Effect of anti-inflammatory diets based on complementary and alternative medicine in multiple sclerosis: a systematic review and meta analysis of clinical trials

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Abstract

Background:

The role of diet in modulating inflammation has garnered attention, particularly regarding anti-inflammatory dietary interventions rooted in complementary medicine. The present study examined the clinical manifestations through which anti-inflammatory diets may influence MS, providing insights for clinician researchers.

Methods:

A thorough search was performed in Scopus, MEDLINE (PubMed), ScienceDirect, EMBASE, Google Scholar, Central Cochrane Library, and the Web of Science, covering trials published until April 2025. Random effect models were used to analyze the quantitative data through $STATA_{14}$.

Results:

After analyzing 246 entries, we found 10 Randomized Controlled Trials (RCTs) with a total of 332 participants, who had an average disease duration of 8.7 years. The combined effect size revealed a decrease in fatigue severity (Weighted Mean Difference [WMD]= -7.10; 95% Confidence Interval [CI] = -13.61, -0.59; P=0.032) and an increase in physical health score (WMD= 2.59; 95% CI= 0.17, 5.00; P=0.036).

Conclusion:

Anti-inflammatory diets may improve MS clinical manifestations especially fatigue and disability, therefore, more researches are needed to confirm the present findings.

MeSH Keywords:

Multiple sclerosis; Anti-inflammatory diet; Complementary Therapies; Inflammation; Meta-analysis; Systematic review

1. Introduction

Multiple Sclerosis (MS) is a chronic autoimmune disorder characterized by neuroinflammation and demyelination of nerve fibers in the central nervous system [1]. MS presents significant challenges not only in the management but also in understanding its complex pathophysiology [2].

The pursuit of holistic treatment options has led to a growing interest in dietary modifications aimed at reducing systemic inflammation. Anti-inflammatory diets encompass various nutritional strategies believed to exert beneficial effects on immune function, mitigate oxidative stress, and promote gut health [3]. While disease-modifying therapies remain the cornerstone of MS treatment, anti-inflammatory diets may serve as a complementary approach [4]. Clinician researchers should investigate patient adherence to dietary changes and their correlation with clinical outcomes.

Anti-inflammatory diets typically emphasize foods rich in specific nutrients known to modulate inflammatory processes. These include omega-3 fatty acids, found abundantly in fatty fish and flaxseeds, which are crucial for producing bioactive lipids such as resolvins [5]. These metabolites not only promote the resolution of inflammation but also encourage the production of anti-inflammatory cytokines like Interleukin-4 (IL-4) while inhibiting pro-inflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-α), IL-17, and high-sensitivity C-Reactive Protein (hs-CRP) [6, 7].

A meta-analysis by Guerrero Aznar et al. [8] showed that dietary intervention is associated with a trend of reduction in fatigue in MS. Another meta-analysis by Snetselaar et al. [9] reported that several dietary interventions may improve physical and mental Quality of Life (QoL) in MS patients. The current review specifically focused on anti-inflammatory diets in the context of complementary and alternative medicine, to create a detailed insight into the

efficacy of dietary intervention in MS. Therefore, we conducted a comprehensive reanalysis of relevant RCTs to determine the effectiveness of the anti-inflammatory diets in MS patients, specifically concerning anthropometric indices, quality of life, and serum inflammation.

2. Materials & Methods

2.1. Protocol

The research protocol was developed in accordance with the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [10], as detailed in Supplementary Table 1. Additionally, this systematic review was formally registered in the International Prospective Register of Systematic Reviews (PROSPERO) database under registration number CRD42022368118 on October 30, 2022.

2.2. Literature Search

Two independent researchers conducted a systematic search of electronic databases up to April 2025, with details provided in Supplementary Table 2. The databases included ISI Web of Science, Embase, MEDLINE (PubMed), Cochrane Central Register of Controlled Trials (CENTRAL), Google Scholar, ScienceDirect, and Scopus.

The search strategy incorporated both Medical Subject Headings (MeSH) and non-MeSH keywords to ensure comprehensive coverage: (("Anti-inflammatory Diet" OR " Complementary and Alternative Medicine" OR "Integrative Medicine" OR "CAM" OR "Diet" OR "Plant-based Diet" OR "Healthy Diet") AND ("Relapsing-Remitting Multiple Sclerosis" OR "Multiple Sclerosis" OR "RRMS" OR "MS") AND ("Intervention" OR "Intervention Study" OR "Intervention Studies" OR "Controlled trial" OR "Randomised" OR "Randomized controlled trial" OR "Randomized clinical trial" OR "Randomized clinical trial" OR "RCT"

OR "Non-Randomized Controlled Trials" OR "Clinical Trials" OR "Clinical Trial" OR "Trial" OR "Trials" OR "Non-Randomized Controlled Trials" OR "Cross-Over study" OR "Cross-Over trial" OR "Cross Over trial" OR "Cross Over study" OR "Double-Blind Method" OR "Double-Blind" OR "Double-Blind trial" OR "Double-Blind study")). Reference lists of included trials were also thoroughly examined to identify additional relevant studies.

