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REVIEW

Linking Mechanisms of Lipoic Acid to Multiple Sclerosis: A Narrative Review

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Abstract: The effect of lipoic acid supplements on patients with multiple sclerosis (MS) has been widely studied, yet the evidence remains inconclusive, and more research is needed to draw definitive conclusions. This review aimed to comprehensively assess the impact of α - lipoic acid (ALA) on oxidative stress, inflammatory responses, and brain atrophy in MS Methods This Narrative review, conducted in February 2025, examines research from multiple databases, including PubMed, Google Scholar, ScienceDirect, Scopus, and EMBASE. It focuses on studies published in the English language that investigate the effects of ALA supplementation on MS, oxidative stress, inflammation, and brain atrophy. MS is a chronic and often progressive neurological disease that leads to the degradation of myelin, the protective sheath surrounding nerve fibers. This MS-related neuronal damage disrupts communication between the brain and body, potentially resulting in severe neurological impairments, including cognitive dysfunction, motor difficulties, and eventually permanent nerve damage. ALA, an antioxidant with multiple biological roles, has been investigated as a promising dietary supplement for MS patients. A total of three studies reported that LA supplementation improved total antioxidant capacity and reduced inflammation and oxidative stress, suggesting that ALA might have therapeutic value in managing MS. However, other studies failed to show consistent or significant results, indicating that further research is needed to validate the therapeutic potential of ALA in MS management. This Narrative review highlights the possible benefits of ALA supplementation but emphasizes the need for more comprehensive studies to explore the underlying mechanisms, consistency of findings, and its effectiveness across diverse populations.

Keywords: multiple sclerosis, lipoic acid, inflammation, oxidative stress, brain atrophy, narrative review

Introduction

Multiple sclerosis (MS) is a debilitating autoimmune disease that primarily affects the central nervous system (CNS), leading to the progressive destruction of myelin, the protective covering of nerve fibers.[1] The breakdown of myelin disrupts nerve signal transmission, resulting in a wide range of neurological symptoms, including visual disturbances, cognitive impairment, motor dysfunction, and autonomic dysfunction and MS is an autoimmune disorder, meaning that the immune system mistakenly attacks the body's own tissues, in this case, the myelin sheaths. The disease's progression is often marked by an initial phase of relapse-remission, followed by a more irreversible secondary progressive phase, leading to increasing disability over time.[2]

MS is particularly prevalent in young adults aged 20–40 years and can result in long-term neurological and physical impairments. However, the demographic landscape is shifting, and the incidence of MS among older adults, particularly those aged 55–64 years, is on the rise due to improved life expectancy and better diagnostic tools. MS significantly impacts patients' quality of life and has profound social and economic consequences. It is estimated that over 2.8 million individuals worldwide suffer from MS, with the highest rates of prevalence observed in developed countries, such as the United States, where the disease is most commonly diagnosed in individuals between the ages of 55 and 64.[3]

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Furthermore, MS's impact is substantial in regions like Khuzestan, Iran, where there has been a marked increase in incidence rates over the past two decades, indicating a growing need for effective treatments.[4]

The symptoms of MS can vary greatly from person to person, depending on the extent of the damage to the CNS and the areas of the brain and spinal cord affected. Common symptoms include visual disturbances, muscle weakness, difficulty walking, fatigue, cognitive decline, sensory disturbances, bladder and bowel dysfunction, and depression.[5] The heterogeneity of the disease means that MS can range from a relatively mild course, where patients can live independently for many years, to a severe, rapidly progressive form that results in complete physical and cognitive disability. The course of MS also varies based on age at onset, gender, and geographical location, with women being more likely to develop the disease than men.[6]

While disease-modifying therapies (DMTs) have shown some promise in managing MS, they often have limited effectiveness in preventing disease progression or alleviating symptoms in later stages of the disease. In light of this, dietary supplements such as vitamins D, E, A, and C, as well as antioxidants like curcumin, have been proposed as complementary therapeutic strategies.[7]

Lipoic acid (LA)(often called α-lipoic acid(ALA))[8] is an endogenous organosulfur compound with potent antioxidant properties and is known to be an essential component for proper mitochondrial function. It exerts prominent anti-inflammatory and antioxidant effects by reducing ROS, inhibiting metal ions, and regulating pathways associated with oxidative stress and inflammation.[9] ALA has a chiral center and exists in two isomers, R and S, as different enantiomers, each of which can have different biological and beneficial effects on health. The R-ALA isomer is the natural form of this compound and is found in food sources, especially meat and some vegetables and antioxidant activity are superior to S-ALA; while the S-ALA isomer is mainly produced through chemical synthesis.[10,11]

Research has suggested that LA can reduce oxidative stress and inflammation, both of which are critical factors in the pathogenesis of MS.[12,13] Furthermore, LA has been shown to have the potential to stimulate myelin regeneration, which is essential for repairing the damage caused by MS. In this context, LA supplementation may offer an effective adjunctive treatment for MS patients, helping to reduce disease progression and improve overall quality of life.[14] This Narrative review discusses the comprehensive mechanisms of α-lipoic acid in MS and assesses evidence of its effects on MS disease activity from various aspects in in vitro and in vivo studies.

