the theoretical foundation of this study (Togia and Malliari, 2017; Jimenez et al., 2024).

The data collection technique was conducted through systematic literature searching and document analysis. Relevant articles were identified using academic databases and then screened based on their relevance to the research objectives. This process involved collecting, reviewing, and organizing literature that discusses oxidative stress, neuroinflammation, mitochondrial dysfunction, and antioxidant-based interventions in Alzheimer's disease. Literature review as a research method enables the integration of diverse findings into a coherent framework, allowing researchers to identify patterns, theoretical developments, and research gaps (Granikov et al., 2020; Kim and Moon, 2024). This approach ensures that the study is grounded in established scientific evidence.

The data analysis procedure followed a qualitative analytical framework consisting of several stages. First, data were systematically organized and examined to identify key themes related to antioxidant neuroprotection. Second, data reduction was performed by selecting relevant information and eliminating redundant or less relevant content. Third, categorization of concepts was conducted by grouping findings into thematic areas such as oxidative stress mechanisms, mitochondrial dysfunction, and antioxidant therapeutic strategies. Finally, conclusions were drawn inductively to develop a comprehensive understanding of the role of antioxidants in Alzheimer's dementia. This iterative and thematic analysis process is consistent with contemporary qualitative data analysis approaches emphasizing coding, categorization, and interpretation (Belotto, 2018; Kalpokaite and Radivojevic, 2018; Fife and Gossner, 2024).

To ensure methodological rigor, inclusion and exclusion criteria were clearly defined. Inclusion criteria comprised articles published in reputable journals, studies focusing on Alzheimer's disease and antioxidants, and publications from recent years to ensure up-to-date evidence. Exclusion criteria included non-peer-reviewed sources, outdated publications, and

studies not directly related to the research focus. This selection process aimed to maintain the quality and relevance of the analyzed literature. Moreover, emphasis was placed on studies that discuss molecular mechanisms such as oxidative stress, amyloid-beta pathology, and mitochondrial dysfunction, as these are central to understanding neuroprotection in Alzheimer's disease (Iliyasu et al., 2023; Martináková et al., 2026).

The validity and reliability of the data were ensured through source triangulation and conceptual consistency. Triangulation was achieved by comparing findings from multiple scholarly sources to confirm the consistency of evidence and interpretations. In addition, the study applied a conceptual peer-review approach by critically evaluating and synthesizing theoretical perspectives across different studies. This strategy enhances the credibility of the findings and minimizes bias. By employing a qualitative descriptive approach through a systematic literature review, this study provides a robust and comprehensive analysis of the neuroprotective effects of antioxidants in Alzheimer's dementia, ensuring that the results are scientifically valid, relevant, and accountable (Zheng et al., 2025; Barnwal et al., 2025).

RESULTS AND DISCUSSION

The results of this literature review reveal that oxidative stress plays a central and unifying role in the pathogenesis of Alzheimer's disease (AD), interacting with multiple pathological mechanisms including amyloid-beta aggregation, tau hyperphosphorylation, mitochondrial dysfunction, and neuroinflammation. Reactive oxygen species (ROS) are consistently identified as key mediators that exacerbate neuronal damage and accelerate cognitive decline (Kim and Moon, 2024). Furthermore, oxidative stress is not an isolated mechanism but acts as a bridge linking neurodegenerative and vascular components, particularly in mixed dementia, where endothelial dysfunction and blood–brain barrier disruption further amplify neuronal injury (Beretti et al., 2025). These findings confirm that targeting oxidative stress is a critical therapeutic strategy in AD management.

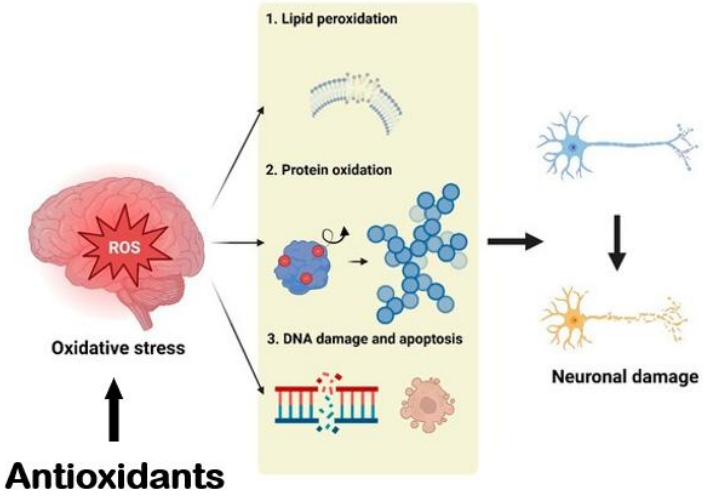

Figure 1. An illustration of how antioxidants work in oxidative stress associated with dementia

Source: Author's own creation, 2026 (adapted from Kim and Moon, 2024; Squillace et al., 2026)

As illustrated in Figure 1, oxidative stress induces neuronal damage through several key molecular mechanisms, including lipid peroxidation, protein oxidation, and DNA damage leading to apoptosis. These processes collectively disrupt cellular integrity and neuronal function, ultimately contributing to neurodegeneration.