2.3. Selection criteria

Inclusion was restricted to trials published in English. Eligible studies comprised those with single-, double-, or triple-blind designs, employing either parallel or crossover methodologies, and featuring at least two arms. These studies evaluated the effects of the anti-inflammatory diets based on complementary and alternative medicine on anthropometric indices (Body Weight [BW], Body Mass Index [BMI], Wrist Circumference [WC]), Expanded Disability Status Scale (EDSS), Modified Fatigue Impact Scale (MFIS), Physical Health Composite Score (PHCS), Mental Health Composite Score (MHCS), inflammatory markers (hs-CRP, IL-4, IL-17), and liver enzymes (Serum Glutamic-Oxaloacetic Transaminase [SGOT], Serum Glutamic Pyruvic Transaminase [SGPT]) in MS patients aged 18-60 years, with corresponding control groups. One author initially screened articles and abstracts for relevance. Subsequently, two authors independently reviewed the full texts of non-duplicate articles, with discrepancies resolved by a third independent reviewer.

2.4. Data Extraction

Data extraction was performed by a single author. Extracted variables included:

- First author of the study,
- Year of publication and study location,

- Study design and duration,
- Baseline participant characteristics (age, gender, disease duration, and Expanded Disability Status Scale (EDSS)),
- Details of intervention and control groups, and
- Primary outcome measures, such as body mass index (BMI) and Modified Fatigue Impact Scale (MFIS).

When data were incomplete or unclear, corresponding authors were contacted via email for clarification.

2.5. Risk of Bias (Quality Assessment)

The quality of included trials was assessed by two researchers using the Cochrane Risk-of-Bias (RoB) tool (version 5.0) [11]. Discrepancies were resolved by a third reviewer. Evaluated domains included:

a. Allocation concealment (selection bias),

b. Random sequence generation (selection bias),

c. Blinding of participants and personnel (performance bias),

d. Blinding of outcome assessment (detection bias),

e. Incomplete outcome data (attrition bias), and

f. Selective reporting (reporting bias).

Each domain was classified as “low risk,” “high risk,” or “some concerns” of bias.

2.6. Statistical analysis

Meta-analysis was conducted using STATA software version 14 (StataCorp LP, College Station, TX, USA). Data were entered as mean differences with standard deviations (m ± SD). A random-effects model was employed to calculate Weighted Mean Differences (WMDs) with

95% Confidence Intervals (CIs). When only Standard Error of the Mean (SEM) was reported, Standard Deviation (SD) was derived using the formula:

$$SD = SEM \times \sqrt{n} \text{ (where n = number of subjects) [12].}$$

For trials reporting median and Interquartile Range (IQR) or 95% CI, mean and SD were estimated per Hozo et al. [13]. Between-study heterogeneity was assessed using the I^2 test. Sensitivity analyses evaluated the impact of excluding individual studies. Publication bias was examined using Begg's rank correlation and Egger's weighted regression tests, with statistical significance set at $P < 0.05$.

3. Results

3.1. Search Details

The initial literature search identified 246 records. After excluding 74 records (92 duplicates, 6 animal studies, and 3 cell-based studies), 97 additional papers were excluded following title and abstract screening, and 38 articles were removed after full-text review. Ultimately, 10 RCTs involving 332 patient records, published between 2013 and 2024, were included for quantitative analysis (**Figure 1**) [6, 14-22].

3.2. Study Characteristics

Key characteristics of the included RCTs are summarized in **Table 1** [6, 14-22]. A total of 332 participants (167 intervention, 165 control) with a mean age of 37.9 years and mean disease duration of 8.7 years were enrolled. Due to an 8.7% average dropout rate, data from 303 participants were analyzed. All RCTs utilized a two-arm parallel design and included both genders (female-to-male ratio: 3.2). Five researches were conducted on RRMS patients [6, 18-

21], four researches on progressive forms [14-17], and one study selected a mixed population [22]. Follow-up durations ranged from 8 to 24 weeks.

3.3. Risk of Bias (Quality) Assessment

Eight RCTs were classified as low risk of bias [14-21], while two raised concerns [6, 22]. Random sequence generation and allocation concealment showed low risk, minimizing selection bias. The Higher rate of risk was noted for performance bias [6, 14-17, 22], and detection bias [6, 22], however, some concerns were identified in terms of reporting bias [6, 14-16, 18-21]. Details are provided in **Figure 2**.