Methods

This Narrative review article was conducted by searching for relevant studies from multiple reputable academic databases, including PubMed, Google Scholar, ScienceDirect, Scopus, and EMBASE. The focus of the narrative review was to identify studies that explored the impact of lipoic acid supplementation on MS, specifically its effects on oxidative stress, inflammation, and brain atrophy. The search strategy utilized the following keywords: "multiple sclerosis," "lipoic acid," "nutrition," and "oxidative stress." To ensure that only high-quality and relevant studies were included, articles published in peer-reviewed journals were selected, while case reports, studies with small sample sizes, and those from non-citable or predatory journals were excluded. In order to capture a broad spectrum of research, the narrative review included studies published in the English language, with no specific time restrictions and shown in PRISMA (Figure 1). By using this comprehensive approach, the narrative review aimed to provide a thorough and up-to-date synthesis of the existing literature on the topic.

The selected studies were then assessed based on their methodological rigor, the population studied, and the outcomes measured. The primary focus was on research that directly investigated the relationship between LA supplementation and its impact on MS symptoms, oxidative stress levels, inflammatory markers, and neurodegeneration. The results of these studies were synthesized to provide an overview of the potential benefits and limitations of LA as a therapeutic agent for MS[15,16] (Tables 1 and 2).

Mechanisms of MS Pathology

The exact cause of MS remains largely unknown, but multiple factors have been identified as potential contributors to the disease's onset and progression. Genetic predisposition plays a significant role, as certain gene variants increase susceptibility to the disease.[4] In addition, environmental factors such as viral infections, smoking, high-fat diets, and vitamin D deficiency are believed to influence the development and exacerbation of MS. Gender is another factor, with women being more likely to develop MS than men, possibly due to hormonal influences on immune function. Although

