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Review Article

Anti-inflammatory Food Parameters in Alzheimer's Disease: A Narrative Review

Ali Sattarian[1], Minoo Akbarzadeh Morshedi[2*]

1. School of Medicine, Isfahan University of Medical Sciences, Kashan, Iran
2. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Science, Kashan University of Medical Sciences, Ravand, Kashan, Iran

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**Corresponding author:*
Minoo Akbarzadeh Morshedi, BSc;
Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Science, Kashan University of Medical Sciences, Ravand, Kashan, Iran.
Tel: +98 9392772650
Email: Mi.akbarzadeh213@gmail.com
Akbarzadeh-m@kaums.ac.ir

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ABSTRACT

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and inflammation. Recent studies suggest that dietary interventions may play a role in modulating inflammatory processes associated with AD. This narrative review aimed to explore the anti-inflammatory food parameters that may influence the pathophysiology of AD. A comprehensive literature search was conducted using databases such as PubMed, Scopus, Science Direct, Cochrane, Ovid, Google Scholar, and Web of Science. Studies focusing on the relationship between dietary components, inflammation, and AD were included utilizing the keywords of anti-inflammatory agents, anti-inflammatory foods, nutraceuticals, Alzheimer's disease, AD, and cognitive decline. The review highlighted several food parameters with anti-inflammatory properties that may benefit AD patients. Omega-3 fatty acids found in fish and flaxseed oil were shown to reduce neuroinflammation. Antioxidant-rich foods like berries and green leafy vegetables were demonstrated to mitigate oxidative stress. Additionally, polyphenols from sources such as tea and dark chocolate were found to have neuroprotective effects. In conclusion, specific anti-inflammatory foods were illustrated to provide a promising adjunctive strategy for managing AD. It seems that further researches are needed to establish definitive dietary guidelines and understand the underlying mechanisms of these food parameters in AD pathology.

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Introduction

Alzheimer's disease (AD) is a complex neurodegenerative disorder characterized by progressive cognitive decline, memory impairment, and behavioral changes (1, 2). It is the most prevalent form of dementia, affecting millions of individuals worldwide and posing significant challenges to healthcare systems (3). The pathophysiology of AD is multifactorial, with neuroinflammation emerging as a critical component in its progression (4). Chronic inflammation in the brain is believed to contribute to neuronal damage and synaptic dysfunction, ultimately leading to cognitive decline (5, 6). Consequently, there is growing interest in exploring dietary interventions that may mitigate inflammatory processes and their potential impact on neurogenerative diseases (7, 8).

A recent research highlighted the role of nutrition in modulating inflammation and promoting brain health (9). Certain dietary patterns, particularly those rich in anti-inflammatory foods, have been associated with a reduced risk of developing AD and other forms of dementia (10). These foods often contain bioactive compounds, such as polyphenols, omega-3 fatty acids, vitamins, and minerals, which exhibit potent anti-inflammatory properties (11, 12). For instance, diets that emphasize fruits, vegetables, whole grains, lean proteins, and healthy fats; such as the Mediterranean diet can positively influence cognitive function and reduce neuroinflammatory markers (13, 14).

Despite the accumulating evidence linking dietary components to inflammatory processes in AD, the specific mechanisms by which these anti-inflammatory food parameters exert their effects remain poorly understood (15). Furthermore, the heterogeneity of study designs and methodologies complicates the establishment of clear dietary recommendations for individuals at risk of or diagnosed with AD. Therefore, a comprehensive narrative review is warranted to synthesize the current literature on anti-inflammatory food parameters in the context of AD. This review aimed to elucidate the relationship between dietary factors and neuroinflammation in AD by examining various anti-inflammatory foods and their potential mechanisms of action. By integrating findings from clinical studies, observational research, and dietary intervention trials, this narrative review seeks to provide a clearer understanding of how specific food parameters may contribute to the prevention and management of AD. The current study also tried to inform future research directions and dietary guidelines that could enhance cognitive health and mitigate the burden of this devastating condition.