3.4. Results of Meta-analysis

3.4.1. Anthropometric Indices

Within the pooled analysis encompassing four studies involving 265 participants (intervention: 133; control: 132) [6, 15, 17, 22], effect of anti-inflammatory diets on BW (WMD= -0.22 kg; 95% CI= -2.42, 1.99; P= 0.846) and BMI (WMD= 0.01 kg/m^2; 95% CI= -0.84, 0.85; P= 0.990) were not statistically significant with no heterogeneity in both (I^2= 0.0 %; P= 0.999, P= 0.978, respectively) (**Figure 3A-B**).

Moreover, the pooled effects of three RCTs investigating the impact of anti-inflammatory diets on WC in 161 MS patients (intervention, 81; control, 80) was not significant (P= 0.364) [15, 17, 22](**Figure 3C**).

3.4.2. EDSS

Pooled analysis of four studies (228 participants: 115 intervention, 113 control) did not show any significant effect (WMD = -0.14; 95% CI: -0.42, 0.14; P = 0.321), and heterogeneity (I^2 = 0.0%; P = 0.709) [16-18, 22](**Figure 4A**).

3.4.3. MFIS

Across three RCTs (244 participants), a significant downward trend for MFIS was observed (WMD = -7.10; 95% CI: -13.61, -0.59; P = 0.032) [6, 14, 17]. Significant heterogeneity was present (I^2 = 79.9%; P = 0.007) (**Figure 4B**).

3.4.4. PHCS & MHCS

Although the pooled estimate did not demonstrate a significant rising in MHCS (WMD = 0.89; 95% CI = -1.01, 2.79, P =0.358), PHCS showed considerable improvement [6, 16, 17](WMD = 2.59; 95% CI = 0.17, 5.00, P =0.036) (**Figure 4D-C**). Moreover, no study heterogeneity was found (I^2 = 0.0%, P = 0.549 for MHCS, P = 0.667 for PHCS).

3.4.5. Serum Inflammation

The pooled estimate analysis did not detect any significant trend for hs-CRP (WMD = -0.12; 95% CI = -0.29, 0.05, P =0.162) [6, 17], IL-4 (WMD = -0.02; 95% CI = -0.48, 0.44, P =0.942) [6, 20], and IL-17 (WMD = -0.06; 95% CI = -0.13, 0.01, P =0.85) [6, 21] (**Figure 5A-C**). Test of heterogeneity did not yield a statistically significant result for hs-CRP (I^2 = 10.3%, P = 0.291), IL-4 (I^2 = 0.0%, P = 0.699), and IL-17 (I^2 = 0.0%, P = 0.822).

3.4.6. Liver Enzymes

While a decreasing trend in SGOT (WMD= -2.93; 95% CI = -7.79, 1.92; P= 0.239) and SGPT (WMD= -0.51; 95% CI = -13.76, 12.74; P= 0.939) was observed (***Figure 5D-E***), the pooled estimate did not indicate a significant enhancement across two RCTs involving 88 participants [19, 22]. Furthermore, there was identified study heterogeneity for SGPT (I^2 = 80.2%, P=0.025), as depicted in ***Figure 5D***.

3.5. Sensitivity Analysis and Publication Bias

Sensitivity analyses showed no significant changes in outcomes. No publication bias was detected for BW (Begg's: P = 0.734; Egger's: P = 0.562), BMI (Begg's: P = 0.734; Egger's: P = 0.403), WC (Begg's: P = 1.000; Egger's: P = 0.910), EDSS (Begg's: P = 0.308; Egger's: P = 0.307), MFIS (Begg's: P = 1.000; Egger's: P = 0.442), PHCS (Begg's: P = 1.000; Egger's: P = 0.937), MHCS (Begg's: P = 1.000; Egger's: P = 0.693), hs-CRP (Begg's: P = 1.000; Egger's: -), IL-4 (Begg's: P = 1.000; Egger's: -), IL-17 (Begg's: P = 1.000; Egger's: -), SGOT (Begg's: P = 1.000; Egger's: -), or SGPT (Begg's: P = 1.000; Egger's: P = -).

4. Discussion

In the current systematic review and meta-analysis comprising 10 RCTs, adherence to the anti-inflammatory diets shown to be effective in fatigue reduction and physical health improvement.

The quest for adjunctive therapies in the management of MS has led to increasing interest in the potential of dietary modifications. Anti-inflammatory diets are believed to have beneficial effects by modulating immune responses, reducing oxidative stress, and improving gut health [23]. This paper examined the pooled effects of anti-inflammatory diets and their potential roles in influencing the cellular and immunological landscape in individuals with MS.

