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Topical Review

Over-the-counter anti-oxidant therapies for use in multiple sclerosis: A systematic review

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Abstract

Background: Anti-oxidant compounds that are found in over-the-counter (OTC) supplements and foods are gaining interest as treatments for multiple sclerosis (MS). They are widely used by patients, sometimes without a clear evidence base.

Objective: We conducted a systematic review of animal and clinical research to determine the evidence for the benefits of OTC anti-oxidants in MS.

Methods: Using predefined criteria, we searched key databases. Two authors scrutinized all studies against inclusion/exclusion criteria, assessed study risk-of-bias and extracted results.

Results: Of the 3507 titles, 145 met criteria and included compounds, α(alpha)-lipoic acid (ALA), anti-oxidant vitamins, *Ginkgo biloba*, quercetin, resveratrol and epigallocatechin-3-gallate (ECGC). The strongest evidence to support OTC anti-oxidants was for compounds EGCG and ALA in animal models; both consistently showed anti-inflammatory/anti-oxidant effects and reduced neurological impairment. Only vitamin E, *Ginkgo biloba* and ALA were examined for efficacy in pilot clinical trials with either conflicting evidence or evidence of no benefit.

Conclusion: OTC anti-oxidants EGCG and ALA show the most consistent benefit, however only in preclinical studies. There is no evidence that they alter MS relapses or progression. Future work should focus on testing more of these therapies for clinical efficacy before recommending them to MS patients.

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Introduction

Multiple sclerosis (MS) is an inflammatory disorder that is characterized by focal damage to white matter, oligodendrocyte cell death and loss of myelin. Clinically available therapies reduce relapses but they do not effectively slow irreversible damage, such as neuronal and axonal injury, which occurs during both the early and late phases of the disease.[1] Cumulative axonal and neuronal injury is thought to be a major contributor to MS progression,[2,3] which will eventually affect the majority of people with MS.[4] Methods that slow or stop axonal injury and brain atrophy are valuable therapeutic targets.[5–7]

Oxidative stress (OS), the overabundance of reactive oxygen species (ROS) or reactive nitrogen species (RNS), is one contributor to neuronal and axonal injury in MS.[8,9] When there is a preponderance of ROS/RNS in the brain and spinal cord that cannot be adequately eliminated by endogenous mechanisms, neural tissue becomes injured. Evidence for a role of ROS/RNS in the pathology of MS is offered by the accumulation of oxidized lipids, nucleotides or proteins. Active and expanding MS lesions express increased oxidized lipid and nucleotide species, especially in degenerating axons and damaged oligodendrocytes.[10,11] Moreover, there is an upregulation of nitric oxide synthase and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase in MS lesions,[12,13] which are enzymes that produce nitric oxide and superoxide, respectively. Together, nitric oxide and superoxide are the important contributors to focal axonal swelling and degeneration.[14]

Table 1. Search terms.

Area	Search terms
Pathology*	Multiple sclerosis, chronic neurological disease, central nervous system (CNS), inflammation, demyelination, remyelination, axonal degeneration, cortical atrophy, virus demyelination, randomized controlled trials, clinical controlled trials, animal model, model, experimental autoimmune encephalomyelitis (EAE), cuprizone, focal demyelination
Intervention*	Anti-oxidant, OS, ROS, RNS, hydroxyl radicals, peroxynitrite, superoxide, metal chelators, iron chelators, dietary intervention, diet plan, dietary supplements, dietary management, anti-inflammatory, poly-unsaturated fatty acids (PUFAs), selenium, blueberries, green tea, *Ginkgo biloba* extracts, coenzyme Q10, turmeric, curcumin, vitamin C, vitamin E, vitamin A, phenolic, polyphenol, flavonoid, carotenoid

*Titles were included if the title or keywords included at least one term from the 'pathology terms' list and one term from the 'intervention terms'.

Anti-oxidant drug therapies, diets, and supplements, purported to counteract ROS and RNS cascades, are available as over-the-counter (OTC) remedies yet their benefits have not been proven. Most people with MS reporting using an OTC supplement despite the lack of a clear evidence base.[15] We undertook this study to systematically and rigorously examine current research findings on the effects of OTC anti-oxidant supplements in animal models and clinical trials in MS. Our aim was to translate research findings to MS clinicians and to identify areas for future research.