Materials and Methods

Literature Search Strategy

A systematic literature search was conducted to identify relevant studies focusing on anti-inflammatory food parameters in AD. The search was performed using multiple electronic databases, including PubMed, Scopus, Science Direct, Cochrane, Ovid, Google Scholar, and Web of Science. The search terms included combinations of keywords: [("Anti-Inflammatory Agents" OR "Anti-Inflammatories" OR "Anti Inflammatory Agents" OR "Antiinflammatories" OR "Anti-inflammatory diet" OR "Nutraceuticals" OR "Plant-Derived Compounds" OR "Dietary interventions" OR "Antioxidants" OR "Anti-Inflammatory Food" OR "Anti-Inflammatory Foods" OR "Anti-Inflammatory Nutrients" OR "Anti-Inflammatory Micronutrients" OR "Anti-Inflammatory Macronutrients") AND ("Alzheimer's Disease" OR "AD" OR "Cognitive Decline" OR "Cognitive Dysfunction" OR "Mental Deterioration" OR "Cognitive Impairment" OR "Cognitive Disorders" OR "Alzheimer's Diseases" OR "Alzheimer Disease")]. The search was limited to articles published in English from January 2000 to May 2025.

Inclusion and Exclusion Criteria

Inclusion criteria for this review encompassed peer-reviewed articles that investigated the relationship between dietary components and inflammatory processes in the context of AD. Studies were selected if they provided original data, reviews, or meta-analyses that discussed specific food parameters known to exert anti-inflammatory effects. Exclusion criteria were non-peer-reviewed articles, conference abstracts, and studies not directly related to AD. Studies with high level of biases were also excluded.

Data Extraction

Based on literature search, 100 research related papers were selected for inclusion in the review. Extracted information was (i) Author(s) and year of publication, (ii) Study design (e.g., observational, clinical trial, review), (iii) Dietary evaluated components (e.g., specific anti-inflammatory foods or nutrients), (iv) Methodology used to assess inflammation (e.g., measured biomarkers), and (v) Key findings related to anti-inflammatory effects and implications for AD.

Synthesis of Findings

A narrative synthesis approach was adopted to summarize and interpret the findings from the selected studies. The synthesis focused on categorizing anti-inflammatory food parameters into relevant groups (e.g., fats, fruits, herbs, spices, probiotic-rich foods, prebiotics, and other specific food parameters) and discussing their potential mechanisms of action in relation to inflammation and AD.

Ethical Considerations

As this study was a narrative review of existing literature, ethical approval was not required. However, all included studies were adhered to ethical guidelines established by their respective institutional review boards.

Results and Discussion

Inflammation and AD

AD is characterized by cognitive decline, neuronal loss, and the accumulation of amyloid-beta (Aβ) plaques and tau neurofibrillary tangles (16, 17). Neuroinflammation, marked by gliosis, is a central mechanism, with microglia and astrocytes playing pivotal roles (18, 19). Pathogenic Aβ and tau induce gliosis, regulating their own pathogenesis, and chronic activation is generally deleterious, suggesting potential therapeutic targets in inhibiting glial responses and pro-inflammatory cytokines (20) (Table 1).

Microglia, derived from monocyte precursors, are activated by Aβ via Pattern Recognition Receptors (PRRs) such as Toll-Like Receptors (TLRs), Nucleotide-Oligomerization binding Domain (NOD) proteins, and C-type lectin receptors, recognizing pathogen-Associated Molecular Patterns (PAMPs) or Damage-Associated Molecular Patterns (DAMPs) (21, 22). This activation leads to the production of Reactive Oxygen Species (ROS), pro-inflammatory cytokines (Interleukin-1β, IL-6, TNF-α, IFN-γ), chemokines (MIP1α, MIP1β, RANTES, MCP1), growth factors (MCSF), and complement factors (C1q, C3, C4, C9) (23-25). Microglia express receptors like Receptor for Advanced Glycation Endproducts (RAGE), Fc receptors, CD40, FP receptors, and scavenger-type receptors, with *in vitro* studies showing Aβ phagocytosis, though limited in AD brains, where peripheral macrophages also contribute (26).

