International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(REVIEW ARTICLE)

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Medium-chain triglyceride supplementation and physical exercise for people with Alzheimer's disease

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International Journal of Science and Research Archive, 2025, 14(03), 1546-1550

Publication history: Received on 08 February 2025; revised on 25 March 2025; accepted on 27 March 2025

Article DOI: https://doi.org/10.30574/ijsra.2025.14.3.0750

Abstract

Alzheimer's disease (MA) is a progressive neurodegenerative disease characterized by the accumulation of beta-amyloid plaques and hyperphosphorylated tau neurofibrillary tangles, resulting in synaptic dysfunction and severe cognitive decline. Brain energy metabolism is compromised due to reduced glucose uptake and insulin resistance in the brain, aggravating oxidative stress and neuroinflammation. In this context, medium-chain triglycerides (MCTs) emerge as a promising metabolic alternative. TCMs are rapidly converted into ketone bodies by the liver, offering an alternative source of energy for affected neurons. Studies show that TCM supplementation can improve memory, reduce neuroinflammation, and modulate biochemical pathways essential to neuronal survival. This article reviews the biochemistry of Alzheimer's and the molecular mechanisms by which MCTs may attenuate disease progression, as well as exploring comparisons with other nutritional approaches. It is concluded that TCM supplementation may represent a viable strategy to slow the progression of the disease, although additional studies are needed to determine its long-term efficacy.

Keywords: Alzheimer's; Physical exercise; Neurodegeneration; Medium-chain triglycerides; Ketone bodies; Brain energy metabolism

1. Introduction

Alzheimer's disease (AM) is a progressive neurodegenerative disease characterized by significant cognitive decline, affecting memory, executive functions, and quality of life in patients. It is one of the main causes of dementia in the elderly and represents a challenge for modern medicine due to its complex etiology and not yet fully understood.

In recent years, research has investigated alternative therapeutic approaches that can slow the progression of the disease or improve the quality of life of patients. Supplementation with medium-chain triglycerides (MCT) has been widely studied as a possible intervention to improve cognition in patients with MA. MCTs are metabolized in the liver and converted into ketone bodies, providing an alternative source of energy for the brain, whose glucose utilization is often compromised in the disease.

This article aims to explore the impact of TCM supplementation in patients with Alzheimer's by reviewing recent scientific literature and analyzing its clinical implications.

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2. Literature Review

2.1. Biochemical Basis of Alzheimer's

Alzheimer's is characterized by the deposition of beta-amyloid plaques and neurofibrillary tangles of hyperphosphorylated tau, leading to synaptic dysfunction and neuronal death (Querfurth & LaFerla, 2021). Studies indicate that neuronal energy metabolism is altered in the disease, resulting in lower glucose uptake and increased oxidative stress (Cunnane et al., 2021).

Mitochondrial function is also compromised, with reduced activity of respiratory chain complexes and increased production of reactive oxygen species (Swerdlow et al., 2022). This energy deficit contributes to the progressive neuronal degeneration seen in the disease.

2.2. Molecular and Biochemical Mechanisms of Neurodegeneration

Alzheimer's-associated neurodegeneration involves the interaction between genetic, metabolic, and environmental factors. Hyperphosphorylated tau protein forms neurofibrillary tangles that compromise microtubule stability and impair axonal transport (Wang et al., 2022). In addition, beta-amyloid toxicity induces oxidative stress and chronic inflammation in the central nervous system (Smith et al., 2023).

Elevated levels of free radicals in the brains of Alzheimer's patients compromise cell membranes and proteins essential for neuronal homeostasis. Oxidative stress dysregulates mitochondrial function, exacerbating neuroinflammation and contributing to programmed cell death (Johnson et al., 2023).

2.3. The Role of Medium-Chain Triglycerides in Brain Metabolism

Medium-chain triglycerides (MCTs) are rapidly metabolized in the liver, producing ketone bodies such as β-hydroxybutyrate and acetoacetate, which can cross the blood-brain barrier and serve as energy substrates for neurons (Newport et al., 2022). This energy alternative is crucial for Alzheimer's patients, as the ability to metabolize glucose is reduced due to brain insulin resistance (Krikorian et al., 2021).

2.4. Effects of MCTs on Metabolic Regulation

TCM-derived ketone bodies have neuroprotective properties, including activating antioxidant pathways, reducing neuroinflammation, and promoting synaptic plasticity (Gao et al., 2023). In addition, TCM stimulates mitochondrial biogenesis, improving the energy function of neurons and reducing cell apoptosis (Henderson et al., 2023).

Studies demonstrate that TCM supplementation can significantly increase the levels of ketone bodies in the blood and cerebrospinal fluid, providing alternative energy to the brain and reducing the progression of cognitive deficit (Fortier et al., 2023).

The metabolization of MCTs occurs primarily in the liver through β-oxidation, resulting in the production of ketone bodies that can be used by neurons as an alternative source of energy. This process reduces glucose dependence, which is impaired in Alzheimer's due to insulin resistance and dysfunction of glucose transporters in the blood-brain barrier (Wilson et al., 2023).