Methods

Search strategy

With the assistance of a librarian expert in systematic reviews and using predefined search terms (Table 1), we searched PubMed, CINAHL, PsychInfo, the Cochrane Library, and the Central Register of Controlled Clinical Trials, including all years up to 1 October 2013 (English language only). Clinical studies were included if the participants had MS or the biological products tested were from people with MS. Animal studies were included if a disease, similar to MS, was induced in animals and included at least behavioral findings.

Data extraction and synthesis

Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,[16] and after duplicates were removed, we merged titles retrieved across search databases. At the title, abstract, and manuscript levels of the search, two authors evaluated inclusion status independently and if the authors disagreed, the article was included. Data extraction and synthesis was conducted on manuscripts that were categorized by compound tested. Reference lists of included articles were hand-searched and two authors scrutinized all titles against inclusion criteria. The data from all studies were extracted into article summary spreadsheets. In order to prevent inflation of findings, we required at least three studies testing a specific compound of interest in order to be included. Each study was assessed for risk-of-bias: the clinical studies using the Cochrane Collaboration risk-of-bias tool;[17] and animal studies using a combination of two previously published checklists.[18,19]

Results

Our review resulted in 3507 titles, of which 400 were reviewed at the manuscript level (Figure 1). Although there were 12 studies examining uric acid, we did not synthesize the findings since there are several recent reviews as well as a clinical trial completed.[20–22] Similarly, there is a recent Cochrane review that summarizes the literature regarding polyunsaturated fatty acids (PUFA).[23] Many compounds had fewer than three studies, which were below our threshold for synthesis; for example, chelation, polyamines, selenium, and others (Figure 1). The final research articles were grouped by category (polyphenols, anti-oxidant vitamins, alpha lipoic acid (ALA), and *Ginkgo biloba*). A summary is provided describing the extent of the research evidence in polyphenols (luteolin, quercetin, curcumin, EGCG, and resveratrol), anti-oxidant vitamins (A, C, and E), *G. biloba* and ALA (Table 2). We found that evidence in animal models consistently supported the benefits of EGCG and ALA. The only evidence supporting use of OTC anti-oxidants among people with MS was in *G. biloba* and ALA, and that evidence was conflicting.

Polyphenols

Polyphenols are the most abundant dietary anti-oxidants, occurring naturally in fruits, vegetables, and cereals.[24] They are believed to function through their