Anti-inflammatory diets, often inspired by complementary and alternative medicine, focus on foods like fish, fruits, vegetables, and whole grains while cutting back on processed foods and red meat [24]. For people with MS, a condition where the immune system attacks the nervous system, these diets might help reduce fatigue and improve physical health by lowering inflammation in the body [25]. Research suggests they work by calming down the immune response and supporting overall health, but the exact benefits can vary from person to person [26]. It seems likely that these diets reduce inflammation through molecular pathways, such as

lowering proinflammatory cytokines like IL-17, IL-1β and IL-6, which are linked to fatigue in MS [27]. Foods rich in omega-3 fatty acids, like fish, may also help by promoting regulatory T cells, which calm the immune system [28]. Fiber from fruits and vegetables supports gut bacteria, producing substances that might protect nerve cells [29]. While these mechanisms are promising, more research is needed to confirm how well they work for everyone.

There are various molecular and biological mechanisms by which anti-inflammatory diets, based on complementary and alternative medicine, may improve fatigue and physical health in MS. Anti-inflammatory diets, such as the Mediterranean diet and DASH diet, are hypothesized to mitigate these effects by modulating immune responses and reducing oxidative stress [30]. Anti-inflammatory diets influence MS through several molecular pathways, primarily targeting inflammation and immune regulation. PUFAs, particularly omega-3 fatty acids, are metabolized into anti-inflammatory prostaglandins (e.g., PGE1, PGE2), which modulate cytokine production and leukocyte migration [31]. Studies indicate that PUFAs induce Peroxisome Proliferator-Activated Receptors (PPAR) in CNS-infiltrating T cells, reducing inflammation [32]. Preclinical models, like the cuprizone-induced demyelination model, show that EPA pretreatment reduces weight loss and increases cerebroside content, suggesting neuroprotection and remyelination [33].

Fruits, vegetables, and whole grains impact gut microbiota, fermenting fiber into Short-Chain Fatty Acids (SCFAs) like butyrate [34, 35]. SCFAs promote Treg differentiation and reduce pro-inflammatory cytokines via GPCR activation (e.g., GPR43) and HDAC inhibition [36-38]. Tryptophan metabolites from cruciferous vegetables activate the Aryl hydrocarbon Receptor (AhR), inducing $FoxP3^{+}$ Tregs and IL-10-producing Tr1 cells, inhibiting Th17 differentiation, and crossing the blood-brain barrier to affect astrocytes [39]. Flavonoids, AhR agonists found in fruits and vegetables, show anti-inflammatory effects, neuroprotection, and remyelination in EAE models [40]. Specific diets like the Mediterranean diet [41], McDougall

diet (very low-fat, plant-based) and Paleolithic diet (lean meats, vegetables, no dairy/grains) may reduce proinflammatory effects through low saturated fat and high fiber, though evidence is preliminary [42, 43].

Genetic factors influence MS susceptibility and response to dietary interventions. Research highlights interactions between diet and polymorphisms in fatty acid biosynthesis genes, particularly FADS2 [44]. Researchers found that FADS2 SNPs rs174611 and rs174618 are associated with lower MS risk, linked to omega-3 PUFA metabolism. Genetic factors might play a role in how well these diets work for MS [45]. For example, certain gene variants, like those in the FADS2 gene related to omega-3 metabolism, could influence MS risk and how someone responds to diet [44]. Foods like seafood, vegetables, and supplements (e.g., vitamin D, folic acid) are often highlighted, but the best mix is still debated.

Anti-inflammatory food agents also include magnesium, niacin, and vitamins D, A, E, found in fruits, vegetables, whole grains, fish, nuts, and dairy [46]. Studies link higher intake of calcium, iron, folic acid, vitamin B12, and C to lower primary progressive MS incidence [47]. Proinflammatory agents include carbohydrates, cholesterol, total fat, saturated fat, trans fat, and red meat, associated with increased MS risk [48]. Researchers found higher fruit/vegetable intake reduces disease activity and disability, with MS studies showing almost 50% decreased relapse risk per cup-equivalent vegetable increase [49].

The Dietary Inflammatory Index (DII) helps measure how inflammatory a diet is, with lower scores linked to better MS outcomes, but individual responses can differ [50]. There's some controversy over which foods are best for MS, with debates about dairy and other items. Lower DII diets, rich in anti-inflammatory foods, may reduce fatigue and improve physical health by mitigating systemic inflammation [51, 52]. While early studies are encouraging, we need more long-term research to be sure these diets are safe and effective for everyone.

Personalized approaches are also exciting, but they're still in early stages, and not all findings apply to every population.