Astrocytes, the most abundant glial cells, are activated by Aβ via TLRs and RAGE, expressing high levels of glial fibrillary acidic protein (GFAP), vimentin, and nestin (27). They phagocytose and degrade Aβ, but intense activation disrupts functions like glutamate homeostasis, leading to neuronal damage (28). They express receptors like RAGE, receptor-like density lipoproteins, proteoglycans, and scavenger receptors, releasing factors like S100β, correlating with dystrophic neurites (29). Oligodendrocytes are affected by Aβ, showing cell death and morphological alterations, with anti-inflammatory agents preventing death but not reversing damage (30). Mutations in presenilin-1 (PS1, e.g., hPS1 M146V) and Aβ accumulation alter Myelin Basic Protein (MBP), increasing neuronal vulnerability and inflammation (31).

The complement system is deregulated in AD, with increased immunoreactivity of C1q, C3b, C4d, C5b-9, and Membrane Attack Complex (MAC) around plaques (31). C1q recognizes fibrillar Aβ 1-42 and Aβ 1-40, but nanomolar C1q decreases phagocytosis in rat cultures (32). C3 synthesis increases 5-10 folds with Aβ exposure (33), and CR1 gene variants link to cognitive impairment and plaque formation (34). A C5a receptor antagonist (C5aR/CD88) reduces Aβ aggregates and hyperphosphorylated tau (35). Cytokines like IL-1 induce APP-β mRNA, promotes S100β synthesis, and increases p38-MAP kinase activity, leading to tau hyperphosphorylation (36).

IL-6 promotes APP-β expression and tau phosphorylation via cdk5/p35 (37). TNF-α stimulates NF-κB, potentially increasing β- and γ-secretase, while Transforming Growth Factor-β (TGF-β) has anti-apoptotic effects but shows decreased receptor type II (TβRII) expression in AD (38). Chemokines, produced by astrocytes and microglia, including MCP-1/CCL2, MIP-1α, MIP-1β, IL-8/CXCL8, promote immune cell migration. Increased CCL2 levels in CSF are correlated with cognitive decline and contribute to disease progression (39). Cyclooxygenases (COX-1, COX-2) are involved with COX-1 high in microglia around Neuritic Plaques (NPs) and COX-2 linked to neurotoxicity are correlated with NPs, NFTs, and cognitive impairment (40). COX-2 overexpression increases Caspase-3 and retinoblastoma protein phosphorylation (S795-pRb) and promotes apoptosis and Aβ formation via γ-secretase (41).

Nitric Oxide (NO), produced by Nitric Oxide Synthase (NOS) isoforms (nNOS, eNOS, iNOS), increases with inflammation (42, 43). Aβ promotes NOS expression, NO, and peroxynitrite formation, causing oxidative damage, mitochondrial dysfunction, and apoptosis, also contributing to NFT formation by increasing tau phosphorylation (44). Genetic factors influence inflammation, with variants in APOE, TREM2, and CD33 affecting glial function and inflammatory responses, modulating AD risk and progression (45). Systemic inflammation,

Table 1: Cellular and molecular mediators of inflammation in AD.

Cell Type	Activation Mechanism	Key Outputs	Impact on AD
Microglia	Aβ via TLRs, RAGE, PRRs	IL-1β, TNF-α, IL-6, ROS, chemokines, complement	Amplifies neuroinflammation, promotes Aβ, tau
Astrocytes	Aβ via TLRs, RAGE	Inflammatory mediators, S100β, disrupts homeostasis	Neuronal damage, synaptic dysfunction
Oligodendrocytes	Aβ, PS1 mutations	Cell death, altered MBP	Increased neuronal vulnerability

AD, Alzheimer's Disease; Aβ, amyloid-beta; TLRs, Toll-Like Receptors; RAGE, Receptor for Advanced Glycation Endproducts; PRRs, Pattern Recognition Receptors; IL, Interleukin; TNF-α, Tumor Necrosis Factor-alpha; ROS, Reactive Oxygen Species; MBP, Myelin Basic Protein.