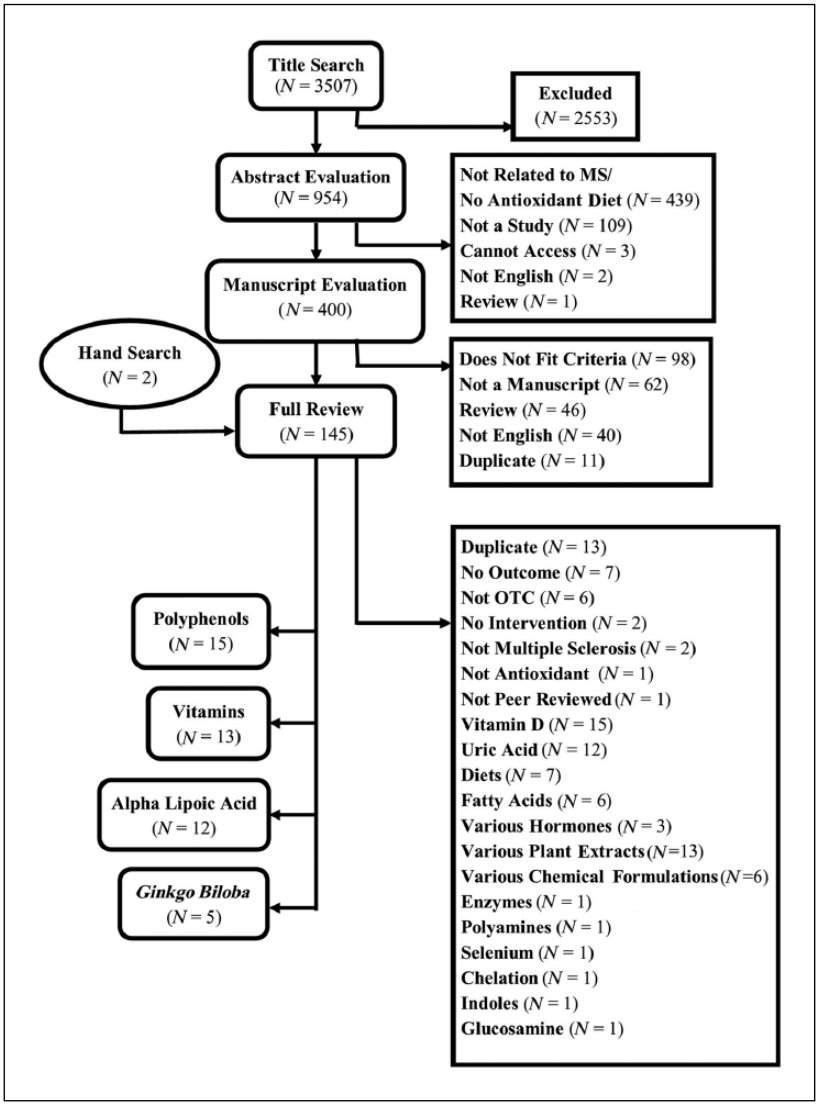

Figure 1. PRISMA diagram. Of 147 articles evaluated by group consensus, seven compounds were excluded because there were too few studies (<3) to proceed. By consensus, we also excluded mixed diets such as the Swank diet, fatty acids, and products that were not available OTC.

anti-oxidant and radical scavenging activities.[25] Our review included 15 studies examining five compounds classified as polyphenols, where some studies examine more than one compound: quercetin,[26–29] luteolin,[26,29,30] curcumin,[29,31,32] resveratrol,[33–36] and epigallocatechin-3-gallate (EGCG).[37–40] Details of the included studies are found in Supplementary Table 3 and assessment of risk-of-bias in Supplementary Figure 2(a) and (b).

Quercetin. There were three animal studies examining quercetin in EAE,[26,27,29] and one *ex vivo* assessment from MS patients.[28] When quercetin was administered by intraperitoneal (i.p.) injection, EAE severity score was less severe, which was associated with decreased immune cell infiltrates in the spinal cord.[26,27] However, when administered orally, mice showed no improvement.[29] In the single clinical study, Peripheral blood mononuclear cells (PBMCs) from RR-MS patients and healthy controls were treated with quercetin or quercetin plus the drug interferon-β (IFN-β) to examine potentially synergistic effects, but nothing conclusive can be drawn as the baseline effect of IFN-β alone was not included.[28]

Luteolin. In the three studies (two in animals and one clinical study) examining luteolin, we see conflicting results.[26,29,30] In EAE animals, luteolin either showed no improvement[29] or a decrease in disease severity;[26] and an *ex vivo* assessment of PBMCs from RR-MS patients

Table 2. Summary of research evidence.

	Luteolin	Quercetin	Curcumin	EGCG	Resveratrol	Vitamin A	Vitamin C	Vitamin E	*Ginkgo biloba*	Alpha lipoic acid (ALA)
	Broccoli*	Cranberries*	Tumeric*	Green tea*	Red grapes*	Spinach*	Red pepper*	Almonds*	Extract*	Organ meats*
Animal models										
Anti-inflammatory/anti-oxidant properties	✓ X	✓	✓	✓	X	O	O	O	O	✓
Decreased damage to nervous system (e.g. relapses)	O	O	O	✓	✓ X	O	O	✓	O	✓
Reduced disease severity	✓ X	✓	✓	✓	✓	✓	X	O	O	✓
MS patients										
Anti-inflammatory/anti-oxidant properties	O	O	O	O	O	O	O	O	O	✓ X
Decreased relapses	O	O	O	O	O	O	O	O	O	O
Reduced disease progression	O	O	O	O	O	O	O	X	✓ X	O

