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Common dietary supplements for cognitive health

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Abstract

Advancing age is a major risk factor for cognitive impairment and dementia. Currently, there are no effective preventive strategies for cognitive decline. Since physicians have no drug therapies to offer, patients and families may turn to complementary and alternative medicine to preserve cognition. Dietary supplements are one of the most common forms of complementary and alternative medicine that patients use and although limited, evidence for their potential interactions with other treatments has been documented. Considering the insufficient evidence for their efficacy, potential for interaction with other therapies and costs to patients, physicians should be aware of the use of dietary supplements among their patients so that they can advise their patients on the potential benefits and harms.

Keywords

ω-3 fatty acids; antioxidants; cognitive impairment; dementia; dietary supplements; folate; ginkgo biloba; vitamin B12; vitamin E

Older adults aged 65 years of age and above currently account for 13% of the US population and this figure is expected to rise to 16% in 2020 and 20% in 2050 [101]. As the population ages, the number of older adults suffering from age-related health problems, such as cognitive decline, is also expected to rise. A recent national survey estimated that the prevalence of cognitive impairment among noninstitutionalized older adults was 4% among the 65–74-year age group but rose to 9 and 20% in the 75–84 and 85 years and above age groups [1]. Other studies have estimated that the prevalence of mild cognitive impairment (MCI), which was defined as a self- or informant-reported cognitive complaint with evidence of impairment on objective cognitive testing but without functional dependency [2,3], among older adults aged 65 years and over, to be between 7.7 and 23.4% [2,4]. On the other hand, the prevalence rate of Alzheimer's disease (AD), the most common cause of dementia, among older adults over 70 years of age is estimated to be 9.5% [5]. The incidence rate of AD increases with age, from 53 per 1000 adults aged 65–74 years, to 231 per 1000 adults 85 years old or older [6]. Other common chronic diseases have also been suggested to be associated with cognitive decline, including cerebrovascular disease,

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cardiovascular disease (CVD), hypertension, diabetes mellitus, chronic lung disease and kidney disease [7–11]. Cognitive impairment is thus prevalent and may lead to devastating consequences including disability, depression, institutionalization and poor quality of life [12–17].

Given the high burden of cognitive impairment and its poor outcomes, it is not surprising that older adults consider that maintaining cognitive health is a key to aging well [18]. Also, since little is known of how healthy older adults can maintain intact cognitive function, it is not surprising that a large proportion of older adults use complementary and alternative medicine (CAM) for cognitive health. In a recent US national survey, almost four out of ten adults had used CAM in the previous 12 months [19]. In community-dwelling older adults, 52% of prescription medication users concurrently used dietary supplements, which are defined as products intended to supplement the diet but not intended to diagnose, treat, cure or prevent any disease, and contain one or more dietary ingredient including vitamins, minerals, herbs or other botanicals and amino acids [20–22,102]. In the USA, unlike drug products, dietary supplements are not subject to US FDA approval for safety or effectiveness before they are marketed to consumers [102]. Out-of-pocket costs on CAM were estimated at US$33.9 billion in the USA in 2007, with 44% on the purchase of nonvitamin and nonmineral natural products [23]. Owing to the potential for interactions with other treatments and costs to patients, physicians should be aware of the use of CAM among their patients so that they can advise their patients on the potential benefits and harms. Therefore, our objective is to review current evidence on the efficacy and harm of the most commonly used dietary supplements for cognitive health. Selected supplements were identified by a Medline® search for studies investigating dietary supplements most commonly used by the general population and older adults for cognition, memory or dementia [20,21,24–26]. For each dietary supplement a Medline search was performed limiting articles to those written in the English language and published since 1990. Search terms used included common and chemical names of each dietary supplement, ‘cognition’, ‘cognitive impairment’, ‘memory’, ‘memory loss’, ‘dementia’ and ‘Alzheimer’s disease’. Inclusion of articles was based on the level of evidence. When available, systematic reviews of randomized controlled trials and reports of randomized controlled trials were preferentially cited over observational studies.