marked by increased blood levels of circulating proinflammatory cytokines and chemokines, may occur due to infection, chronic disease, or stress, promoting a proinflammatory environment in the central nervous system by crossing the blood-brain barrier, signaling through endothelial cells or circumventricular organs, and stimulating the vagus nerve. Inflammation in AD is a double-edged sword of acute responses that may aid Aβ clearance, but chronic neuroinflammation, driven by sustained glial activation, cytokine release, and oxidative stress that exacerbates pathology. Understanding these mechanisms is crucial for developing targeted therapies, with ongoing research exploring anti-inflammatory agents and immunotherapy (46-48).

Anti-inflammatory Food Parameters in Alzheimer's Disease

Fats

Omega-3 Polyunsaturated Fatty Acids (PUFAs), particularly Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) from fatty fish, and Alpha-Linolenic Acid (ALA) from flaxseed oil, have been studied for their potential to mitigate this inflammation, with varying degrees of evidence supporting their efficacy in AD (49, 50) (Table 2).

Table 2: Key studies evaluating anti-inflammatory food parameters in AD.

Authors	Year	Intervention	Duration	Population	Outcome	Reference
Chiu *et al.*	2008	0.72 g DHA + 1.08 g EPA	6 months	MCI patients	Improved cognitive function (ADAS-cog)	56
Lee *et al.*	2013	1.3 g DHA + 0.45 g EPA	12 months	MCI subjects	Significant cognitive improvement	57
Ogawa *et al.*	2023	3.7 g flaxseed oil (2.2 g ALA)	12 weeks	Healthy older adults	Improved verbal fluency, predictor of AD	62
Hou *et al.*	2024	Urolithin A supplementation	Long-term	AD mouse models	Improved cognition, reduced neuroinflammation	67
Krikorian *et al.*	2010	Blueberry supplementation	12 weeks	Older adults with MCI	Improved memory performance	68
Subash *et al.*	2014	Pomegranate extract	15 months	AD models	Decreased LPO and protein carbonyl levels and restoration in the activities of SOD, catalase, GPx, GSH, and GST	73
Cheng *et al.*	2023	Avocado consumption	Cross-sectional	Multi-ethnic cohort	Lower inflammatory markers	76
Sangeet and Khan	2025	*Bacopa Monnieri* phytochemicals	Various	AD models	Reduced Aβ, anti-inflammatory effects	82
Dwivedi *et al.*	2013	*Bacopa Monnieri* extracts at 40-80 mg/kg	13 days	Rats	Reduced neuronal loss, neuroinflammation	84
Wan *et al.*	2016	EGb 761 (extract of *Ginkgo Biloba*)	Various	APP/PS1 mice	Reduced pro-inflammatory cytokines, improved cognition	90
Banerjee *et al.*	2025	diAcCA (carnosic acid from rosemary)	Various	Mouse models	Enhanced memory, reduced brain inflammation	99
Small *et al.*	2018	90 mg curcumin twice daily	18 months	Adults with MCI	28% memory improvement, reduced amyloid/tau	105
Ringman *et al.*	2012	2-4 g/day Curcumin C3 Complex	24 weeks	Mild-moderate AD	Safe, no cognitive improvement	106
Rasi *et al.*	2022	15 mg Saffron twice daily + donepezil	12 weeks	Mild-moderate AD	Reduced IL-1β, improved inflammation	108
Babaei *et al.*	2025	EGCG with different doses of 25, 50, and 100 mg/kg	21 days	AD model rats	Increased levels of hippocampal BDNF, improved spatial memory deficits	120

AD, Alzheimer's Disease; DHA, Docosahexaenoic Acid; EPA, Eicosapentaenoic Acid; MCI, Mild Cognitive Impairment; ALA, Alpha-Linolenic Acid; LPO, Lipid Peroxidation; SOD, Superoxide Dismutase; GPx, Glutathione Peroxidase; GSH, Glutathione; GST, Glutathione S-Transferase; Aβ, Amyloid-Beta; EGCG, Epigallocatechin-3-Gallate; IL, Interleukin; BDNF, Brain-Derived Neurotrophic Factor.