*Examples of natural sources of compounds. Most studies examined in this review tested purified extracts or synthesized products. ✓ evidence to support; X evidence that there is no benefit; O no evidence.

treated with luteolin plus IFN-β provide no conclusive data as a critical control group was missing.[30]

Curcumin. Curcumin is the main ingredient of turmeric and a lipophilic compound that crosses membranes easily, making it a promising oral therapy.[41] The three studies reviewed all employed animal models that showed consistent anti-inflammatory benefits.[29,31,32] It decreased the T cell production of IFN-γ;[29] prevented the differentiation of T helper 1 (Th1) cells;[31] and decreased the amount of Th17-differentiated cells.[32] As the included studies administered curcumin before the onset of clinical symptoms, only preventative effects were assessed.[29,31,32] One clinical trial examining curcumin as an adjunct therapy to IFN-β1a is in recruitment phase (clinicaltrials.gov, NCT01514370).

EGCG. EGCG is the most abundant of the biologically active catechins present in green tea. Four studies examined the ability of purified EGCG (95%) to decrease the severity of EAE disease (Table 2 and Supplementary Table 3).[37–40] EGCG-fed animals consistently showed decreased severity scores compared to control-fed animals, which was associated with suppressed immune cell infiltrates,[37–39] decreased demyelination in the spinal cord,[39,42] and a decreased production of inflammatory cytokines that promote Th1 and Th17 differentiation.[37,39,40] Furthermore, EGCG enhanced the viability and outgrowth of hippocampal cells in vitro.[37,38] To date, there are six ongoing trials investigating EGCG as an adjunct therapy in MS listed on clinicaltrials.gov (NCT00525668, NCT02011451, NCT00799890, NCT00836719, NCT01451723, and NCT01417312). Most of these studies focus on the safety and the neuroprotective ability of EGCG by assessing levels of neuronal marker *N*-acetyl aspartate, used to identify the number of neurons and their metabolism.

Resveratrol. Resveratrol is found predominantly in grapes and red wine.[43] It is known to have poor bioavailability, so most studies administer SRT501, a pharmaceutical formulation of resveratrol that has enhanced systemic absorption.[33,43] In four studies reviewed (all in animal models), both resveratrol and SRT501 consistently decreased EAE severity,[33–36] which coincided with reduced optic nerve damage and prevention of retinal ganglion cell loss.[33,35] Resveratrol did not alter the levels of infiltrating immune cells into the spinal cord of EAE animals, suggesting it functions through a neuroprotective mechanism;[33–35] though one group reported decreased levels of peripheral pro-inflammatory cytokines.[36]

Anti-oxidant vitamins

Vitamins A (β-carotene and retinol), C (ascorbic acid) and E (α-tocopherol), having anti-oxidant properties, were examined in 13 studies (animal models $n = 4$; clinical $n = 7$; population wide $n = 2$).[44–56] Details of the included studies are found in Supplementary Table 4 and risk-of-bias in Supplementary Figure 3(a) and (b).

Vitamin A. There was a single animal study[55] and two small clinical studies from the same cohort examining vitamin A.[45,46] Treatment of vitamin A following EAE increased the number of animals without EAE symptoms.[55] The two clinical studies were small, with fewer than 20 subjects treated for 6 months with 25,000 IU vitamin A, finding decreased peripheral immune cell proliferation, but only when cells were cultured with fetal calf serum and not when cultured with human serum.[46] In the same cohort, vitamin A treatment increased the inflammatory marker C-reactive protein indicating that vitamin A may also induce certain aspects of inflammation.[45] There is currently a registered clinical trial of vitamin A (clinicaltrials.gov 01225289).

Vitamin E. Vitamin E is a group of fat-soluble antioxidants that include tocotrienols and tocopherols.[57] Vitamin E can decrease protein kinase C, an important cellular signaling molecule;[58] it can also regulate the inflammatory arachadonic acid cascade by increasing cytosolic phospholipase A2 and cyclooxygenase activities.[59] In the animal studies, vitamin E either protected myelin or promoted myelin regeneration.[44,53] In a small cohort of people with MS, nine subjects treated for 30 months, vitamin E alone did not decrease annual relapse rate.[50] However, whether annual relapse rate meaningfully captures the protective effects of an anti-oxidant therapy is unclear. No studies examined measures of brain atrophy or lesion accumulation.