A major finding across the reviewed studies is the strong association between mitochondrial dysfunction and oxidative damage in AD progression. Mitochondrial abnormalities, including impaired bioenergetics, disrupted mitophagy, and increased ROS production, significantly contribute to neuronal degeneration (Wang et al., 2025). Supporting this, Coenzyme Q10 (CoQ10), a mitochondrial antioxidant, has been shown to play a crucial role in restoring mitochondrial function and reducing oxidative stress, although clinical outcomes remain inconsistent despite promising preclinical evidence (Jiménez-Jiménez et al., 2023; Fišar and Hroudová, 2024). These findings highlight mitochondria as a primary therapeutic target.

In addition to mitochondrial dysfunction, lipid peroxidation has emerged as an important biomarker of oxidative stress in AD. Elevated levels of lipofuscin-like pigments (LFP), derived from lipid peroxidation, were found to be significantly higher in AD patients compared to controls and correlated with established biomarkers such as amyloid-beta and phosphorylated tau (Martináková et al., 2026). This suggests that oxidative damage can be quantitatively measured and may serve as a diagnostic indicator, strengthening the biological link between oxidative stress and disease progression.

Another key finding is the involvement of enzymatic sources of ROS, particularly NADPH oxidase (NOX), in AD pathology. NOX-derived ROS significantly contribute to oxidative imbalance, neuroinflammation, and neuronal damage (Kim and Moon, 2024). Additionally, dysregulation of signaling pathways such as GSK-3β further links oxidative stress with tau pathology and amyloid-beta production, emphasizing the interconnected nature of molecular mechanisms in AD (Rekha et al., 2025).

The review also highlights the crucial role of neuroinflammation in amplifying oxidative stress. Activation of microglia and astrocytes, while initially protective, can become detrimental when dysregulated, leading to increased production of pro-inflammatory cytokines and ROS (Topalis et al., 2025). This bidirectional relationship creates a feedback loop that accelerates neurodegeneration, reinforcing the need for therapeutic approaches that simultaneously target oxidative stress and inflammation.

One of the most significant findings concerns the neuroprotective effects of antioxidants, particularly natural vitamins and plant-derived compounds. Natural vitamin antioxidants such as vitamins A, C, and E demonstrate variable efficacy, with vitamin E showing the most consistent neuroprotective effects in reducing oxidative stress and improving cognitive outcomes (Squillace et al., 2026). However, their effects are often limited by bioavailability and inconsistent clinical translation.

In contrast, mitochondria-targeted antioxidants (MTAs), such as MitoQ and SkQ1, exhibit more robust and consistent effects in improving mitochondrial function, reducing oxidative damage, and enhancing cognitive performance in animal models (Squillace et al., 2026). This suggests that targeted therapeutic strategies may be more effective than conventional antioxidant approaches.

The findings also demonstrate that several bioactive compounds derived from natural sources possess multi-target neuroprotective properties. For example, curcumin has been shown to reduce oxidative stress, inhibit neuroinflammation, and modulate amyloid-beta and tau pathology (Azzini et al., 2024). Similarly, resveratrol exhibits antioxidant and anti-amyloidogenic effects, although its clinical efficacy is limited by poor bioavailability (Braidy et al., 2016).

Flavonoids such as quercetin and naringenin also show significant neuroprotective potential through antioxidant, anti-inflammatory, and anti-amyloid mechanisms (Kaur et al., 2024; Goyal et al., 2022). Additionally, epigallocatechin gallate (EGCG) from green tea has been reported to regulate oxidative stress, reduce tau aggregation, and promote neuronal survival (Valverde-Salazar et al., 2023). These findings indicate that plant-derived antioxidants act through multiple pathways, making them promising therapeutic candidates.

Experimental studies further support the efficacy of antioxidants in improving cognitive function. For instance, Trolox, a vitamin E analog, significantly reduced amyloid-beta levels, tau phosphorylation, oxidative stress, and neuroinflammation while improving synaptic function and memory in animal models (Tahir et al., 2024). Similarly, CoQ10 delivered via exosomes enhanced memory, neuronal proliferation, and neurotrophic factors such as BDNF (Sheykhhasan et al., 2022).