Limitations

The current meta-analysis presents several limitations that warrant attention. The most significant limitation of this systematic review and meta-analysis is the limited number of studies available. Certain variables were reported in only two studies, which adversely impacted the pooled effect analysis. Additionally, a considerable degree of heterogeneity was noted in certain outcomes, and the sources of heterogeneity could not be explored through subgroup analysis. Finally, further RCTs with larger sample sizes would be require for confirming the present results.

5. Conclusion

This systematic review and meta-analysis suggest the anti-inflammatory diets may effectively normalize physical health as a QoL indicator in MS patients. A slight reduction in fatigue severity was also observed, however, additional trials assessing serological, functional, and physical outcomes are warranted to fully evaluate anti-inflammatory diets efficacy in MS management.

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Conflicts of interest

The authors declare no conflicts of interest.

Figure Legends:

Figure 1. PRISMA flow diagram of the selected studies

Figure 2. Risk of bias assessment

Figure 3. Pooled effect sizes describing the efficacy of anti-inflammatory diets based on complementary and alternative medicine on anthropometric indices "BW (A)(P= 0.846), BMI (B) (P= 0.990), and WC (C) (P= 0.364). BW, body weight; BMI, body mass index; WC, waist circumference.

Figure 4. Pooled effect sizes describing the efficacy of anti-inflammatory diets based on complementary and alternative medicine on EDSS (A)(P= 0.321), MFIS (B) (P= 0.032), PHCS (C) (P= 0.036), and MHCS (D) (P= 0.358). EDSS, expanded disability status scale; MFIS, modified fatigue impact scale; PHCS, physical health composite score; MHCS, mental health composite score. PHCS and MHCS are two main final scores of Multiple Sclerosis Quality of Life-54 items (MSQOL) questionnaire.

Figure 5. Pooled effect sizes describing the efficacy of anti-inflammatory diets based on complementary and alternative medicine on hs-CRP (A)(P= 0.162), IL-4 (B)(P= 0.942), IL-17 (C)(P= 0.085), SGOT (D)(P= 0.236), and SGPT (E)(P= 0.939). hs-CRP, high sensitive C-reactive protein; IL interleukin; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase.

References:

1. Mirashrafi S, Hejazi Taghanaki SZ, Sarlak F, Moravejolahkami AR, Hojjati Kermani MA, Haratian M. Effect of probiotics supplementation on disease progression, depression, general health, and anthropometric measurements in relapsing-remitting multiple sclerosis patients: A systematic review and meta-analysis of clinical trials. Int J Clin Pract. 2021;75(11):e14724. https://doi.org/10.1111/ijcp.14724.

2. Moravejolahkami AR, Paknahad Z, Chitsaz A. Association of dietary patterns with systemic inflammation, quality of life, disease severity, relapse rate, severity of fatigue and anthropometric measurements in MS patients. Nutr Neurosci. 2020;23(12):920-30. https://doi.org/10.1080/1028415X.2019.1580831.

3. van Zonneveld SM, van den Oever EJ, Haarman BC, Grandjean EL, Nuninga JO, van de Rest O, et al. An Anti-Inflammatory Diet and Its Potential Benefit for Individuals with Mental Disorders and Neurodegenerative Diseases—A Narrative Review. Nutrients. 2024;16(16):2646.

4. Shin S, Chen S, Xie K, Duhun SA, Ortiz-Cerda T. Evaluating the anti-inflammatory and antioxidant efficacy of complementary and alternative medicines (CAM) used for management of inflammatory bowel disease: a comprehensive review. Redox Rep. 2025;30(1):2471737. https://doi.org/10.1080/13510002.2025.2471737.

5. Bo C, Liu X, Liu Y, Xu L, Huang Q. Resolvin D1 accelerates resolution of neuroinflammation by inhibiting microglia activation through the BDNF/TrkB signaling pathway. European Journal of Medical Research. 2025;30(1):189.

6. Mousavi-Shirazi-Fard Z, Mazloom Z, Izadi S, Fararouei M. The effects of modified anti-inflammatory diet on fatigue, quality of life, and inflammatory biomarkers in relapsing-remitting multiple sclerosis patients: a randomized clinical trial. Int J Neurosci. 2021;131(7):657-65. https://doi.org/10.1080/00207454.2020.1750398.

7. Ricker MA, Haas WC. Anti-Inflammatory Diet in Clinical Practice: A Review. Nutr Clin Pract. 2017;32(3):318-25. https://doi.org/10.1177/0884533617700353.

8. Guerrero Aznar MD, Villanueva Guerrero MD, Cordero Ramos J, Eichau Madueno S, Morales Bravo M, Lopez Ruiz R, et al. Efficacy of diet on fatigue, quality of life and disability status in multiple sclerosis patients: rapid review and meta-analysis of randomized controlled trials. BMC Neurol. 2022;22(1):388. https://doi.org/10.1186/s12883-022-02913-w.