EPA and DHA exert anti-inflammatory effects by modulating inflammatory pathways, reducing pro-inflammatory cytokine production, and enhancing resolution of inflammation (51, 52). EPA and DHA decrease cytokines and monocytic chemotactic protein-1 levels by suppressing Nuclear Factor-kappa B (NF-κB), a key regulator of inflammation. They also inhibit COX-2 and NOS-2 activities and reduce oxidative stress and neuroinflammation (53, 54).

Preclinical research, such as Thomas *et al.* demonstrated that DHA supplementation reduces markers of inflammation in the hippocampus of adult C57Bl/6 mice, suggesting neuroprotective effects (55). Clinical trials have further supported these findings. Chiu *et al.* reported that 0.72 g of DHA + 1.08 g EPA daily for 6 months could significantly improve cognitive function in patients with mild cognitive impairment, a precursor to AD, likely due to reduced neuroinflammation (56). Similarly, Lee *et al*. found that 1.3 g of DHA + 0.45 g EPA over 12 months could improve cognitive function that is attributed to anti-inflammatory and neuroprotective properties (57). Researches showed that DHA-derived neuroprotectin D1 mediated anti-inflammatory and survival signaling, potentially reducing amyloid-β release and supporting neuronal health in AD (58).

Flaxseed oil, rich in ALA (about 57%), has been investigated for the anti-inflammatory potential, though the benefits for AD are less direct due to the inefficient conversion of ALA to EPA and DHA (59). A meta-analysis in 2019 found that flaxseed intake significantly reduced circulating high-sensitivity C-Reactive Protein (hs-CRP) with a weighted mean difference (WMD) of -0.75 (95% CI: -1.19, -0.30; $p<0.001$), indicating systemic anti-inflammatory effects (60). The presence of Secoisolariciresinol Diglucoside (SDG) in flaxseed, with antioxidant and anti-inflammatory properties reduced leukocyte adhesion and migration across the blood-brain barrier by ~50% (61), which may be relevant for AD given the blood-brain barrier's role in disease progression. A randomized controlled trial by Ogawa *et al.* showed that 3.7 g/day flaxseed oil (2.2 g ALA) for 12 weeks improved verbal fluency in healthy older adults, a cognitive domain predictive of AD development, suggesting potential cognitive benefits (62). However, direct studies on anti-inflammatory effects of flaxseed oil in AD are limited, and the efficacy may be lower compared to EPA and DHA from fatty fish, which provide immediate anti-inflammatory benefits. Fatty fish, such as salmon and mackerel, are rich sources of EPA and DHA, offering stronger evidence for reducing neuroinflammation and supporting cognitive function in early AD stages (63).

Fruits

Dietary interventions rich in anti-inflammatory compounds, such as berries, pomegranate, and avocados, have been explored for their potential to mitigate inflammation (64) and potentially slow AD progression (65) (Table 2). Berries, particularly those rich in anthocyanins such as blueberries and strawberries, have demonstrated significant anti-inflammatory effects in AD (66). A study by Hou *et al.* revealed urolithin A as a gut microbial metabolite of ellagic acid to be found in berries like strawberries, and improve cognitive function and reduces neuroinflammation in AD mouse models. Specifically, urolithin A restored mitophagy and lysosomal functions, modulated immune responses, and reduced Aβ and tau pathologies, highlighting its potential as a therapeutic agent (67). Another study by Krikorian *et al.* exhibited that blueberry supplementation improved memory performance in older adults with mild cognitive impairment, likely due to reduced oxidative stress and inflammation, though direct AD-specific effects were not detailed (68). These findings suggest that high antioxidant content of berries, particularly anthocyanins, can neutralize ROS and reduce pro-inflammatory cytokine production, potentially mitigating AD-related neuroinflammation (69).

