

# Flavanols for Age-related Memory Loss: A Promising Nutritional Intervention

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[journals.sagepub.com/home/aon](http://journals.sagepub.com/home/aon)Mariam Shahabi<sup>1</sup>  and Rahma Idrees<sup>1</sup>

As the global population ages, healthcare systems face the challenge of providing quality care that addresses the unique needs of older adults, including age-related memory loss (ARML).<sup>1</sup> Although considered a normal part of aging, ARML nevertheless impairs the quality of life and limits opportunities for older adults. Neuroscientific research has been focused on understanding the molecular and cellular characteristics of the aging brain and exploring potential interventions to reduce the risk of age-related cognitive decline. One area of interest is the impact of nutritional interventions, with studies showing promising results for flavanols, a group of plant-based compounds with antioxidant and anti-inflammatory properties, found in foods such as fruits, vegetables, tea, cocoa, and red wine, shown to have a protective effect on neurocognition of aging adults.<sup>2</sup>

Flavanols are part of a larger family of health-promoting phytochemicals called polyphenols, which can be classified as flavonoids (flavonols, flavanols, flavones, flavanones, isoflavones, and anthocyanins) and non-flavonoids (phenolic acids, hydroxycinnamic acids, lignans, stilbenes, and tannins).<sup>3</sup> Flavanols, specifically, have been found to account for approximately 80% of flavonoid intake in the United States, with smaller amounts of other flavonoids consumed.<sup>4</sup>

The neuroprotective effects of flavanols can be attributed to various cellular and physiological mechanisms. Flavanols such as catechins and epicatechins have good absorption in the human body and are detectable in the bloodstream as early as 30 min after ingestion.<sup>5</sup> They have been shown to cross the blood-brain barrier, suggesting a direct impact on brain functioning.<sup>6</sup> Flavanols are associated with strong antioxidant and anti-inflammatory properties, in addition to aiding neuroplasticity, which involves the formation of new neural pathways.<sup>7</sup> They also enhance cerebral blood flow, which is crucial for oxygenation, waste metabolite excretion, and glucose supply to neurons.<sup>8</sup>

Results from the COcoa Supplement and Multivitamin Outcomes Study (COSMOS)-Web, an ancillary trial that involved 3960 participants from the COSMOS, were published recently.<sup>9</sup> Participants were randomized to a daily dose of 500 mg cocoa flavanols or placebo for 3 years. Individuals in the intervention arm experienced a modest

improvement in hippocampal-dependent memory, which involves the ability to recall specific facts, knowledge, events, and locations. These benefits were more pronounced among older adults who had a poor intake of flavanols at baseline. These individuals showed an average increase of 10.5% in memory scores compared with the placebo group, and a 16% increase in their memory scores from baseline. These findings are consistent with those from an earlier study that involved 37 participants and used functional magnetic resonance imaging (fMRI) and cognitive testing to establish that dietary flavanol consumption can enhance the functioning of the dentate gyrus, a region within the hippocampal formation associated with episodic memory.<sup>10,11</sup>

Despite promising results, there is significant heterogeneity in previous randomized controlled trials (RCTs) investigating flavanols' neurocognitive effects on older adults. Differences in sample size, study duration, and flavanol dosage have contributed to mixed outcomes. Some smaller-scale studies with high flavanol doses and shorter exposure durations reported positive correlations between flavanol consumption and cognitive outcomes.<sup>12,13</sup> However, larger RCTs, like the COSMOS-Mind trial involving over 2200 elderly participants, found no association between cocoa flavanol consumption and cognitive outcomes over a 3-year period.<sup>14</sup> More evidence from large-scale longitudinal studies is needed to establish the effectiveness of flavanol-rich diets in maintaining cognitive health during aging.

Consumption of flavonoids in general has been associated with a slower rate of cognitive decline, according to large prospective cohort studies.<sup>15,16</sup> However, these studies employ food frequency questionnaires, which because of their reliance on self-reported data from participants, can introduce bias into the study.<sup>17</sup>

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Despite the limitations of currently available literature, flavanols and other polyphenols found in foods still offer a promising avenue for supporting cognitive health. The PNAS study suggests a daily intake of 500 mg, which is easily achieved, considering that these compounds occur in a variety of fruits, teas, and cocoa.<sup>9</sup> It is no secret that neurodegenerative diseases and even ARML have a profound healthcare burden; nutritional therapies are easy to implement, and can be a low-cost, low-risk way to improve cognitive function and reduce the risk of neurodegenerative disease in the elderly population.

## Authors' Contribution

Mariam Shahabi contributed to the conceptualization and drafting of the manuscript; Rahma Idrees contributed to the drafting and finalization of the manuscript. Both authors drafted the manuscript, critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and have read and approved the final manuscript.