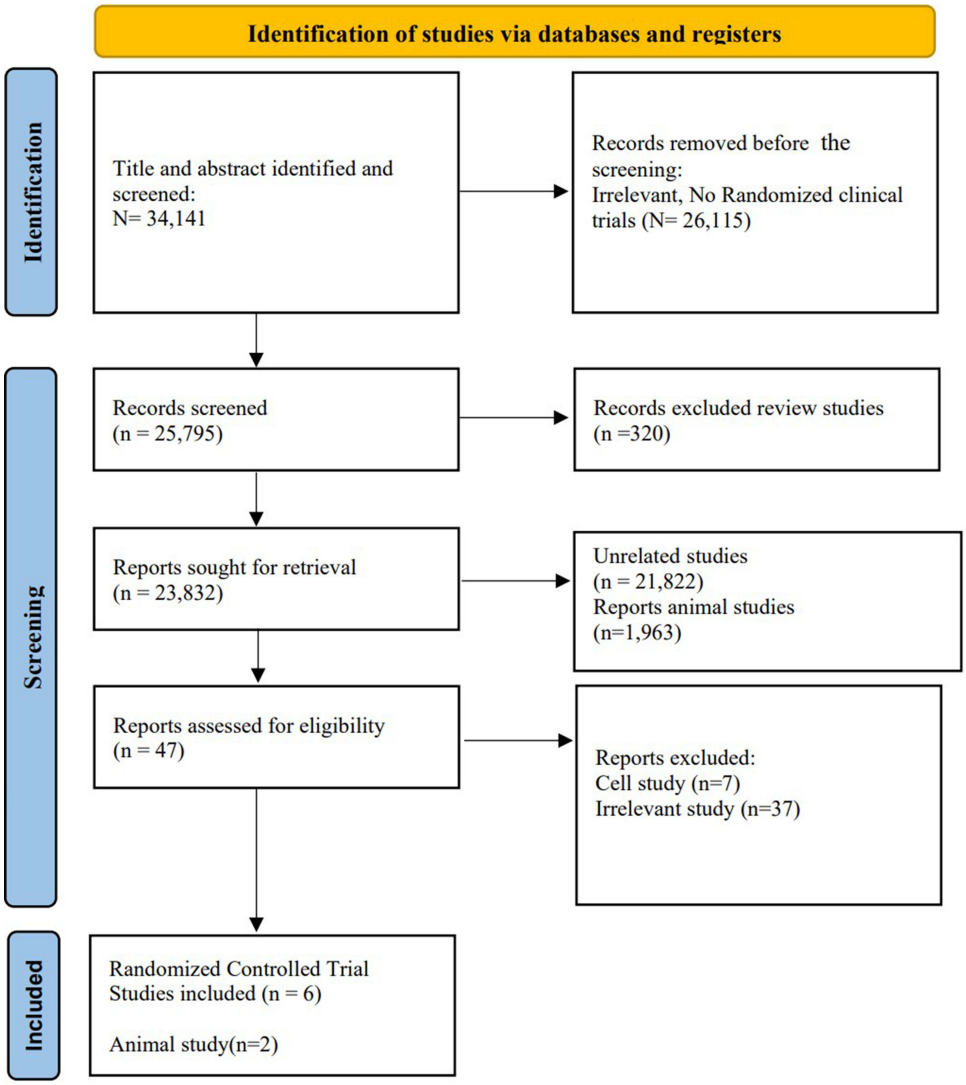

Figure 1 Identification of studies via databases and registers.

genetic factors cannot be controlled, the influence of environmental factors can be mitigated through lifestyle changes, including smoking cessation and dietary modification.[24]

MS is characterized by the activation of the immune system, particularly autoreactive T cells, which mistakenly attack the myelin in the CNS and this immune response triggers inflammation, demyelination, and axonal damage.[25] Oxidative stress is another key factor in MS pathology, as it leads to further cellular damage and mitochondrial dysfunction. The combination of inflammation, oxidative stress, and neuronal damage results in the progressive neurological impairments seen in MS patients, As the disease advances, myelin regeneration becomes more difficult, and axonal loss leads to irreversible functional impairments.[26] Understanding these underlying mechanisms is critical for developing effective treatments that target the root causes of the disease.

Lipoic Acid Supplementation in MS

Effect of Lipoic Acid on Mechanisms of MS Symptoms Such as Brain Atrophy

Brain atrophy, particularly in gray and white matter, is a hallmark feature of MS and is associated with disease progression and functional decline.[27] Longitudinal studies have shown that MS patients experience significant reductions in brain volume, which are linked to cognitive impairment and worsening physical disability. Brain atrophy in MS

Table 1 Summary of Included Study on Lipoic Acid in MS Patients

Author (Year)	Study Design	Participants	Duration	Intervention	Outcomes Measured	Key Findings
Spain et al[17] (2017).	RCT	50 patients with SPMS, age 40–70	2 years	LA 1200 mg/ day vs placebo	Annualized PCBV, atrophy of brain/ spinal/retinal structures, disability, QOL, safety	Significant reduction in brain volume loss rate; supports neuroprotective effect of LA.
Cameron et al[18] (2020).	RCT	20 patients with progressive MS	7–10 days	600 mg R-LA vs 1200 mg racemic LA	Serum LA absorption, GI tolerability	600 mg R-LA had better GI tolerance and equivalent absorption compared to 1200 mg racemic mixture.
Yadav et al[19] (2005).	RCT	33 patients with MS	2 weeks	LA 1200 mg or 2400 mg	MMP-9, sICAM-1, pharmacokinetics	Dose-dependent reduction in MMP-9 and sICAM-1; higher serum LA correlated with lower MMP-9.
Loy et al[20] (2018).	RCT	21 patients with SPMS	2 years	LA 1200 mg/ day	Gait (Timed Up and Go test), EDSS	Medium effect size in improving mobility (TUG); better outcomes in less disabled patients (EDSS < 6).
Khalili et al[21] (2014).	RCT	52 patients with RRMS, age 18–50	12 weeks	LA 1200 mg/ day vs placebo	TAC, SOD, GPx, MDA	Significant increase in TAC in LA group; no significant change in SOD, GPx, or MDA.
Khalili et al[22] (2017).	RCT	24 patients with RRMS	12 weeks	LA 1200 mg/ day vs placebo	EDSS, ADMA	Significant decrease in ADMA within LA group; between-group difference not statistically significant.