Ginkgo biloba

Ginkgo biloba is an herb that many older adults have used for cognitive health. In the year 2000 alone, it was estimated that Americans spent US$250 million on this supplement [22]. The hypothesized mechanisms of ginkgo biloba that may lead to improved brain function include changes in cerebrovascular circulation through cerebral vasodilation, a reduction in blood viscosity, a reduction of oxygen free radicals and a reduction in the age-related decrease in neurotransmitter receptors [27,28]. The most commonly used dosage, both in the community and in prior studies, was 120–240 mg daily. Several randomized controlled trials have been conducted to examine the efficacy of ginkgo biloba for primary prevention of dementia and cognitive decline, but these studies were small [29–31]. More recently, a larger, more definitive study, the Gingko Evaluation of Memory (GEM) study, has been conducted using 3069 participants randomized into gingko biloba treatment and placebo treatment groups to determine if ginkgo biloba supplementation can prevent dementia among older adults who were cognitively intact or had MCI at baseline [32]. The study followed participants for a median of 6.1 years and found that there was no difference in dementia incidence in all participants (odds ratio [OR]: 1.12; 95% CI: 0.94–1.33; $p = 0.21$), or in the rate of progression to dementia in participants with MCI between the ginkgo biloba treatment group and the placebo group (OR: 1.13; 95% CI: 0.85–1.50; $p = 0.39$). The study investigators also found that ginkgo biloba did not slow the rate of cognitive decline in all

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participants, regardless of their baseline cognitive status [27]. For adults who had been diagnosed with dementia, ginkgo biloba also did not reduce the rate of cognitive decline [33].

Conversely, ginkgo biloba use may be associated with harm. Because most older adults use at least one prescription medication, drug interaction with these supplements needs to be considered [20]. Although the evidence for harm is limited, ginkgo biloba may interact with antiplatelet or anticoagulant medications which may lead to bleeding; in the GEM study, although not statistically significant, there were twice as many hemorrhagic strokes in the ginkgo biloba group compared with placebo [32,34]. In addition, ginkgo biloba may also interact with medications metabolized in the CYP2C19 pathway, such as omeprazole, valproic acid and phenytoin, because it induces the CYP2C19 enzyme [34]. In summary, despite the theoretical basis for ginkgo biloba in the prevention of cognitive decline, there is no convincing evidence that ginkgo biloba is efficacious in preventing dementia or delaying cognitive decline among older adults who are cognitively intact, or those who have MCI or dementia. Also, given the potential harm from medication interactions, clinicians should ask if their patients are taking this supplement, and advise them on potential risks of drug interactions.