Pomegranate is rich in polyphenols such as ellagitannins, punicalagins, and ellagic acid (70) that can attenuate neuroinflammation associated with AD (71). A review highlighted that pomegranate extracts reduced microgliosis, Aβ plaque deposition, and pro-inflammatory cytokine expression in AD models, suggesting its role in suppressing inflammatory signaling pathways (72). An animal study by Subash *et al.* demonstrated that pomegranate peel extract improved spatial memory and reduced biomarkers of inflammation and oxidative stress in a mouse model of neurodegeneration, indicating neuroprotective effects (73). Furthermore, a cell culture experiment confirmed that punicalagin and ellagic acid from pomegranate significantly lessened Nuclear Factor of Activated T-cells (NFAT) bioassay and decreased Aβ-stimulated TNF-α secretion through murine microglia, supporting its anti-inflammatory potential in AD (74). These findings collectively suggest that bioactive compounds of pomegranate exert antioxidant and anti-inflammatory effects, potentially slowing AD progression by reducing neuroinflammation and supporting neuronal health (70-74).

While avocados are not as extensively studied in the context of AD, their anti-inflammatory properties are well-documented and may indirectly benefit brain health (75). A study by Cheng *et al.* from the Multi-Ethnic Study of Atherosclerosis

(MESA) found that avocado consumption was associated with lower levels of inflammatory markers such as IL-1β and CRP in a population-based cohort, suggesting systemic anti-inflammatory effects (76). Although this study did not specifically address AD, chronic inflammation is a key driver of AD pathology, reduces systemic inflammation and indirectly supports cognitive function (77). Additionally, avocados contain monounsaturated fats, antioxidants like lutein and β-carotene, and bioactive phenolics, which may improve vascular health and reduce oxidative stress, both implicated in AD (78). However, direct evidence linking avocados to AD-specific anti-inflammatory effects remains limited, warranting further research.

Herbs

Herbal interventions, particularly those with anti-inflammatory properties, have emerged as promising candidates for mitigating AD progression (Table 2). *Bacopa monnieri*, *Ginkgo biloba*, Ashwagandha, and Rosemary have been extensively studied for their anti-inflammatory effects, with recent human and animal studies providing robust evidence for their therapeutic potential (79-81). *B. Monnieri* has demonstrated significant anti-inflammatory effects in AD through the bioactive components, particularly bacosides. A study published in 2025 highlighted the potential of *B. monnieri* phytochemicals as BACE1 inhibitors, which are crucial for reducing Aβ production, while also exhibited anti-inflammatory properties (82). Additionally, some researchers noted that *B. monnieri* extracts reduced neuroinflammation by modulating oxidative stress markers and restoring antioxidant enzymes, such as glutathione peroxidase, in animal models (83). Specific studies, such as Dwivedi *et al.* showed that *B. monnieri* extracts at 40 and 80 mg/kg body weight for 13 days reduced neuronal loss and neuroinflammation in rats with Okadaic Acid-induced memory dysfunction (84). *In vitro*, *B. monnieri* protected SK-N-SH cells against oxidative stress by inhibiting ROS generation and modulating redox regulatory proteins like NF-κB, which are central to inflammatory pathways (85). Other animal studies further supported the neuroprotective and anti-inflammatory effects of *B. monnieri* (86, 87).

G. biloba, particularly its standardized extract EGb 761, has been extensively studied for its anti-inflammatory effects in AD. EGb 761 inhibits inflammatory processes by reducing pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α, while increasing anti-inflammatory cytokines like IL-4, IL-13, and TGF-β (88). This modulation is linked to microglia activation, where EGb 761 reduces cytotoxic mediators and supports neuronal repair mechanisms (89). Wan *et al.* demonstrated that EGb 761 regulated inflammatory responses in APP/PS1 mice, a transgenic model of AD, by reducing pro-inflammatory cytokines and enhancing cognitive function (90). Additional research by Gargouri *et al.* revealed anti-neuroinflammatory effects in LPS-activated primary microglial cells (91). Hao *et al.* confirmed synergistic effects with bone marrow-derived mesenchymal stem cells in reducing inflammation in experimental autoimmune encephalomyelitis. These findings suggest that anti-inflammatory properties of *G. biloba* to be critical for the neuroprotective effects in AD (92).