Additional plant-based interventions, such as Ginkgo biloba, demonstrated improvements in cognitive function and neuropsychiatric symptoms in several clinical trials, although results were not universally consistent (Pagotto et al., 2024). Likewise, plant extracts such as Guiera senegalensis and Terminalia macroptera showed significant antioxidant, anti-inflammatory, and neuroprotective effects, including improvements in memory and reductions in amyloid-beta and tau levels in animal models (Foyet et al., 2024; Ambamba et al., 2025).

Table 1. Summary of Key Findings on Neuroprotective Effects of Antioxidants in Alzheimer's Disease

Category	Key Findings	Representative Studies
Oxidative Stress Mechanisms	ROS drives Aβ, tau, and neuronal damage	(Kim and Moon, 2024; Beretti et al., 2025)
Mitochondrial Dysfunction	Impaired mitochondria increase ROS and neurodegeneration	(Wang et al., 2025; Fišar and Hroudová, 2024)
Biomarkers	LFP correlates with AD biomarkers	(Martináková et al., 2026)
Antioxidant Vitamins	Mixed efficacy, Vitamin E most consistent	(Squillace et al., 2026)
Targeted Antioxidants	MTAs more effective than conventional antioxidants	(Squillace et al., 2026)
Natural Compounds	Curcumin, resveratrol, flavonoids show multi-target effects	(Azzini et al., 2024; Kaur et al., 2024)
Experimental Evidence	Improved cognition and reduced pathology in models	(Tahir et al., 2024; Sheykhhasan et al., 2022)

Source: Compiled by the author from reviewed studies (Kim and Moon, 2024; Beretti et al., 2025; Wang et al., 2025; Squillace et al., 2026; Azzini et al., 2024; Kaur et al., 2024; Tahir et al., 2024)

Despite these promising findings, a consistent pattern across studies is the gap between preclinical success and clinical application. Many antioxidants demonstrate strong neuroprotective effects in vitro and in animal models but fail to produce consistent results in human trials (Jiménez-Jiménez et al., 2023). This discrepancy is largely attributed to limitations such as poor bioavailability, inadequate blood–brain barrier penetration, and the multifactorial nature of AD.

In comparison with earlier research, recent studies emphasize a shift from single-target therapies toward multi-target and systems-based approaches. Modern evidence highlights the importance of combining antioxidant effects with anti-inflammatory, mitochondrial, and metabolic interventions to achieve more effective outcomes (Barnwal et al., 2025; Zhou et al., 2025). This represents a significant advancement over traditional approaches that focused primarily on amyloid-beta or tau pathology alone. Thus, the findings demonstrate that antioxidants have substantial potential as neuroprotective agents in Alzheimer's dementia, particularly when designed to target multiple pathological pathways. However, further research is needed to optimize delivery systems, improve bioavailability, and validate clinical efficacy.

The findings of this literature review strongly support the theoretical framework that oxidative stress plays a central role in the pathogenesis of Alzheimer's disease (AD). Excessive production of reactive oxygen species (ROS) contributes significantly to neuronal damage and is closely associated with the accumulation of amyloid-beta (Aβ) plaques and tau protein hyperphosphorylation, which are the primary pathological hallmarks of AD (Iliyasu et al., 2023). These results align with the oxidative stress hypothesis, which posits that redox imbalance is a key driver of neurodegeneration. Furthermore, the involvement of NADPH oxidase (NOX) enzymes as major contributors to ROS production reinforces the concept that oxidative stress is not merely a secondary effect but a primary pathological mechanism in AD progression (Kim and Moon, 2024).

In addition, the findings are consistent with the mitochondrial dysfunction hypothesis, which emphasizes the role of impaired mitochondrial function in accelerating neurodegeneration. Mitochondrial abnormalities lead to increased ROS production, disrupted energy metabolism, and neuronal vulnerability, thereby contributing to disease progression (Wang et al., 2025). The role of Coenzyme Q10 (CoQ10) as a mitochondrial antioxidant further supports this theory, as it is essential for maintaining mitochondrial bioenergetics and reducing oxidative damage (Fišar and Hroudová, 2024). Moreover, dysregulation of signaling pathways such as glycogen synthase kinase-3β (GSK-3β) provides additional evidence linking oxidative stress to tau pathology and amyloid processing, highlighting the interconnected nature of molecular mechanisms in AD (Rekha et al., 2025).

The interaction between oxidative stress and neuroinflammation represents another critical aspect of AD pathophysiology. The reviewed studies demonstrate that oxidative stress and inflammation form a self-amplifying cycle in which activated microglia and astrocytes release pro-inflammatory cytokines and ROS, leading to further neuronal damage (Topalis et al., 2025). This interaction is further complicated by vascular factors, as oxidative stress also contributes to endothelial dysfunction and blood–brain barrier disruption, particularly in mixed dementia conditions (Beretti et al., 2025). These findings suggest that AD should be understood as a multifactorial disorder involving not only neuronal degeneration but also systemic and vascular dysfunction.