## Declaration of Conflicting Interests

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## References

- Jakovljevic M, Kumagai N, Ogura S. Editorial: Global population aging – Health care, social and economic consequences, volume II. *Front Public Health* 2023; 11: 1184950. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10150406/>
- Cheng N, Bell L, Lamport DJ, et al. Dietary flavonoids and human cognition: A meta-analysis. *Mol Nutr Food Res*. 2022 Nov 1; 66(21): e2100976. <https://pubmed.ncbi.nlm.nih.gov/35333451/>
- Di Lorenzo C, Colombo F, Biella S, et al. Polyphenols and human health: The role of bioavailability. *Nutrients* 2021 Jan 1; 13(1): 1–30. <https://pubmed.ncbi.nlm.nih.gov/33477894/>
- Bonetti F, Brombo G and Zuliani G. Nootropics, functional foods, and dietary patterns for prevention of cognitive decline. *Nutrition and Functional Foods for Healthy Aging* 2017 Jan 1; 211–232.
- Nehlig A. The neuroprotective effects of cocoa flavanol and its influence on cognitive performance. *Br J Clin Pharmacol* 2013 Mar; 75(3): 716. <https://pmc/articles/PMC3575938/>
- Faria A, Pestana D, Teixeira D, et al. Insights into the putative catechin and epicatechin transport across blood-brain barrier. *Food Funct* 2011 Jan; 2(1): 39–44. <https://pubmed.ncbi.nlm.nih.gov/21773584/>
- Cichon N, Saluk-Bijak J, Gorniak L, et al. Flavonoids as a natural enhancer of neuroplasticity—an overview of the mechanism of neurorestorative action. *Antioxidants (Basel)* 2020 Nov 1; 9(11): 1–19. <https://pubmed.ncbi.nlm.nih.gov/33114058/>
- Lamport DJ, Pal D, Moutsiana C, et al. The effect of flavanol-rich cocoa on cerebral perfusion in healthy older adults during conscious resting state: A placebo controlled, crossover, acute trial. *Psychopharmacology (Berl)* 2015 Sep 14; 232(17): 3227–3234. <https://pubmed.ncbi.nlm.nih.gov/26047963/>
- Brickman AM, Yeung LK, Alschuler DM, et al. Dietary flavanols restore hippocampal-dependent memory in older adults with lower diet quality and lower habitual flavanol consumption. *Proc Natl Acad Sci U S A* 2023 Jun 6; 120(23): e2216932120. <https://pubmed.ncbi.nlm.nih.gov/37252983/>
- Amaral DG, Scharfman HE and Lavenex P. The dentate gyrus: Fundamental neuroanatomical organization (dentate gyrus for dummies). *Prog Brain Res* 2007; 163: 3–22. <https://pubmed.ncbi.nlm.nih.gov/17765709/>
- Brickman AM, Khan UA, Provenzano FA, et al. Enhancing dentate gyrus function with dietary flavanols improves cognition in older adults. *Nat Neurosci* 2014; 17(12): 1798–1803. <https://pubmed.ncbi.nlm.nih.gov/25344629/>
- Sloan RP, Wall M, Yeung LK, et al. Insights into the role of diet and dietary flavanols in cognitive aging: Results of a randomized controlled trial. *Sci Rep* 2021 Dec 1; 11(1): 3837. <https://pubmed.ncbi.nlm.nih.gov/33589674/>
- Mastroiacovo D, Kwik-Urbe C, Grassi D, et al. Cocoa flavanol consumption improves cognitive function, blood pressure control, and metabolic profile in elderly subjects: The cocoa, cognition, and aging (CoCoA) study—a randomized controlled trial. *Am J Clin Nutr* 2015 Mar 1; 101(3): 538–548. <https://pubmed.ncbi.nlm.nih.gov/25733639/>
- Baker LD, Manson JE, Rapp SR, et al. Effects of cocoa extract and a multivitamin on cognitive function: A randomized clinical trial. *Alzheimers Dement* 2023; 19(4): 1308–1319. <https://pubmed.ncbi.nlm.nih.gov/36102337/>
- Holland TM, Agarwal P, Wang Y, et al. Association of dietary intake of flavonols with changes in global cognition and several cognitive abilities. *Neurology* 2023 Feb 14; 100(7): E694–E702. <https://pubmed.ncbi.nlm.nih.gov/36414424/>
- Yeh TS, Yuan C, Ascherio A, et al. Long-term dietary flavonoid intake and subjective cognitive decline in US men and women. *Neurology* 2021 Sep 7; 97(10): e1041–e1056. <https://pubmed.ncbi.nlm.nih.gov/34321362/>
- Kristal AR, Peters U, Potter JD. Is it time to abandon the food frequency questionnaire? *Cancer Epidemiol Biomarkers Prev* 2005; 14(12): 2826–2828. <https://pubmed.ncbi.nlm.nih.gov/16364996/>