Table 2 Summary of Included Animal Study on Lipoic Acid in MS Patients

Author(Year)	Treatment Group	Texture of Interest	Dose of LA	Results
Ibrahim Fouad G[14] (2023).	7 rats	Nervous system and myelin of the brain	600 mg of ALA per tablet	1. Reduce oxidative stress and neural inflammation Strengthen the myelin repair.
Chaudhary P et al[23] (2019).	6 Adult female rats were C57BL	Microglia brain tissue	LA (25, 50, 100 μg/mL, Sigma, #T1395) and vehicle for 24 additional hours	1. Reduce microglia activation (based on cell size) 2. Phagocytosis ability to suppress them (based on fluorescence and molecular markers)

patients typically begins early in the disease course and can be observed even in the absence of overt lesions on MRI scans. This has prompted researchers to investigate potential therapies that could slow or prevent brain atrophy.[28]

Lipoic acid has shown promise in this regard. Preclinical studies have suggested that LA can protect against neurodegeneration by modulating key cellular pathways involved in inflammation, oxidative stress, and neuronal survival.[29,30] In experimental models of MS, LA supplementation has been shown to reduce the rate of brain volume loss, particularly in patients with secondary progressive MS (SPMS), a stage of the disease that is characterized by more rapid progression and irreversible disability.[17,23] MRI studies in SPMS patients have demonstrated that LA supplementation may help preserve brain structure and function by reducing brain atrophy. However, these findings are preliminary, and further studies are needed to determine the long-term effects of LA on brain atrophy in MS patients.[29,31]

Effect of Lipoic Acid on Mechanisms of MS Pathogenesis Such As Oxidative Stress

Oxidative stress is a key contributor to the pathophysiology of MS, as it can damage neurons, myelin, and other critical structures in the CNS. The brain is particularly vulnerable to oxidative stress because it consumes a significant amount of

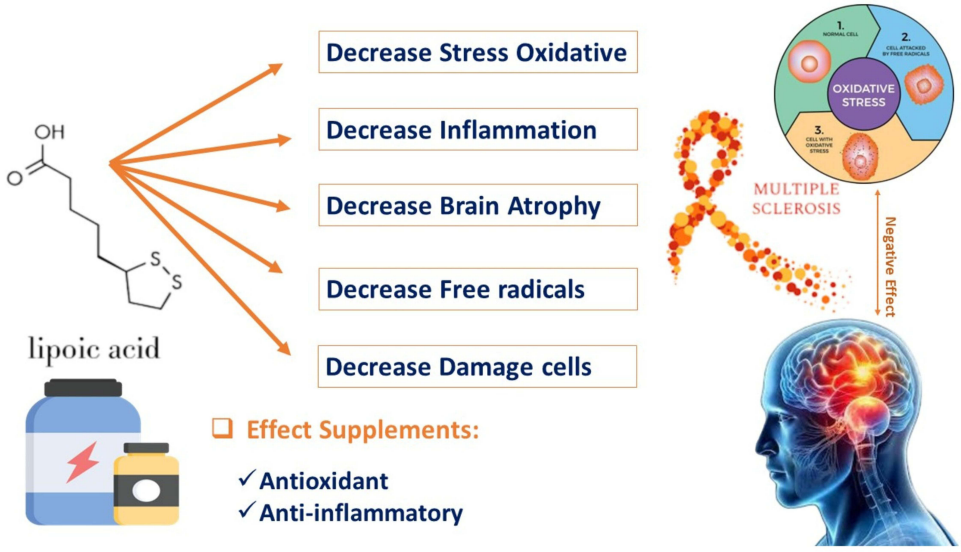

Figure 2 The possible mechanisms of alpha-lipoic acid in multiple sclerosis include antioxidant and anti-inflammatory roles. This compound acts by reducing oxidative stress, inhibiting inflammatory processes, decreasing brain atrophy, neutralizing free radicals, and restricting cell damage.

oxygen during energy production, generating free radicals as by products.[27,28] LA acts as a potent antioxidant, neutralizing these free radicals and protecting against oxidative damage. It has been shown to increase the activity of other antioxidants, such as glutathione, and can regenerate other antioxidants like vitamin C, further reducing oxidative stress. LA's ability to cross the blood-brain barrier is crucial for its potential as a therapeutic agent for MS, as it can directly target oxidative damage in the CNS[25] (Figure 2).