Vitamins B6, B9 & B12

Previous studies have examined the effect of vitamin B supplementation, which included vitamin B6, B9 (folate) and B12 (cyanocobalamin), on cognition. Because elevated homocysteine levels have been associated with an increased risk of dementia and as the most common causes of homocysteine elevation are deficiencies in vitamins B6, B9 or B12 [35], enhanced homocysteine metabolism through vitamin B supplementation may have a beneficial effect on reducing the risk of dementia. Vitamin B6 is an essential cofactor in homocysteine metabolism; vitamin B9 acts as a donor of methyl groups for the methylation of homocysteine to methionine; and vitamin B12 is also required for the methylation of homocysteine to methionine [36–38]. Systematic reviews, which included small trials on the use of B vitamins to prevent or halt the progression of cognitive decline in healthy or cognitively impaired older adults, had not shown any benefit to recommend their use [36–38]. In a recent randomized controlled trial conducted by Ford *et al.*, vitamin B supplementation (400 μg B12, 25 mg B6, 2 mg folic acid) did not result in better cognition over a period of 24 months compared with placebo among cognitively intact older men aged 75 years and older. In the same study, at 8 years follow-up, there was a nonsignificant decrease in the risk of cognitive impairment (OR: 0.72; 95% CI: 0.25–2.09) and dementia (hazard ratio: 0.72; 95% CI: 0.29–1.78) [39]. In another randomized controlled trial of cognitively intact older adults with elevated homocysteine levels, supplementation with B vitamins (500 μg B12, 10 mg B6, 1000 μg folate) for 2 years lowered homocysteine levels, but did not demonstrate any improvement in cognitive performance compared with placebo [40]. Another large trial was conducted in older adults with mild-to-moderate dementia (with a mean Mini-Mental State Examination score of 21); 18 months of high-dose B vitamin supplementation with (25 mg vitamin B6, 1 mg vitamin B12, 5 mg folate) showed no benefit on the rate of decline in the AD Assessment Scale-Cognitive subscale score (0.372 points per month for placebo vs 0.401 points per month for vitamin group; 95% CI: of rate difference, -0.06–0.12; p = 0.52) [41]. Most studies cited above did not report any significant adverse events with vitamin B supplementation [36–39]. However, the study by Aisen *et al.* noted an increased incidence of depression in the high-dose supplement group [41].

Although prior studies did not demonstrate substantial benefit of vitamin B supplementation on cognition, vitamin B is one of the most commonly used supplements [42].

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Adequate intake of B vitamins is essential for health maintenance as they participate in key metabolic processes. However, there is no clear benefit in high-dose vitamin B supplementation for preventing cognitive decline.

Vitamin E

Vitamin E is the collective name for the derivatives of tocopherol and tocotrienol; α-tocopherol is the standard form for medical use [43]. It is a lipid-soluble antioxidant and its lipid solubility allows it to cross the blood–brain barrier and exert its effects in cell membranes. Because oxidative stress is hypothesized to contribute to the development of dementia, antioxidants such as vitamin E have been used for its prevention and treatment [43–45]. Several studies have investigated the use of vitamin E for preventing dementia among healthy adults and adults with MCI, and for delaying cognitive decline among those with dementia.

Prevention of dementia in healthy adults

A large population-based observational study found that healthy older adults who used anti-oxidants including vitamin E, vitamin C and multivitamin combinations were 50% less likely to experience cognitive decline at 5 years follow-up compared with those who did not (OR: 0.51; 95% CI: 0.29–0.90). However, a risk reduction in incident dementia was not seen [46]. Subsequently, a randomized placebo-controlled study – the Women's Health Study – compared vitamin E supplementation (600 IU every other day) to placebo in women aged 65 years or older. Participants' cognitive performance were followed at 2-year intervals for a mean of 9.6 years using standardized tests. There was no difference in cognitive performance between the vitamin E-treated group and placebo group [47]. An additional study by the same group randomized women who may have an elevated risk of cognitive decline due to cardiovascular risk factors to vitamin E supplementation (600 IU every other day) and placebo. They also failed to find any difference in cognitive performance over a 5-year follow-up [48]. Recently, a large prospective cohort study with 5395 participants, who were followed for 9.6 years, found that those with the highest intake of vitamin E-rich foods were 25% less likely to develop dementia when compared with the lowest tertile of vitamin E intake [49]. Although these results were encouraging, it is important to note that there is a difference between dietary intake of vitamin E-rich foods and vitamin E supplementation. The benefit seen in this study may be due to other ingredients rather than vitamin E. Also, these results may have been confounded by other health behaviors.

Prevention of dementia in adults with MCI

Older adults with MCI have an elevated risk of dementia [50]. Vitamin E supplementation has been examined as a treatment option to reduce the rate of progression to dementia. A randomized controlled trial was conducted comparing vitamin E supplementation (2000 IU daily) with placebo and with donepezil alone. Upon 3 years' follow-up, there was no difference in the probability of progression from MCI to AD with vitamin E supplementation (OR: 1.02; 95% CI: 0.74–1.41) [50].