Vitamin combinations. We found five clinical studies that tested anti-oxidant combinations including vitamins A, C, or E[47–50,52] (Supplementary Table 4). In one small clinical study (9–12 participants per treatment arm), a mixture of several PUFAs, monosaturated fatty acids, and saturated fatty acids along with vitamin E and vitamin A significantly reduced relapse rate compared to control.[50] The authors reported that vitamin E was a necessary component in this combination; however, it is difficult to draw definitive conclusions. In population studies it was found that that the levels of vitamin intake were not associated with increased risk of MS or disease progression when adjusted for age, time period, latitude of birthplace, smoking, and total energy.[51,56]

Alpha lipoic acid (ALA)

Found in very small amounts in foods such as organ meats, spinach, and broccoli, ALA is synthesized in the liver and is considered to be a naturally-occurring anti-oxidant.[60] ALA is a direct scavenger of free radicals and acts indirectly as a metal chelator thereby lessening free-radical damage.[61] Of the 12 studies included in this review, one reported findings in both humans and animals[62] and four examined the effects of ALA supplements in people with MS or their blood products from two samples of patients.[62–65] The remaining preclinical studies utilized the EAE rodent model.[42,62,66–71] Detailed information is found in Supplementary Table 5 and risk-of-bias assessments in Supplementary Figure 4(a) and (b).

In terms of the effects of ALA on anti-oxidant/inflammatory mediators, peripheral T cell activity in ALA-specific studies showed conflicting results.[42,69] Marracci et al. reported no effect of ALA on pro-inflammatory T cells[69] while Wang et al. reported suppression of CD^+ T cells obtained from ALA-treated animals.[42] In five studies there was a consistent reduction in T cell infiltration into the CNS with ALA treatment: spinal cord,[42,67,69,71] optic nerve,[66] and cerebellum.[42,71]

The six studies examining the effects of ALA on mediators of inflammation, such as matrix metallopedtidase-9 (MMP-9) or soluble cell adhesion molecule (ICAM), in animal models[42,67,70] and people with MS,[63,64,72] reported varying results. In serum obtained from people with MS, 1200 mg LA administered daily for 14 days did not change serum levels of MMP-9, TIMP-1, or soluble cell adhesion molecule (ICAM).[72] However, Khalili and group reported significant reductions in pro-inflammatory markers IFN-γ, ICAM-1, TGF-β, and IL-4 after 12 weeks of treatment.[64] Studies in animal models showed more consistent beneficial findings. ALA treatment reduced immunostimulators MMP, IFN-γ, and IL-4;[70] increased endogenous PPAR-γ, which acts to counteract OS;[42] and reduced expression of ICAM in spinal cord tissue.[67] Two animal studies reported dose-dependent effects of ALA, with higher dosages (100 μg/ml versus 25 μg/ml) being more beneficial and oral ingestion being less effective than injection.[67,70]

Effects of ALA on recovery and repair were evaluated in two ways: quantification of demyelination and axonal injury,[66,69,70] and behavioral/clinical neurological impairment score. The three studies examining the effects of ALA on demyelination and axonal damage in optic nerve, spinal cord, and brain consistently showed that ALA-treated EAE animals had reduced damage in the CNS,[66,69,70] which was dependent on timing and route of administration. ALA administered by i.p. injection seven days or directly following immunization protected axons from demyelination and damage.[66,69,70] Delayed ALA administration reduced damage to optic nerve but not as robustly as immediate treatment.[66] Oral administration was only protective when instituted immediately, but not delayed, following EAE immunization.[70]

All eight studies examining the behavioral effects of ALA in the EAE model showed reduced disease severity in ALA-treated animals.[42,62,66–71] There was no change in Expanded Disease Severity Scale (EDSS) score in the five studies among people with MS, although the longest intervention was only 12 weeks.[64,65] Four animal studies showed both dosage and timing effects: low dosages of less than 10 mg/kg/day,[69,71] or delayed dosage[70] were of minimal benefit. However, one study showed that both early and late administration of ALA abolished the EAE-related impairment during the 24 day length of the experiment.[66] Yadav and group reported that EAE-related impairment was correlated with serum levels of ALA in EAE animals.[62] Importantly, two studies showed that when ALA treatment is halted, impairments return.[68,69] Study durations in EAE models were less than 40 days so the long-term benefits are unknown. Furthermore, the effects of ALA on MS progression, relapse, or recovery have not been tested in people with MS, although several trials are posted in clinicaltrials.gov (02133664, 00676156, 01188811).