9. Snetselaar LG, Cheek JJ, Fox SS, Healy HS, Schweizer ML, Bao W, et al. Efficacy of Diet on Fatigue and Quality of Life in Multiple Sclerosis: A Systematic Review and Network Meta-analysis of Randomized Trials. Neurology. 2023;100(4):e357-e66. https://doi.org/10.1212/WNL.0000000000201371.

10. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Annals of internal medicine. 2009;151(4):W-65-W-94.

11. Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. https://doi.org/10.1136/bmj.l4898.

12. Peng W, Mao P, Liu L, Chen K, Zhong Y, Xia W, et al. Effect of carnosine supplementation on lipid profile, fasting blood glucose, HbA1C and insulin resistance: A systematic review and meta-analysis of long-term randomized controlled trials. Complement Ther Med. 2020;48:102241. https://doi.org/10.1016/j.ctim.2019.102241.

13. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005;5(1):13. https://doi.org/10.1186/1471-2288-5-13.

14. Moravejolahkami AR, Chitsaz A, Hassanzadeh A, Paknahad Z. Anti-inflammatory-antioxidant modifications and synbiotics improved health-related conditions in patients with progressive forms of multiple sclerosis: A single-center, randomized clinical trial. Complement Ther Clin Pract. 2023;53:101794. https://doi.org/10.1016/j.ctcp.2023.101794.

15. Moravejolahkami AR, Chitsaz A, Hassanzadeh A, Paknahad Z. Effects of anti-Inflammatory-antioxidant-rich diet and co-supplemented synbiotics intervention in patients with progressive forms of multiple sclerosis: a single-center, single-blind randomized clinical trial. Nutr Neurosci. 2023;26(11):1078-89. https://doi.org/10.1080/1028415X.2022.2128010.

16. Moravejolahkami AR, Chitsaz A, Hassanzadeh A, Paknahad Z. Co-supplementation of synbiotics and anti-inflammatory-antioxidant rich diet in patients with progressive forms of multiple sclerosis: A single-center, randomized clinical trial. Mediterranean Journal of Nutrition and Metabolism. 2024;17(2):133-47.

17. Moravejolahkami AR, Hadi S, Hadi V, Mirghazanfari SM, Mohajeri M. Effects of Dietary Modification Based on Complementary and Alternative Iranian Medicine in Patients with Secondary-Progressive Multiple Sclerosis: A Randomized Controlled Clinical Trial. J Integr Complement Med. 2023;29(11):747-56. https://doi.org/10.1089/jicm.2023.0037.

18. Rezapour-Firouzi S, Arefhosseini SR, Ebrahimi-Mamaghani M, Baradaran B, Sadeghihokmabad E, Mostafaei S, et al. Alteration of delta-6-desaturase (FADS2), secretory phospholipase-A2 (sPLA2) enzymes by Hot-nature diet with co-supplemented hemp seed, evening primrose oils intervention in multiple sclerosis patients. Complement Ther Med. 2015;23(5):652-7. https://doi.org/10.1016/j.ctim.2015.07.003.

19. Rezapour-Firouzi S, Arefhosseini SR, Ebrahimi-Mamaghani M, Baradaran B, Sadeghihokmabad E, Torbati M, et al. Activity of liver enzymes in multiple sclerosis patients with Hot-nature diet and co-supplemented hemp seed, evening primrose oils intervention. Complement Ther Med. 2014;22(6):986-93. https://doi.org/10.1016/j.ctim.2014.10.004.

20. Rezapour-Firouzi S, Arefhosseini SR, Ebrahimi-Mamaghani M, Farhoudi M, Baradaran B, Ali TM, et al. Erythrocyte membrane fatty acids in multiple sclerosis patients and hot-nature dietary intervention with co-supplemented hemp-seed and evening-primrose oils. Afr J Tradit Complement Altern Med. 2013;10(6):519-27. https://doi.org/10.4314/ajtcam.v10i6.22.

21. Rezapour-Firouzi S, Arefhosseini SR, Mehdi F, Mehrangiz EM, Baradaran B, Sadeghihokmabad E, et al. Immunomodulatory and therapeutic effects of Hot-nature diet and co-supplemented hemp seed, evening primrose oils intervention in multiple sclerosis patients. Complement Ther Med. 2013;21(5):473-80. https://doi.org/10.1016/j.ctim.2013.06.006.

22. Riccio P, Rossano R, Larocca M, Trotta V, Mennella I, Vitaglione P, et al. Anti-inflammatory nutritional intervention in patients with relapsing-remitting and primary-progressive multiple sclerosis: A pilot study. Exp Biol Med (Maywood). 2016;241(6):620-35. https://doi.org/10.1177/1535370215618462.