Ashwagandha (*Withania somnifera*) has also shown promising anti-inflammatory effects in AD. A narrative review revealed how Ashwagandha reduced pro-inflammatory cytokines such as TNF-α, IL-1β, IL-6, and MCP-1, while decreasing β and γ-secretase activity, which are involved in Aβ production (93). Withaferin A as a key bioactive compound has inhibited amyloid-β production and suppressed gene expression of neuroinflammatory molecules related to NF-κB (94). In transgenic mice, half-purified Ashwagandha root extract increased LRP1 level, reduced amyloid-β, and reversed behavioral deficits (95, 96). Additionally, Withanolide A and other compounds like witanoside IV and V were shown to reduce β-amyloid aggregation, a hallmark of AD, with studies demonstrating neuroprotective effects against neuronal stressors and improved blood-brain barrier function (97). Ashwagandha extract on human embryonal neuroblastoma SK-N-SH cells modulated cholinergic transmission, potentially inhibited acetylcholinesterase activity, and reduced free radical generation that further supported its anti-inflammatory and neuroprotective effects. These studies collectively indicate that anti-inflammatory and neuroprotective effects of Ashwagandha are mediated through multiple pathways, making it a valuable candidate for AD therapy (98).

Rosemary (*Rosmarinus officinalis*) has gained attention for the anti-inflammatory potential in AD, particularly through its diterpenes like carnosic acid. Some researchers reported that a stable form of carnosic acid, diAcCA, exhibited significant anti-inflammatory effects in mouse models of AD, enhancing memory, increasing synaptic density, and reducing brain inflammation. The compound also decreased phosphorylated-tau and amyloid-β levels, key pathological features of AD (99). Earlier research noted that rosemary diterpenes possessed antioxidant, metal chelation, and anti-inflammatory properties (100). In silico studies from 2024 further explored rosemary diterpenes as

Acetylcholinesterase (AChE) inhibitors, suggesting potential for preventing and treating AD. These findings suggest that rosemary could play a significant role in reducing neuroinflammation and supporting cognitive function in AD (101).

Spices

Spices are rich in bioactive compounds and with anti-inflammatory and antioxidant properties. They have been explored for their potential to mitigate this inflammation and potentially slow AD progression too (102-104) (Table 2). Turmeric, particularly its active compound curcumin, has been extensively studied for the anti-inflammatory effects in AD. A double-blind, placebo-controlled study by Small *et al.* involved 40 adults aged 50 to 90 years with mild memory complaints, finding that curcumin (90 mg twice daily) improved memory by 28% over 18 months, with PET scans showing reduced amyloid and tau in the amygdala and hypothalamus compared to placebo (105). However, a randomized controlled trial by Ringman *et al.* in Alzheimer's therapy found that curcumin (Curcumin C3 Complex® at 2 g/day or 4 g/day) was safe and well-tolerated but did not significantly improve cognition or function in 36 mild-to-moderate AD patients over 24 weeks, possibly due to bioavailability issues (106).

Saffron has emerged as a promising candidate for reducing inflammation in many diseases including AD (107, 108). A randomized, double-blind, placebo-controlled clinical trial by Rasi Marzabadi *et al.* showed the effects of saffron in combination with donepezil in 60 mild-to-moderate AD patients. The study illustrated that saffron (15 mg twice daily) significantly reduced serum level of the pro-inflammatory cytokine IL-1β ($p=0.036$) and improved inflammatory profiles compared to placebo. Additionally, saffron decreased oxidative stress markers (e.g., malondialdehyde) and increased total antioxidant capacity. However, no significant improvements in cognitive outcomes were observed beyond those provided by donepezil alone (108). A systematic review concluded that saffron had comparable efficacy in cognitive outcomes with approved drugs like donepezil and memantine, but supplementation did not add beneficial effects, reinforcing the anti-inflammatory potential (109).