Delay of cognitive decline in adults with AD

Vitamin E supplementation (2000 IU daily) has been found to delay disease progression in patients with moderate AD in a study by Sano *et al.* [51]. Using a composite end point of any one of the following outcomes: death, institutionalization, loss of two out of three basic activities of daily living and severe dementia measured using the Clinical Dementia Rating scale, the investigators were able to demonstrate that vitamin E supplementation delayed the occurrence of the composite end point from a median of 440 days to 670 days ($p = 0.001$). Although the study did not find improvement in cognitive performance test scores, a delay

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of clinically relevant composite end points should be considered as an important potential benefit from vitamin E supplementation.

More recently, vitamin E supplementation in doses higher than 400 IU daily was found to be harmful. A meta-analysis found that supplementation with vitamin E for a year was associated with an increase in all-cause mortality; the pooled risk difference was 39 per 10,000 persons (95% CI: 3–74 per 10,000 persons) and the risk ratio was 1.04 (95% CI: 1.01–1.07; p = 0.035) [52]. Also, a randomized placebo-controlled trial, in which a dose of 400 IU of vitamin E was given daily with a follow-up period of 7 years, found that compared with the placebo group, subjects in the supplementation group had higher rates of heart failure and hospitalizations for heart failure (relative risk: 1.13; 95% CI: 1.01–1.26; p = 0.03; and relative risk: 1.21; 95% CI: 1.00–1.47; p = 0.045) [53]. This raises concern that despite the potential benefits of vitamin E supplementation for delaying clinical deterioration in moderate AD, there may be a small risk associated with it. A rational approach may be to consider supplementation among those without significant CVD and risk factors, guided by a discussion of individual patient's goals and preferences.

ω-3 fatty acids

ω-3 fatty acids (FAs) are a group of polyunsaturated FAs (PUFAs) characterized by a C=C bond at position n-3. They include the shorter-chain α-linolenic acid and its longer-chain derivatives docosahexaenoic acid (DHA), eicosapentaenoic acid and docosapentaenoic acid [54,55]. Mechanisms for their benefit in cognition and dementia include reduction in CVD and stroke, reduction in the synthesis of pro-inflammatory cytokines implicated in the pathogenesis of AD, maintenance of brain cell membrane integrity and neuronal function, and reduction of β-amyloid by decreasing production and increasing clearance [54–56].

Prevention of dementia in healthy adults

Prior observational studies suggested that ω-3 FAs and high fish intake may have a protective effect on cognition in cognitively intact adults [57,58]; however, this has not been demonstrated consistently [55,56,59]. A large prospective cohort study of elderly men in the Veterans Affairs Normative Aging Study did not find any association between fish or ω-3 PUFA intake and better cognitive function or less cognitive decline in over 6 years of follow-up; the mean ω-3 PUFA intake was 0.28 g per day [59]. Dangour *et al.* conducted a trial on cognitively intact older adults between 70 and 79 years of age using ω-3 long-chain PUFA supplementation with 200 mg of eicosapentaenoic acid plus 500 mg of DHA, compared with olive oil placebo for 24 months. Their primary outcome measure was the California Verbal Learning Test, and at 24 months there was no difference in California Verbal Learning Test scores between the groups: the mean difference in total number of words recalled over three trials was −0.5 words (95% CI: −1.2–0.2; p = 0.14), and mean difference in delayed recall of list A in the California Verbal Learning Test was 0.1 words (95% CI: −0.2–0.4; p = 0.46). The investigators did not find any difference in secondary cognitive outcome measures either. The lack of cognitive decline in the total sample suggests that a longer follow-up may be needed [60].