Several studies have investigated the effects of LA on oxidative stress in MS. These studies suggest that LA supplementation may help reduce oxidative markers in the serum and cerebrospinal fluid of MS patients, which could potentially slow the progression of the disease.[29,30] Additionally, LA has been shown to enhance total antioxidant capacity (TAC), which is an important indicator of the body's ability to counteract oxidative stress. Despite these promising results, the findings are not entirely consistent, with some studies failing to demonstrate significant improvements in oxidative stress markers.[17,23] This inconsistency may be due to differences in study designs, patient populations, or dosages of LA used, indicating the need for more standardized research to confirm its efficacy.[17,27]

Inflammation

Inflammation plays a central role in the pathogenesis of MS.[32] The entry of autoreactive T cells into the CNS triggers a cascade of immune responses that result in the activation of microglia, astrocytes, and other immune cells, leading to further inflammation and neuronal damage. This inflammatory process contributes to the formation of MS lesions and accelerates disease progression. In addition to T cells, B cells, macrophages, and other myeloid cells are also involved in the inflammatory response in MS.[33]

Lipoic acid has been shown to have potent anti-inflammatory effects, which could make it a valuable therapeutic agent for MS.[34] By inhibiting key inflammatory pathways, including the NF-κB pathway, LA can reduce the production of pro-inflammatory cytokines such as TNF-α, IL-6, and INF-γ.[35–37] These cytokines are implicated in the development and progression of MS lesions.[38] Several studies have demonstrated that LA supplementation can decrease the secretion of these inflammatory markers and reduce immune cell activation, suggesting that LA may help modulate the immune response in MS patients.[39] Furthermore, LA has been shown to enhance the production of cAMP, a molecule that plays a key role in regulating immune responses and inflammation.[40–42] By increasing cAMP levels, LA may inhibit the activation of inflammatory pathways and help to reduce the autoimmune response in MS.[31,43]

According to animal studies, similar results have been shown to decrease inflammation and oxidative stress[23] and improve the myelin repair.[14]

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Discussion

LA presents as a promising neuroprotective and anti-inflammatory agent for patients with multiple sclerosis (MS).[18] The compound's antioxidant properties can help mitigate oxidative stress, a major factor contributing to the progression of MS.[44] Additionally, LA's ability to modulate inflammatory responses and protect against brain atrophy makes it a potential complementary therapy for MS management.[19,20] Results from a 2014 study by Khalili et al showed that daily intake of 1200 mg LA significantly improved total antioxidant capacity in patients with MS, although other markers of oxidative stress were not affected.[21] While another randomized clinical trial conducted by Khalili et al in 2017, daily intake of 1200 mg of ALA helped reduce plasma Asymmetric dimethylarginine (ADMA) levels in patients with multiple sclerosis and prevented progression of Expanded Disability Status Scale (EDSS) score. However, no significant change was observed compared to the control group and larger studies are needed to confirm its clinical effects.[22] In a clinical trial conducted by Spain et al[17] in 2017 over a two-year period in patients with secondary progressive MS, daily administration of 1200 mg of LA reduced the rate of whole-brain atrophy and showed signs of improvement in motor function. This effect may be related to the duration of this study. In another study, oral administration of LA was well tolerated in patients with multiple sclerosis and resulted in reduced serum levels of matrix metalloproteinase-9 (MMP-9) and intercellular adhesion molecule-1 (sICAMP-1), indicating potential anti-inflammatory and inhibitory effects on T cell migration into the central nervous system. These findings suggest a possible role for LA in reducing inflammation and limiting demyelinating damage in MS.[19] Given that LA exists in different forms, a study showed that pure RLA caproate was better gastrointestinally tolerated and provided similar serum absorption than the racemic R, S-LA mixture. These findings suggest that the choice of LA form can influence the safety and clinical acceptability of the supplement, and that the use of R-LA may be a suitable option for long-term treatment.[18] Nonetheless, daily administration of 1200 mg of lipoic acid in patients with progressive multiple sclerosis in a study improved walking performance, indicating the potential effect of LA in preserving motor function and reducing the progression of physical limitations in secondary progressive multiple sclerosis (SPMS).[20] The potential mechanisms of the neuroprotective and anti-inflammatory effects of LA in animal models of MS are also reflected in the results of studies that LA can alter the activity of primary mouse microglia, including inhibition of phagocytosis, actin rearrangement, and formation of membrane blebs, and also reduce brain atrophy.[23] In another animal study, ALA supplementation demonstrated myelin regenerative activity and indicated neuroprotective and regenerative effects by reducing oxidative stress, neuroinflammation, and increasing the expression of major myelin proteins (MBP and PLP). These findings underscore the potential of ALA to stimulate remyelination and neuroprotection in MS.[14]

While evidence from preclinical and clinical studies suggests that LA supplementation may offer benefits, the findings are not entirely consistent, and further research is required to confirm its effectiveness and some supplements may be harmful and have the opposite results.[37] Long-term, multicenter, well-designed studies are necessary to determine the optimal dosages, administration methods, and potential combination therapies that could improve outcomes for MS patients.[45]

Strength and Limitations

Despite the promising effects of lipoic acid in clinical and animal studies, the results of some studies have been inconsistent. The differences may be due to variability in dose, duration of administration, type of LA form (R-LA or racemic mixture), patient population, and study design. Also, clinical studies often have small sample sizes and short durations, and animal and cellular models are unable to fully represent the complexity of human MS. These limitations make interpretation of the effects of LA cautious.