23. Guerrero Aznar MD, Villanueva Guerrero MD, Beltrán García M, Hernández Cruz B. Specific Composition Diets and Improvement of Symptoms of Immune-Mediated Inflammatory Diseases in Adulthood—Could the Comparison Between Diets Be Improved? Nutrients. 2025;17(3):493.

24. Zhang Y, Iob E, Tapia Munoz T. Identifying leading anti-inflammatory dietary determinants of depression and loneliness in older adults. Brain Behav Immun Health. 2025;46:101000. https://doi.org/10.1016/j.bbih.2025.101000.

25. Guglielmetti M, Ferraris C, Neri LdCL, Frias-Toral E, Tagliabue A, Tavazzi E, et al. Dietary Inflammatory Score (DIS)'s and Lifestyle Inflammatory Score (LIS)'s Impact on Multiple Sclerosis Severity. Nutrients. 2025;17(3):526.

26. Yu X, Pu H, Voss M. Overview of anti-inflammatory diets and their promising effects on non-communicable diseases. British Journal of Nutrition. 2024:1-21.

27. Atabilen B, Akdevelioglu Y, Acar Ozen P, Tuncer A. Examining dietary habits in the context of multiple sclerosis: A comprehensive investigative approach. Mult Scler Relat Disord. 2024;83:105467. https://doi.org/10.1016/j.msard.2024.105467.

28. Jerab D, Blangero F, da Costa PCT, de Brito Alves JL, Kefi R, Jamoussi H, et al. Beneficial Effects of Omega-3 Fatty Acids on Obesity and Related Metabolic and Chronic Inflammatory Diseases. Nutrients. 2025;17(7):1253. https://doi.org/10.3390/nu17071253.

29. Barcutean L, Maier S, Burai-Patrascu M, Farczadi L, Balasa R. The Immunomodulatory Potential of Short-Chain Fatty Acids in Multiple Sclerosis. Int J Mol Sci. 2024;25(6):3198. https://doi.org/10.3390/ijms25063198.

30. Solsona EM, Tektonidis T, Reece JC, Simpson-Yap S, Black LJ, Rad EY, et al. Associations between diet and disease progression and symptomatology in multiple sclerosis: A systematic review of observational studies. Multiple Sclerosis and Related Disorders. 2024:105636.

31. Al-Naqeb G, Kalmpourtzidou A, De Giuseppe R, Cena H. Beneficial Effects of Plant Oils Supplementation on Multiple Sclerosis: A Comprehensive Review of Clinical and Experimental Studies. Nutrients. 2023;15(22):4827. https://doi.org/10.3390/nu15224827.

32. Yu H, Bai S, Hao Y, Guan Y. Fatty acids role in multiple sclerosis as "metabokines". Journal of Neuroinflammation. 2022;19(1):157.

33. Di Biase A, Salvati S, Di Benedetto R, Attorri L, Martinelli A, Malchiodi F. Eicosapentaenoic acid pre-treatment reduces biochemical changes induced in total brain and myelin of weanling Wistar rats by cuprizone feeding. Prostaglandins Leukot Essent Fatty Acids. 2014;90(4):99-104. https://doi.org/10.1016/j.plefa.2013.11.004.

34. Moravejolahkami AR, Hojjati Kermani MA, Balouch Zehi Z, Mirenayat SMS, Mansourian M. The effect of probiotics on lipid profile & anthropometric indices in diabetic nephropathy; a systematic review and meta-analysis of clinical trials. J Diabetes Metab Disord. 2021;20(1):893-904. https://doi.org/10.1007/s40200-021-00765-8.

35. Bohlouli J, Namjoo I, Borzoo-Isfahani M, Hojjati Kermani MA, Balouch Zehi Z, Moravejolahkami AR. Effect of probiotics on oxidative stress and inflammatory status in diabetic nephropathy: A systematic review and meta-analysis of clinical trials. Heliyon. 2021;7(1):e05925. https://doi.org/10.1016/j.heliyon.2021.e05925.

36. Moravejolahkami AR, Paknahad Z, Chitsaz A. Dietary intake of energy and fiber in MS patients; an approach to prebiotics role. Nutrition & Food Science. 2019;49(6):1039-50.

37. Askari G, Ghavami A, Shahdadian F, Moravejolahkami AR. Effect of synbiotics and probiotics supplementation on autoimmune diseases: A systematic review and meta-analysis of clinical trials. Clin Nutr. 2021;40(5):3221-34. https://doi.org/10.1016/j.clnu.2021.02.015.

38. Fang C, Zuo K, Liu Z, Xu L, Yang X. Disordered GPR43/NLRP3 expression in peripheral leukocytes of patients with atrial fibrillation is associated with intestinal short chain fatty acids levels. European Journal of Medical Research. 2024;29(1):233.