Delay in cognitive decline in adults with AD

In an 18-month randomized, double-blind, placebo-controlled trial, DHA supplementation (2 g per day) compared with placebo in individuals with mild-to-moderate AD (Mini-Mental State Examination mean score 20.7 and standard deviation 3.6) did not demonstrate any benefit in the rate of change in both AD Assessment Scale-Cognitive subscale score and Clinical Dementia Rating sum of boxes score. AD Assessment Scale-Cognitive subscale score increased by a mean of 7.98 points (95% CI: 6.51–9.45) in the DHA group and 8.27

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points (95% CI: 6.72–9.82) in the placebo group (p = 0.41). Clinical Dementia Rating sum of boxes score increased by 2.87 points (95% CI: 2.44–3.30) for the DHA group and 2.93 points (95% CI: 2.44–3.42) for the placebo group (p = 0.68) [61].

ω-3 FA is well tolerated. There were a few cases of subtherapeutic international normalized ratio in participants also taking warfarin [61]; thus, it is possible that there may be an interaction between warfarin and DHA supplements. While there is some benefit observed in cohort studies examining dietary intake, additional supplementation in high-quality studies failed to demonstrate any further benefits for the prevention and treatment of dementia. On the other hand, supplementation with ω-3 FAs may be associated with a reduced risk of cardiovascular events [62,63]; whether this may lead to improved outcomes in cognition warrants further investigation.

Vitamins A & C

Vitamin A and vitamin C have antioxidant activity, which has led to their use in enhancing cognition and preventing cognitive decline and dementia [64]. Vitamin A, which refers to retinol and biologically active oxidized metabolites retinaldehyde and retinoic acid, is derived from either preformed retinoids or provitamin carotenoids; β-carotene is the most prevalent in the food supply. Vitamin C, ascorbic acid and its biologically active oxidized product dehydroascorbic acid, is readily available in the food supply.

Prevention of dementia in healthy adults

A large randomized, placebo-controlled trial of β-carotene supplementation (50 mg on alternating days; Physicians Health Study [PHS] II) was conducted to examine the short- and long-term effects of β-carotene supplementation on cognition. Participants who continued their participation from the original PHS had a long treatment duration with a mean of 18 years, and additional subjects were newly recruited and were followed for a mean of 1 year. The investigators found that short-term use had no impact on cognitive performance but long-term use may provide cognitive benefits compared with placebo as measured by the global score on cognitive testing (combined result of cognitive battery including Telephone Interview of Cognitive Status, immediate and delayed recall measures of the East Boston Memory Test, delayed recall of a 10-word list and 1-min animal naming); global score difference was 0.047 (95% CI: 0.00–0.09; p = 0.03) [65]. While these results are encouraging, it is not clear whether a small difference in cognitive test scores translates to clinically relevant outcomes. Also, the sample is limited to male physicians, and thus, the results may not be generalizable. In addition, as the investigators also point out, cognitive testing was only performed near termination of the β-carotene arm which may be an issue for the continuing PHS participants who may have had differences in cognitive function at baseline. In another randomized controlled trial, the Women's Antioxidant and Cardiovascular Study (WACS), participants were women aged 65 years and older and were at high risk of cognitive decline from existing CVD or prevalent cardiovascular risk factors (at least three coronary risk factors). They were randomized to β-carotene supplementation (50 mg on alternating days) or placebo; treatment duration was a mean of 8.9 years. β-carotene supplementation was not associated with any differences in cognitive change in 5.4 years of follow-up [48]. These conflicting reports on the effects of β-carotene suggest that additional studies are needed to further examine the role of β-carotene in preserving cognition. The WACS also examined the effect of vitamin C supplementation (500 mg daily) on cognition and found that vitamin C supplementation was associated with a better performance on the last assessment, which was around the 5-year follow-up; but it was not associated with better cognitive change over time. In further subgroup analysis, the investigators found that vitamin C was only associated with better cognitive change from baseline among those who developed cardiovascular events during follow-up [48]. Those

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with significant cardiovascular risk factors at baseline did not have better cognition with vitamin C supplementation. Because the subgroup who had cognitive benefits could not be identified prior to vitamin C supplementation, these results have limited clinical applicability. However, it suggests a direction for future research.