In all except one study[70] in animal models ALA was delivered by injection. When comparing injection of ALA to delivery in drinking water, injection was more effective at reducing severity of disease and indicators of inflammation. In humans, ALA was provided orally in pill form and the most common side effects were gastrointestinal upset, malodorous urine, and rash.[72] In people with MS, there was wide variability in absorption and clearance of ALA between individuals.[62] Furthermore, ALA obtained from different suppliers had different rates of metabolism.[62,72] These findings make it difficult to know how much ALA dosage is required in humans.

Ginkgo biloba

Ginkgo biloba (*G. biloba*) extract is obtained from *G. biloba* tree leaves, and the commercially available products contain a mixture of biologically active compounds.[73] The percentage of each compound within a *G. biloba* extract varies between suppliers; however, the most common research formulation is EGb-761, which contains approximately 24% flavone

glycosides, 7% proanthocyanidins, and 6% terpene lactones.[73] Our search revealed five studies examining *G. biloba* in MS, all of which were clinical trials focusing on cognitive outcomes. Our search revealed no preclinical trials in animal models of MS. Three of the clinical trials were placebo-controlled, administering 240 mg of *G. biloba* daily,[74–76] and two of these were from the same research group, in which a small study was followed by a larger trial.[75,76] One open-label trial was conducted using a dose of 240 mg per day; however, one participant received a dose of 120 mg due to a history of gastritis.[77] Lastly, one paper reanalysed data from a previously conducted placebo-controlled study.[78] All of these studies used commercially available *G. biloba*, but only two used the EGb-761 formulation.[74,75] Details of the included studies are found in Supplementary Table 4, and risk-of-bias is outlined in Supplementary Figure 5.

Four of the clinical studies reviewed examined the effects of *G. biloba* on cognitive impairment in MS with between 12 and 30 subjects in the treatment groups. These studies used different cognitive assessment tools, making it difficult to compare results. In an eight week open-label trial, MS subjects had significant improvement on the Wechsler memory test after treatment.[77] A placebo-controlled study conducted by Lovera et al. demonstrated that eight weeks of *G. biloba* treatment improved scores on the Stroop memory test, indicating increased cognitive flexibility.[76] Using data derived from their 2006 clinic study, Diamond and group reported that the *G. biloba* treated group had enhanced processing speed on the Visual Threshold Serial Addition Test and emitted less verbal intrusions on the California Verbal Learning Test compared to a placebo group.[78] However the largest study examining *G. biloba* in 120 persons with MS with 61 randomized to *G. biloba* failed to show any benefit on cognitive function.[75] Despite minimal effects on impairment or disability, two studies reported that *G. biloba* improved self-reported symptoms and quality of life.[74,75,78]

All of the studies included in this review studied the effects of *G. biloba* administered orally in capsule, 240 mg per day divided in either 2 or 4 doses, though the commercial sources of the *G. biloba* extract varied between studies. *G. biloba* was well tolerated in most cases. In one study a few participants reported mild nausea.[77] No severe adverse events related to *G. biloba* were observed during the trials reviewed.

Discussion

In an effort to combat the OS associated with injury in MS, researchers are exploring anti-oxidant therapies to reduce MS pathology. Our review focused on a subset of this research: readily-available dietary anti-oxidant compounds available OTC. We did not include compounds that were examined in fewer than three studies such as chelation, glucosamine, selenium, and others. We also did not review compounds that had already been subjected to rigorous review and synthesis: uric acid[20–22] or PUFAs.[23] The largest body of research examined ALA (12 studies) and *G. biloba* (5 studies), with the remaining compounds having fewer than four peer-reviewed studies. Only vitamin E, *G. biloba*, and ALA were examined in people with MS with either conflicting evidence or evidence of no benefit (Table 2). The strongest evidence to support OTC anti-oxidants was for compounds EGCG and ALA in animal models; both compounds consistently showed anti-inflammatory/anti-oxidant effects, decreased damage to the nervous system along with reduced neurological impairment (Table 2).