Metabolic dysfunction is also identified as a significant contributor to AD progression. Impairments in glucose metabolism, insulin signaling, and lipid homeostasis exacerbate oxidative stress and synaptic dysfunction, reinforcing the concept of AD as a systemic disease rather than a purely neurological disorder (Barnwal et al., 2025). This broader perspective highlights the need for integrative therapeutic approaches that address multiple pathological pathways simultaneously.

From a therapeutic standpoint, the findings indicate a clear shift from single-target interventions toward multi-target strategies. Conventional antioxidants such as vitamins A, C, and E have shown inconsistent clinical outcomes, although vitamin E appears to have relatively more consistent neuroprotective effects (Squillace et al., 2026). In contrast, mitochondria-targeted antioxidants (MTAs) demonstrate greater efficacy by directly targeting the primary source of ROS production, suggesting that subcellular targeting may enhance therapeutic effectiveness (Squillace et al., 2026). Additionally, natural compounds such as curcumin, quercetin, resveratrol, and epigallocatechin gallate (EGCG) exhibit multi-target properties, including antioxidant, anti-inflammatory, and anti-amyloid effects, making them promising candidates for AD therapy (Azzini et al., 2024; Kaur et al., 2024; Valverde-Salazar et al., 2023; Braidy et al., 2016).

Despite these promising findings, several factors influence the variability of research outcomes. One of the main challenges is the low bioavailability of many natural compounds, which limits their therapeutic efficacy (Azzini et al., 2024). Additionally, the blood–brain barrier (BBB) presents a significant obstacle for drug delivery, preventing sufficient concentrations of therapeutic agents from reaching the brain (H.S. and P.V., 2025). Differences between preclinical models and human physiology also contribute to inconsistent results, as many compounds that show efficacy in animal studies fail to demonstrate similar benefits in clinical trials (Jiménez-Jiménez et al., 2023). Variability in study design, dosage, and duration further complicates the interpretation of results.

Several limitations are evident in the current body of research. Most studies are preclinical, relying on in vitro or animal models, which limits the generalizability of findings to human populations. Additionally, there is a lack of long-term clinical trials evaluating the efficacy and safety of antioxidant therapies. Pharmacokinetic challenges, such as poor absorption, rapid metabolism, and limited BBB penetration, also hinder clinical translation (Grabska-Kobyłecka et al., 2023). Furthermore, the heterogeneity of AD as a multifactorial disease makes it difficult to develop universally effective treatments.

Future research should focus on overcoming these limitations by developing advanced drug delivery systems, such as nanotechnology-based approaches, to improve BBB penetration and bioavailability (H.S. and P.V., 2025). There is also a need for large-scale, well-designed clinical trials to validate preclinical findings and establish standardized treatment protocols. Additionally, exploring combination therapies that target multiple pathological pathways may enhance therapeutic outcomes. The identification of reliable biomarkers, such as lipid peroxidation products, may also improve early diagnosis and treatment monitoring (Martináková et al., 2026).

Overall, this study contributes to the field by reinforcing the central role of oxidative stress in AD pathogenesis and highlighting the importance of multi-target therapeutic strategies. It underscores the interconnected nature of oxidative stress, mitochondrial dysfunction,

inflammation, and metabolic dysregulation in AD. Moreover, it provides evidence supporting the potential of both natural and synthetic antioxidants as neuroprotective agents. These findings contribute to a paradigm shift toward more integrative and systemic approaches in the prevention and treatment of Alzheimer's disease.

CONCLUSION

This research concludes that oxidative stress plays a fundamental and integrative role in the pathogenesis of Alzheimer's disease by interacting with key mechanisms such as amyloid-beta accumulation, tau hyperphosphorylation, mitochondrial dysfunction, neuroinflammation, and metabolic dysregulation, thereby reinforcing the concept of Alzheimer's as a multifactorial and systemic disorder. The findings demonstrate that antioxidants, particularly mitochondria-targeted and natural multi-target compounds, possess significant neuroprotective potential; however, their clinical application remains limited due to challenges such as low bioavailability and restricted blood–brain barrier penetration. These results contribute to the advancement of theoretical understanding by supporting integrative and systems-based approaches while also offering practical implications for developing more effective therapeutic strategies. Therefore, it is recommended that practitioners adopt multi-target antioxidant approaches in prevention and treatment, while researchers should expand studies using multidisciplinary perspectives, methodological triangulation, and advanced delivery systems to enhance efficacy. Future research is encouraged to conduct large-scale clinical trials, explore combination therapies, and identify reliable biomarkers to strengthen translational outcomes and deepen the understanding of neuroprotective mechanisms in Alzheimer's disease.

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