Evidence for the protective effects of vitamins A and C against cognitive decline, impairment or dementia is inconsistent and insufficient to recommend vitamin A or C supplementation for cognitive health [48,65]. Furthermore, potential benefits must be balanced with potential toxicity and risk of adverse effects, especially in high doses. For example, high doses of carotenoids are associated with an increased risk of lung cancer in smokers; vitamin A toxicity associated with chronic use (15 mg per day or more in adults for months) may have several manifestations including hypercalcemia, bone demineralization and pain, and features of pseudotumor cerebri with increased intracranial pressure and papilledema. Vitamin C, while mostly well tolerated, may also induce hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency [64].

Vitamin D

Vitamin D is a secosteroid hormone with bone and nonbone targets. Its effects are mediated by vitamin D receptors, which are found in most tissues [64,66,67]. Vitamin D is synthesized in the skin as vitamin D3 (cholecalciferol) or obtained from dietary sources or supplements as vitamin D3 or D2 (ergocalciferol). Vitamins D3 and D2 are metabolized in the liver to 25-hydroxyvitamin D and in the kidneys to biologically active 1,25-dihydroxyvitamin D (calcitriol), which functions as a steroid-like hormone [66]. In the brain, vitamin D binds to vitamin D receptors which have been identified in the human cortex and hippocampus, which are key areas for cognition; it exerts antineuro-degenerative action through neurotrophic, anti-inflammatory, antioxidative and anti-ischemic properties [67,68].

To our knowledge, there are no available randomized control trials of vitamin D supplementation for the enhancement of cognition or prevention of cognitive decline and dementia. A systematic review which included five observational studies showed that there is some association between serum 25-hydroxyvitamin D concentrations and cognitive performance [68]. A cross-sectional study of older community-dwelling women from the Epidémiologie de l'Ostéoporose (EPIDOS) study demonstrated an association between inadequate weekly dietary intake of vitamin D (defined as ≤35 μg per week) and poorer cognitive performance (OR: 1.3; 95% CI: 1.0–1.6; $p = 0.02$). Cognitive function was assessed using the Short Portable Mental State Questionnaire [67]. Another cross-sectional study with adults aged 65 years and older from the Third National Health and Nutrition Examination Survey (NHANES III), a nationally representative cross-sectional study of the US noninstitutionalized population, showed that vitamin D deficiency (defined as serum 25-hydroxyvitamin D levels <75 nmol/l) was associated with an increased risk of cognitive impairment [69]. Findings on the association of vitamin D and cognition were limited by study designs to demonstrate causal relationships of vitamin D supplementation and cognitive change. Further well-designed clinical trials are needed.

Phospholipids: phosphatidylserine & phosphatidylcholine

The phospholipids phosphatidylserine (PS) and phosphatidylcholine are the second most frequently endorsed substances for older adults with memory complaints by proprietors of dietary supplements [70]. Because aging is associated with changes in lipid composition in the brain, supplementation with phospholipids, which are fundamental components of neuronal membranes, has been suggested to be effective therapy for preventing cognitive decline [71]. PS is a phospholipid in the inner leaflet of mammalian plasma membranes and it plays a key role in the function of neuronal membranes, such as in signal transduction,