Optimal outcomes to assess the benefits of anti-oxidants

There was a paucity of mechanistic outcomes in the studies included in this review. We found the reduction of pro-inflammatory markers as a common feature among animal studies, but the direct cause of the reduced inflammation was more often undetermined. Furthermore, considering that OTC anti-oxidants are purported to provide neuroprotection and repair, there were no studies that examined longer term outcomes such as reduced lesion accumulation or disability progression. With the ongoing degeneration that is associated with progressive MS and the presence of OS at sites of degeneration,[2,8,9,79,80] determining the utility of anti-oxidant therapies to protect neural tissue or promote repair is a major research gap. In this review, we found that only EGCG,[37,38] vitamin E,[44,53] reservatrol,[33,35] and ALA[66,69,70] promoted remyelination and/or protected neurons from inflammatory-mediated damage (in animal models). Resveratrol consistently provided neuroprotection in EAE, though this was independent of any anti-inflammatory benefits.[33,35] Clinical studies included in this review provided short term outcomes (predominantly 12 weeks post-treatment) with no effects of OTC anti-oxidants on the disease course (EDSS score). If it is purported that anti-oxidants convey their benefits by interfering with the inflammatory cascade and preventing axonal damage then longer term outcomes, such as lesion accumulation, number of relapses, or recovery post-relapse, should be included in future studies. In other neurodegenerative diseases, for example, vitamin E for six months to four years significantly slowed functional decline among people with Alzheimer's

disease.[81] There are also opportunities to develop new degenerative models that exhibit ROS-related nervous system injury to test potentially neuroprotective compounds.[82]

Translating preclinical results to clinical trials

Patients with MS likely ingest OTC anti-oxidants, and all the clinical studies we reviewed used oral administration. However, in most animal studies, anti-oxidant compounds were administered by either subcutaneous or i.p. injection, making it challenging to translate to the clinical setting. At least with ALA treatment of EAE, injection was superior to oral administration.[26,29,70] For other compounds, direct administration into the blood may not always improve bioavailability; passage through the gastrointestinal tract could be needed to see any beneficial effects.[83] Several studies showed that absorption of the product varied extensively between individuals and by product formulation, such as ALA[62,72] and *G. biloba*.[84] Still, bioavailability in the circulation does not necessarily mean that compounds can affect the CNS. For many of the compounds studied, it was unclear whether they crossed the blood-brain barrier to the site of their potential action. More studies examining pharmacokinetics particularly blood-brain barrier penetration, are required.[84–86]

Another key concern for the safety of people with MS is toleration of anti-oxidant diets and supplements. Our findings suggest that in both humans and animals, anti-oxidant products were reasonably tolerated. Studies did not report animal mortality related to the intervention; and side effects experienced in clinical trials were mild, such as gastrointestinal upset (*G. biloba* 240 mg/day, ALA 1200 mg/day).

Improving the quality of anti-oxidant research in MS

We assessed risk-of-bias using validated tools for both the clinical studies and studies involving animal models. We identified four areas for improvement for future research. In addition to mode of compound administration and duration of assessment mentioned above, we noted that about half of the protocols did not include blinding of assessors, and there was extensive use of subjective rating scales of behavioral outcomes. Since the behavioral and clinical measures require subjectivity by the assessor, this is a concern. As discussed by researchers in other fields, strengthening preclinical research methodology facilitates knowledge translation.[18,19]

In summary, our review provides a preliminary framework for the benefits of anti-oxidant diets in alleviating the progression of MS and describes key areas of improvement for future animal and clinical studies. Although some preclinical results are promising, at this time, the evidence suggests that OTC anti-oxidants do not alter the disease in people with MS.

Conflict of interest

None declared.

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