TCM-induced ketogenesis also regulates the expression of neuroprotection-related genes, such as PGC-1α, which modulates mitochondrial biogenesis and antioxidant response (Clark et al., 2023). In addition, studies indicate that ketone bodies directly influence the dynamics of the Krebs cycle, optimizing ATP production and reducing neuroinflammation (Huang et al., 2023).

The biochemical effects of MCTs on Alzheimer's also involve epigenetic regulation, with histone modulation associated with memory and synaptic plasticity (Santos et al., 2023). Recent research shows that TCM supplementation can reduce the expression of pro-inflammatory genes and increase the synthesis of neurotrophins essential for neuronal survival (Martins et al., 2023).

2.5. Impact of MCTs on Cognitive Function

Clinical research shows that TCM supplementation improves memory and executive function in patients with mild to moderate Alzheimer's (Castellano et al., 2021). In a randomized controlled trial, individuals who consumed MCT daily performed better on neuropsychological tests compared to the placebo group (Henderson et al., 2020).

In addition, MCTs demonstrate anti-inflammatory properties by reducing microglial activation and expression of pro-inflammatory cytokines, which contributes to the reduction of oxidative stress and neurodegeneration (Gibson et al., 2023).

2.6. Comparison to Other Nutritional Strategies

Other nutritional approaches, such as ketogenic diets, have been explored as potential therapies for Alzheimer's. However, adherence to these diets can be challenging for seniors due to the severe dietary restrictions. TCM supplementation, on the other hand, offers a more affordable and practical approach to increasing ketone body levels without the need for radical dietary changes (Krikorian et al., 2021).

Additionally, studies indicate that combining MCT with essential fatty acids and antioxidants may enhance its neuroprotective effects, reducing oxidative stress and promoting synaptic integrity (Swerdlow et al., 2022).

3. Biochemical Mechanisms of Exercise-Induced Neuroprotection

3.1. Regulation of Oxidative Stress

Oxidative stress plays a crucial role in the pathogenesis of Alzheimer's, as excess reactive oxygen species (ROS) leads to oxidation of lipids, proteins, and DNA, contributing to neurodegeneration (Butterfield & Halliwell, 2021). Physical exercise promotes the activation of the Nrf2 (nuclear factor erythroid 2-related factor 2) pathway, which regulates the expression of antioxidant enzymes, such as superoxide dismutase (SOD) and catalase (CAT), thereby reducing oxidative damage to neurons (Radak et al., 2022).

3.2. Increased Levels of Neurotrophic Factors

Brain-derived neurotrophic factor (BDNF) is a protein that is essential for synaptic plasticity, neuronal survival, and memory formation (Loprinzi et al., 2022). Alzheimer's patients often have reduced BDNF levels, which is associated with synaptic loss and cognitive decline. Studies demonstrate that regular aerobic exercise significantly increases BDNF levels in the hippocampus, improving neuroplasticity and cognition (Voss et al., 2023).

3.3. Modulation of Chronic Inflammation

Neuroinflammation is one of the main pathogenic mechanisms of Alzheimer's, being mediated by the exacerbated activation of microglia and astrocytes, which secrete pro-inflammatory cytokines such as TNF-α and IL-1β (Heneka et al., 2021). Physical exercise reduces the expression of inflammatory cytokines through the activation of the AMPK (AMP-activated protein kinase) pathway, promoting an anti-inflammatory environment that protects neurons from further damage (Valenzuela et al., 2022).

3.4. Improved Brain Energy Metabolism

Glucose hypometabolism is one of the main biochemical changes observed in the brains of Alzheimer's patients, leading to a deficiency in ATP production and increased oxidative stress (Cunnane et al., 2021). Physical exercise improves insulin signaling in the brain and stimulates fatty acid oxidation, reducing dependence on glucose as an energy source (Ryan et al., 2023).

3.5. Beta-Amyloid Removal

The accumulation of beta-amyloid is one of the main pathogenic factors of Alzheimer's. Physical exercise improves the brain's lymphatic system's ability to remove these toxic plaques through the activation of the autophagy pathway, a cellular process essential for the degradation of abnormal protein aggregates (Kang et al., 2022). In addition, increased expression of LRP1 (low-density lipoprotein receptor-related protein 1) facilitates the clearance of beta-amyloid in cerebrospinal fluid (Tarasoff-Conway et al., 2023).

4. Conclusion

Supplementation with medium-chain triglycerides emerges as a promising strategy to mitigate cognitive decline in patients with Alzheimer's disease. The reviewed literature suggests that regular administration of TCM may improve cognition and provide an alternative source of energy for the disease-affected brain.

Regular physical exercise plays an essential role in mitigating the pathological processes of Alzheimer's disease, acting on several biochemical mechanisms that include the reduction of oxidative stress, increase of neurotrophic factors, regulation of inflammation, improvement of brain metabolism and removal of beta-amyloid. Studies indicate that the practice of aerobic and resistance exercises can offer a positive impact on cognition and disease progression. Although more research is needed to define optimal intervention protocols, existing evidence reinforces the potential of physical exercise as an essential therapeutic tool in the treatment of Alzheimer's.

Although the results are encouraging, long-term studies are still needed to establish standardized supplementation protocols and evaluate their effects at different stages of the disease. The development of additional research can provide a more solid foundation for the clinical implementation of this nutritional approach.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest is to be disclosed.

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