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cell-to-cell communication and cell growth regulation [71]. Because cytidine 5′-diphosphocholine is a precursor essential for the synthesis of phosphatidylcholine, which is one of the cell membranes degraded during cerebral ischemia to highly toxic free FAs and free radicals, administration of cytidine 5′-diphosphocholine may protect cell membranes by accelerating phospholipid resynthesis [72]. A review by the Cochrane Collaboration on cytidine 5′-diphosphocholine, at 600–1000 mg daily for the treatment of cognitive, emotional and behavioral impairment in older patients with cognitive impairment or dementia, suggests a positive effect on memory and behavior in the short and medium term especially in patients with cognitive deficits associated with cerebrovascular disorders [72]. In a recent randomized trial with 157 participants, PS supplementation, which contained PS and an ω-3 long-chain PUFA attached to its backbone (300 mg PS and 79 mg of DHA plus eicosapentaenoic acid [PS-DHA]), was associated with better cognitive performance in 15 weeks' follow-up compared with placebo in nondemented older adults with memory complaints [71]. In another randomized trial with 120 participants with age-associated memory impairment, soybean-derived PS at a dose of 300 and 600 mg daily for up to 12 weeks did not affect memory or other cognitive functions [73]. No serious adverse events were reported with short-term PS and phosphatidylcholine supplementation. Current evidence for the use of phospholipids for cognitive enhancement is limited; trials are relatively small, short-term, and with heterogeneous dosing, modalities of administration and outcome measures [72]. Larger trials are needed to confirm these findings before recommending the use of phospholipid supplementation.

Ginseng

Ginseng is one of the most popular herbal supplements and has been used for cognitive enhancement [70,74]. In the alternative medicine literature, it is an 'adaptogen', a substance that increases resistance to physical, chemical and biologic stress and builds vitality, including mental capacity [74]. Ginseng saponins or ginsenosides are the major active components; ginsenosides may attenuate β-amyloid-induced toxicity and may have an antioxidative effect, which may be useful in treating AD [74]. A recent report published by the Cochrane Collaboration reviewed the efficacy and adverse effects of different types of ginseng used by healthy adults and by adults with cognitive impairment or dementia [74]. Included in the review were small randomized controlled trials with heterogeneous outcome measures, duration, dosage and effects. Although improvements in some aspects of cognitive function were reported, general conclusions on the benefits of ginseng could not be drawn because of the heterogeneity of the studies. No serious adverse events have been found with ginseng supplementation. For adults with cognitive impairment or dementia, there were no randomized, placebo-controlled trials assessing the effect of ginseng [75]. Further larger randomized controlled trials are needed to demonstrate the benefits of ginseng.

Conclusion

Older adults commonly use dietary supplements despite their costs; however, there is little information available to guide clinicians on their use for cognition. Small trials, which are more prone to bias and chance, may have found certain benefits in these supplements, but larger, high-quality trials have mostly failed to find clinically relevant benefit. The exception may be in vitamin E supplementation among older adults with moderate dementia, but its potential harms need to be considered. Although dietary supplements are commonly considered to be safe, they may interact with prescription medications. Thus, clinicians need to ask their patients about the use of these supplements in order to assess for potential interactions. Furthermore, clinicians may advise their patients that most of these supplements lack benefit for cognition. Until further studies are available to better

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demonstrate the benefits of supplements on cognition, encouraging a balanced diet that contains essential vitamins and nutrients may reap more health benefits.

Future perspective

Over the next decades, the proportion of older adults will increase, as will the prevalence of cognitive impairment and dementia. With few options available to prevent cognitive decline, older adults will likely continue to turn to the use of dietary supplements for cognition. Further clinical trials on dietary supplements, especially those with promising results in observation studies, are needed to establish their efficacy and safety including interactions with other therapies to better guide clinicians in caring for their older patients.

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Executive summary

- There is no effective prescription medication to prevent cognitive decline in healthy older adults.
- Older adults use dietary supplements to preserve cognition, often without the advice and knowledge of their physicians.
- Older adults may not be aware that manufacturer claims of safety and efficacy for dietary supplements are not subject to the same US FDA regulations as drug products before they are marketed to consumers and should therefore be cautioned appropriately.
- Evidence from high-quality trials does not support the use of dietary supplements for the prevention of cognitive decline or treatment of dementia.
- The use of dietary supplements must be balanced with potential adverse effects, including potential interactions with prescription drugs.