Research Gaps and Novelty

Given the limitations, future research should focus on large-scale, long-term, multicenter clinical trials to determine the optimal dose, appropriate form (R-LA or R, S-LA), and combination strategies with conventional therapies. The long-term effects of LA on myelin repair, motor function, microglial activity, and central immune responses also need to be investigated. Clarification of these issues may clarify the true role of LA in reducing disease progression and neuroprotection in MS.

Abbreviations

MS, Multiple sclerosis; LP, Lipoic acid; ALA, Alpha-lipoic acid; CNS, Central nervous system; OAMS, Older adults diagnosed with MS; TNF-α, Tumor necrosis factor alpha; INF-γ, Interferon gamma; BBB, Blood-brain barrier; NMR, Nuclear magnetic resonance; EAE, Experimental autoimmune encephalomyelitis; TAC, Total antioxidant capacity; RRMS, Relapsing-remitting multiple sclerosis; SPMS, Secondary progressive multiple sclerosis; MRI, Magnetic resonance imaging; GM, Gray matter; WM, White matter; EDSS, Expanded Disability Status Scale; ADMA, Asymmetric dimethylarginine; PKB, Protein kinase B; ON, Optic neuritis; Nrf2, Nuclear factor (erythroid-derived 2)-like 2; SPMS, Secondary progressive multiple sclerosis; PCBV, Percent change in brain volume; TBI, Traumatic brain injury; LPS, Lipopolysaccharide; SCI, Spinal cord injury; GPx, Glutathione peroxidase; hs-CRP, High-sensitivity C-reactive protein; SOD, Superoxide dismutase; SAH, Subarachnoid hemorrhage; RA, Rheumatoid arthritis; **Th**, T-helper cells; **IL**, Interleukin.

Data Sharing Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Cotsapas C, Mitrovic M, Hafler D. Multiple sclerosis. *Handb Clin Neurol*. 2018;148:723–730.
2. Hollenbach JA, Oksenberg JR. The immunogenetics of multiple sclerosis: a comprehensive review. *J Autoimmun*. 2015;64:13–25. doi:10.1016/j.jaut.2015.06.010
3. Walton C, King R, Rechtman L, et al. Rising prevalence of multiple sclerosis worldwide: insights from the Atlas of MS. *Mult Scler*. 2020;26(14):1816–1821. doi:10.1177/1352458520970841
4. Dastoorpoor M, Nabavi SM, Majdinasab N, Zare Javid A, Ahmadi Angali K, Seyedtabib M. A case-control study of drinking beverages and the risk of multiple sclerosis in Iran. *J Health Popul Nutr*. 2023;42(1):22. doi:10.1186/s41043-023-00364-8
5. Sîrbu CA, Thompson DC, Plesa FC, et al. Neurorehabilitation in multiple sclerosis-a review of present approaches and future considerations. *J Clin Med*. 2022;11(23):7003. doi:10.3390/jcm11237003
6. Jayasinghe M, Prathiraja O, Kayani AMA, et al. The role of diet and gut microbiome in multiple sclerosis. *Cureus*. 2022;14(9):e28975. doi:10.7759/cureus.28975
7. Guan JZ, Guan WP, Maeda T. Vitamin E administration erases an enhanced oxidation in multiple sclerosis. *Can J Physiol Pharmacol*. 2018;96(11):1181–1183. doi:10.1139/cjpp-2018-0246
8. Higdon J. Lipoic Acid 2002–2025. Available from: https://lpi.oregonstate.edu/mic/dietary-factors/lipoic-acid. Accessed February 10, 2026.
9. Tripathi AK, Ray AK, Mishra SK, Bishen SM, Mishra H, Khurana A. Molecular and therapeutic insights of alpha-lipoic acid as a potential molecule for disease prevention. *Rev Bras Farmacogn*. 2023;33(2):272–287. doi:10.1007/s43450-023-00370-1
10. Golbidi S, Badran M, Laher I. Diabetes and alpha lipoic Acid. *Front Pharmacol*. 2011;2:69. doi:10.3389/fphar.2011.00069
11. Espíndola KMM, Varela ELP, de Albuquerque RFV, et al. Alpha-lipoic acid and its enantiomers prevent methemoglobin formation and DNA damage induced by dapsone hydroxylamine: molecular mechanism and antioxidant Action. *Int J Mol Sci*. 2022;24(1):57. doi:10.3390/ijms24010057
12. Salehi B, Berkay Yılmaz Y, Antika G, et al. Insights on the Use of α-Lipoic Acid for Therapeutic Purposes. *Biomolecules*. 2019;9(8):356. doi:10.3390/biom9080356
13. Xie H, Yang X, Cao Y, Long X, Shang H, Jia Z. Role of lipoic acid in multiple sclerosis. *CNS Neurosci Ther*. 2022;28(3):319–331. doi:10.1111/cns.13793
14. Ibrahim Fouad G, Ahmed KA. Remyelinating activities of Carvedilol or alpha lipoic acid in the Cuprizone-Induced rat model of demyelination. *Int Immunopharmacol*. 2023;118:110125. doi:10.1016/j.intimp.2023.110125
15. Toyokuni S. Reactive oxygen species-induced molecular damage and its application in pathology. *Pathol Int*. 1999;49(2):91–102. doi:10.1046/j.1440-1827.1999.00829.x
16. Benveniste EN. Cytokine actions in the central nervous system. *Cytokine Growth Factor Rev*. 1998;9(3–4):259–275. doi:10.1016/S1359-6101(98)00015-X
17. Spain R, Powers K, Murchison C, et al. Lipoic acid in secondary progressive MS: a randomized controlled pilot trial. *Neurol Neuroimmunol Neuroinflamm*. 2017;4(5):e374. doi:10.1212/NXI.0000000000000374