While ginger is well-known for the anti-inflammatory properties, recent human studies specifically examining their effects on AD are limited. Preclinical studies have shown that its active compounds, such as gingerol and shogaol, can inhibit COX-2 and NF-κB pathways, reduce neuroinflammation, and protect against Aβ-induced toxicity in animal models (110, 111). Similarly, cinnamon has demonstrated anti-inflammatory effects in animal models, with cinnamaldehyde inhibiting inflammatory mediators (e.g., COX-2, 5-LOX) and oxidative stress (112). A systemic review by Nakhaee *et al.* showed that cinnamon significantly improved cognitive function in terms of memory and learning across 40 studies, but only two were human clinical trials and neither focused specifically on AD's anti-inflammatory effects. Thus, while ginger and cinnamon showed promise, more human studies are needed to establish their anti-inflammatory efficacy in AD (113).

Other Specific Foods

Dark Chocolate and Green Tea

Dark chocolate and green teas have been explored for their potential to mitigate this inflammation and potentially slow AD progression. Dark chocolate, particularly varieties with high cacao content (≥70%), contains flavonoids such as epicatechin and catechin, which exhibit potent antioxidant and anti-inflammatory properties (114). An *in vitro* study demonstrated that cocoa polyphenols can trigger neuroprotective effects in a human AD model by modulating the brain-derived neurotrophic factor (BDNF) signaling pathway, thereby counteracting oxidative stress and promoting neuronal survival (115). Furthermore, a systematic review in 2022 found that consuming dark chocolate with at least 70% cacao reduced stress and inflammation; while improving memory, immunity, and mood, although it did not specifically focus on AD patients (116).

Green tea is rich in catechins such as Epigallocatechin-3-Gallate (EGCG) has been extensively studied for AD prevention and treatment. Green tea catechins possess antioxidant and anti-inflammatory activities, which are crucial for reducing neuronal inflammation and oxidative stress associated with AD (117). Specifically, EGCG has been shown to inhibit lipopolysaccharide-induced inflammation in microglia, reducing the production of pro-inflammatory cytokines and nitric oxide (118). EGCG can also ameliorate learning and memory deficits in animal models by modulating neuroinflammation, with studies showing preadministration of EGCG prevented lipopolysaccharide-induced memory impairment and suppressed increases in cytokines and inflammatory proteins in mice (119, 120) (Table 2). Green tea compounds can reduce amyloid plaque formation and protect neuron function, with anti-inflammatory properties playing a significant role. These studies collectively suggest that anti-inflammatory effects of green tea may help mitigate AD pathology

by reducing neuroinflammation and supporting neuronal health (121).

Conclusion

The role of anti-inflammatory foods in AD management is increasingly recognized, with emerging evidences suggesting their potential to mitigate neuroinflammation and slow disease progression. Foods rich in omega-3 fatty acids, such as fatty fish, have been shown to reduce pro-inflammatory cytokines and improve cognitive function in mild cognitive impairement patients. Berries, particularly blueberries and strawberries, contain antioxidants that lower oxidative stress and neuroinflammation, as demonstrated in both animal models and human studies. Spices like turmeric, with its active compound curcumin, exhibit anti-inflammatory properties by inhibiting NF-κB activation and reducing amyloid-beta aggregation. Dark chocolate and green tea are rich in flavonoids and catechins, respectively and show promise in reducing oxidative stress and inflammatory markers. However, while preclinical and observational studies are encouraging, randomized controlled trials are needed to establish the efficacy of these dietary interventions in human AD populations, particularly in advanced stages of the disease. Future researches should focus on optimizing dosages, identifying synergistic effects, and understanding the long-term impact of these foods on AD progression. Nonetheless, incorporating these anti-inflammatory foods into a balanced diet may offer a complementary approach to managing AD, supporting overall brain health and potentially delaying cognitive decline.

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Authors' Contribution

A.S: Conceptualization, Literature Search, Data Extraction, and Writing – Original Draft of the Narrative Review. M.A.M: Supervision, Methodological Guidance, Critical Revision, and Final Approval of the Manuscript.

Conflict of Interest

None of the authors had a conflict of interest.

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