39. Arifuzzaman M, Collins N, Guo CJ, Artis D. Nutritional regulation of microbiota-derived metabolites: Implications for immunity and inflammation. Immunity. 2024;57(1):14-27. https://doi.org/10.1016/j.immuni.2023.12.009.

40. Zhou F, Guo YX, Gao R, Ji XY, Tang YX, Wang LB, et al. Quercetin regulates dendritic cell activation by targeting STAT4 in the treatment of experimental autoimmune encephalomyelitis. Toxicol Appl Pharmacol. 2024;488:116980. https://doi.org/10.1016/j.taap.2024.116980.

41. Moravejolahkami AR, Shakibaei M, Sharma M, Mohammadnezhad M, Devarakonda SLS. Effect of Mediterranean diet on body mass index and fatigue severity in patients with multiple sclerosis:

A systematic review and meta-analysis of clinical trials. Heliyon. 2024;10(18):e37705. https://doi.org/10.1016/j.heliyon.2024.e37705.

42. Paknahad Z, Sheklabadi E, Moravejolahkami AR, Chitsaz A, Hassanzadeh A. The effects of Mediterranean diet on severity of disease and serum Total Antioxidant Capacity (TAC) in patients with Parkinson's disease: a single center, randomized controlled trial. Nutritional neuroscience. 2022;25(2):313-20.

43. Moravejolahkami A, Chitsaz A. Mediterranean-style diet Co-supplemented with synbiotics improved quality of life, fatigue and disease activity in five secondary progressive multiple sclerosis patients. Ann Med & Surg Case Rep: AMSCR. 2019;2019(02):1-3.

44. Stojković LS, Stefanović M, Ranković S, Đorđević A, Kuveljić J, Dinčić E, et al. Relations of circulating long chain polyunsaturated fatty acids, lipid peroxidation product and FADS2 gene variants differentiate between patients with relapsing-remitting and secondary progressive multiple sclerosis. Multiple Sclerosis Journal. 2024:P1354/2227.

45. Medoro A, Graziano F, Cardinale G, Voccola S, Zotti T, Intrieri M, et al. The influence of FADS1 and ELOVL2 genetic polymorphisms on polyunsaturated fatty acid composition in response to fish oil supplementation. Lipids Health Dis. 2025;24(1):102. https://doi.org/10.1186/s12944-025-02513-w.

46. Napiórkowska-Baran K, Treichel P, Dardzińska A, Majcherczak A, Pilichowicz A, Szota M, et al. Immunomodulatory Effects of Selected Non-Nutritive Bioactive Compounds and Their Role in Optimal Nutrition. Current Issues in Molecular Biology. 2025;47(2):89.

47. Orywal K, Socha K, Iwaniuk P, Kaczynski P, Farhan JA, Zon W, et al. Vitamins in the Prevention and Support Therapy of Neurodegenerative Diseases. Int J Mol Sci. 2025;26(3):1333. https://doi.org/10.3390/ijms26031333.

48. Korat AVA, Duscova E, Shea MK, Jacques PF, Sebastiani P, Wang M, et al. Dietary Carbohydrate Intake, Carbohydrate Quality, and Healthy Aging in Women. JAMA Network Open. 2025;8(5):e2511056-e.

49. Valburg C, Sonti A, Stern JN, Najjar S, Harel A. Dietary factors in experimental autoimmune encephalomyelitis and multiple sclerosis: A comprehensive review. Mult Scler. 2021;27(4):494-502. https://doi.org/10.1177/1352458520923955.

50. Bohlouli J, Namjoo I, Borzoo-Isfahani M, Poorbaferani F, Moravejolahkami AR, Clark CCT, et al. Modified Mediterranean diet v. traditional Iranian diet: efficacy of dietary interventions on dietary inflammatory index score, fatigue severity and disability in multiple sclerosis patients. Br J Nutr. 2022;128(7):1274-84. https://doi.org/10.1017/S000711452100307X.

51. Moravejolahkami AR, Paknahad Z, Chitsaz A, Hojjati Kermani MA, Borzoo-Isfahani M. Potential of modified Mediterranean diet to improve quality of life and fatigue severity in multiple sclerosis patients: a single-center randomized controlled trial. International Journal of Food Properties. 2020;23(1):1993-2004.

52. Mirashrafi S, Borzoo-Isfahani M, Namjoo I, Hojjati Kermani MA, Moravejolahkami AR. A Mediterranean-type diet improved systemic inflammation in multiple sclerosis patients, as compared to the traditional Iranian diet: A single-center randomized controlled trial. Mediterranean Journal of Nutrition and Metabolism. 2021;14(3):289-304.