18. Cameron M, Taylor C, Lapidus J, Ramsey K, Koop D, Spain R. Gastrointestinal tolerability and absorption of r- versus r,s-lipoic acid in progressive multiple sclerosis: a randomized crossover trial. *J Clin Pharmacol*. 2020;60(8):1099–1106. doi:10.1002/jcph.1605
19. Yadav V, Marracci G, Lovera J, et al. Lipoic acid in multiple sclerosis: a pilot study. *Mult Scler*. 2005;11(2):159–165. doi:10.1191/1352458505ms1143oa
20. Loy BD, Fling BW, Horak FB, Bourdette DN, Spain RI. Effects of lipoic acid on walking performance, gait, and balance in secondary progressive multiple sclerosis. *Complement Ther Med*. 2018;41:169–174. doi:10.1016/j.ctim.2018.09.006
21. Khalili M, Eghtesadi S, Mirshafiey A, et al. Effect of lipoic acid consumption on oxidative stress among multiple sclerosis patients: a randomized controlled clinical trial. *Nutr Neurosci*. 2014;17(1):16–20. doi:10.1179/1476830513Y.0000000060
22. Khalili M, Soltani M, Moghadam SA, Dehghan P, Azimi A, Abbaszadeh O. Effect of alpha-lipoic acid on asymmetric dimethylarginine and disability in multiple sclerosis patients: a randomized clinical trial. *Electron Physician*. 2017;9(7):4899–4905. doi:10.19082/4899
23. Chaudhary P, Marracci G, Pocius E, Galipeau D, Morris B, Bourdette D. Effects of lipoic acid on primary murine microglial cells. *J Neuroimmunol*. 2019;334:576972. doi:10.1016/j.jneuroim.2019.576972
24. Lewis JE, Poles J, Shaw DP, et al. The effects of twenty-one nutrients and phytonutrients on cognitive function: a narrative review. *J Clin Trans Res*. 2021;7(4):575–620.
25. van Horssen J, Schreibelt G, Drexhage J, et al. Severe oxidative damage in multiple sclerosis lesions coincides with enhanced antioxidant enzyme expression. *Free Radic Biol Med*. 2008;45(12):1729–1737. doi:10.1016/j.freeradbiomed.2008.09.023
26. Miller ED, Dziedzic A, Saluk-Bijak J, Bijak M. A review of various antioxidant compounds and their potential utility as complementary therapy in multiple sclerosis. *Nutrients*. 2019;11(7):1528. doi:10.3390/nu11071528
27. Bergsland N, Horakova D, Dwyer MG, et al. Gray matter atrophy patterns in multiple sclerosis: a 10-year source-based morphometry study. *Neuroimage Clin*. 2018;17:444–451. doi:10.1016/j.nicl.2017.11.002
28. Alvarez E, Nair KV, Hoyt BD, et al. Brain atrophy rates in patients with multiple sclerosis on long term natalizumab resembles healthy controls. *Mult Scler Relat Disord*. 2021;55:103170. doi:10.1016/j.msard.2021.103170
29. Dietrich M, Helling N, Hilla A, et al. Early alpha-lipoic acid therapy protects from degeneration of the inner retinal layers and vision loss in an experimental autoimmune encephalomyelitis-optic neuritis model. *J Neuroinflammation*. 2018;15(1):71. doi:10.1186/s12974-018-1111-y
30. Ozbal S, Cankurt U, Tugyan K, et al. The effects of α-lipoic acid on immature rats with traumatic brain injury. *Biotech Histochem*. 2015;90(3):206–215. doi:10.3109/10520295.2014.977950
31. Fiedler SE, Yadav V, Kerns AR, et al. Lipoic acid stimulates camp production in healthy control and secondary progressive ms subjects. *Mol Neurobiol*. 2018;55(7):6037–6049. doi:10.1007/s12035-017-0813-y
32. Waldburger KE, Hastings RC, Schaub RG, Goldman SJ, Leonard JP. Adoptive transfer of experimental allergic encephalomyelitis after in vitro treatment with recombinant murine interleukin-12. Preferential expansion of interferon-gamma-producing cells and increased expression of macrophage-associated inducible nitric oxide synthase as immunomodulatory mechanisms. *Am J Pathol*. 1996;148(2):375–382.
33. Traugott U, Reinherz EL, Raine CS. Multiple sclerosis. Distribution of T cells, T cell subsets and Ia-positive macrophages in lesions of different ages. *J Neuroimmunol*. 1983;4(3):201–221. doi:10.1016/0165-5728(83)90036-X
34. Panitch HS, Hirsch RL, Schindler J, Johnson KP. Treatment of multiple sclerosis with gamma interferon: exacerbations associated with activation of the immune system. *Neurology*. 1987;37(7):1097–1102. doi:10.1212/WNL.37.7.1097
35. Lock C, Hermans G, Pedotti R, et al. Gene-microarray analysis of multiple sclerosis lesions yields new targets validated in autoimmune encephalomyelitis. *Nat Med*. 2002;8(5):500–508. doi:10.1038/nm0502-500
36. Ando DG, Clayton J, Kono D, Urban JL, Sercarz EE. Encephalitogenic T cells in the B10.PL model of experimental allergic encephalomyelitis (EAE) are of the Th-1 lymphokine subtype. *Cell Immunol*. 1989;124(1):132–143. doi:10.1016/0008-8749(89)90117-2
37. Bettelli E, Sullivan B, Szabo SJ, Sobel RA, Glimcher LH, Kuchroo VK. Loss of T-bet, but not STAT1, prevents the development of experimental autoimmune encephalomyelitis. *J Exp Med*. 2004;200(1):79–87. doi:10.1084/jem.20031819
38. Packer L, Witt EH, Tritschler HJ. alpha-Lipoic acid as a biological antioxidant. *Free Radic Biol Med*. 1995;19(2):227–250. doi:10.1016/0891-5849(95)00017-R
39. Kohm AP, Carpentier PA, Anger HA, Miller SD. Cutting edge: CD4+CD25+ regulatory T cells suppress antigen-specific autoreactive immune responses and central nervous system inflammation during active experimental autoimmune encephalomyelitis. *J Immunol*. 2002;169(9):4712–4716. doi:10.4049/jimmunol.169.9.4712
40. Bharti AC, Aggarwal BB. Nuclear factor-kappa B and cancer: its role in prevention and therapy. *Biochem Pharmacol*. 2002;64(5–6):883–888. doi:10.1016/S0006-2952(02)01154-1
41. Siritho S, Freedman MS. The prognostic significance of cerebrospinal fluid in multiple sclerosis. *J Neurol Sci*. 2009;279(1–2):21–25. doi:10.1016/j.jns.2008.12.029
42. Haase S, Linker RA. Inflammation in multiple sclerosis. *Ther Adv Neurol Disord*. 2021;14:17562864211007687. doi:10.1177/17562864211007687
43. Salinthone S, Yadav V, Schillace RV, Bourdette DN, Carr DW. Lipoic acid attenuates inflammation via cAMP and protein kinase A signaling. *PLoS One*. 2010;5(9). doi:10.1371/journal.pone.0013058
44. Mirtaheri E, Gargari BP, Kolahi S, et al. Effects of alpha-lipoic acid supplementation on inflammatory biomarkers and matrix metalloproteinase-3 in rheumatoid arthritis patients. *J Am Coll Nutr*. 2015;34(4):310–317. doi:10.1080/07315724.2014.910740
45. Mohammadi V, Khalili M, Eghtesadi S, et al. The effect of alpha-lipoic acid (ALA) supplementation on cardiovascular risk factors in men with chronic spinal cord injury: a clinical trial. *Spinal Cord*. 2015;53(8):621–624. doi:10.1038/sc.2015.35