



Herbal Solutions for Age-Related Cognitive Decline

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1

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2

1

Disclosures

- I am receiving compensation from Gaia to prepare and present this webinar

3

Topics Covered

- What is Cognitive decline?
- Risk factors
- The role of diet and lifestyle
- Key herbs and Gaia products



4

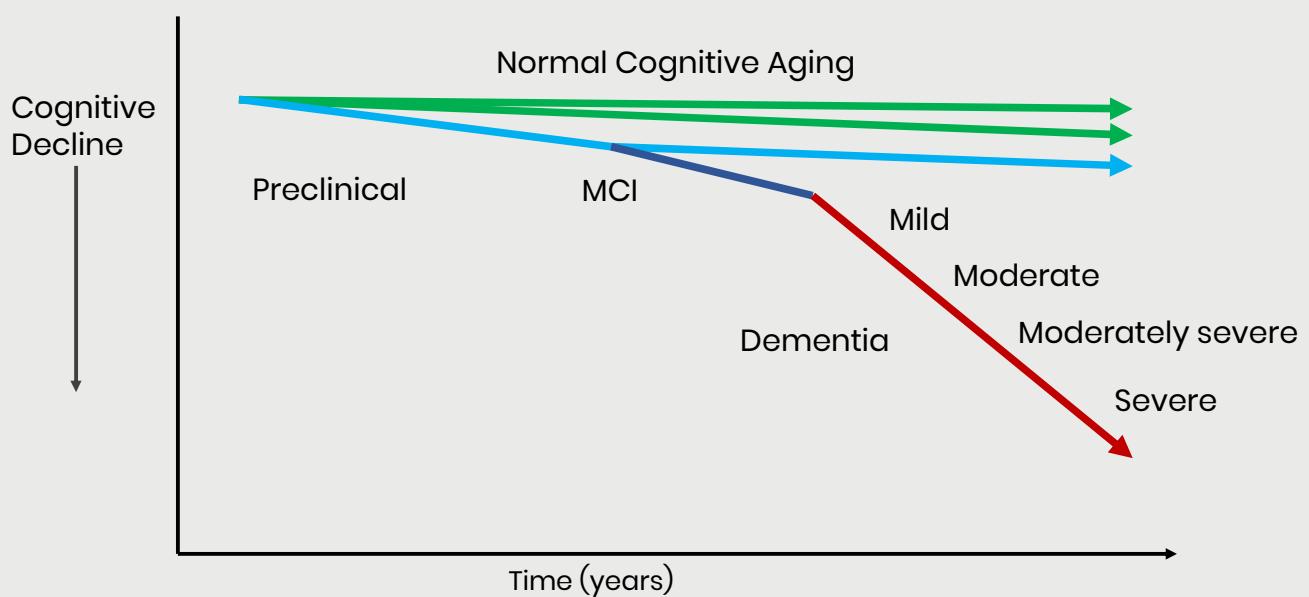
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Definitions

- Age-related cognitive decline
 - Gradual reduction in cognitive abilities that occurs as individuals age
- Mild Cognitive Impairment (MCI) → Mild Neurocognitive Decline
 - An intermediate stage between age-related cognitive decline and more severe conditions such as dementia
- Dementia → Major Neurocognitive Decline
 - Not a specific disease
 - An umbrella term encompassing various progressive neurological disorders

5

The Complexity of Cognitive Decline?



6

3

Types of Dementia

- Alzheimer's Disease
- Vascular Dementia
- Dementia with Lewy Bodies
- Mixed Dementia
- Limbic-predominant age-related TDP-43 encephalopathy (LATE)
- Frontotemporal Dementia
- Parkinson's Disease Dementia
- Huntington's Disease
- Creutzfeldt-Jakob Disease
- Down Syndrome
- Normal Pressure Hydrocephalus
- Posterior Cortical Atrophy
- Korsakoff Syndrome

www.alz.org/alzheimers-dementia Accessed February 12, 2024
Duong MT, Wolk DA. Limbic-Predominant Age-Related TDP-43 Encephalopathy: LATE-Breaking Updates in Clinicopathologic Features and Biomarkers. *Curr Neurol Neurosci Rep.* 2022 Nov;22(11):689–698. PMID: 36190653

7

Risk Factors Dementia and AD

- Age (older) and sex (female)
- Lower educational attainment (15%)
- Lifestyle:
 - Smoking (current) (4%)
 - Physical inactivity (18%)
 - Poor diet
 - ↓ cognitive, social engagement & intellectual activity
 - Excessive alcohol intake

Baumgart M, Snyder HM, Carrillo MC, et al. *Alzheimer's & Dementia.* 2015 Jun;11(6):718–26.
Crous-Bou M, Minguillón C, Gramunt N, et al. *Alzheimer's research & therapy.* 2017 Dec;9(1):71.
Kalaria RN, Maestre GE, Arizaga R et al. *Lancet Neurol* 2008; 7(9): 812–826

8

4

Risk Factors Dementia and AD

- Family history & Genetics (*APOE ε4* allele)
- Cardiovascular:
 - Diabetes (2%)
 - Obesity (mid-life) (17%)
 - Hypertension (mid-life) (14%)
 - Hyperlipidemia
- Traumatic or repetitive brain injury
- Depression (8%)
- Poor sleep & breathing disordered sleep

Baumgart M, Snyder HM, Carrillo MC, et al. *Alzheimer's & Dementia*. 2015 Jun 1;11(6):718–26.
Crous-Bou M, Mingüellón C, Gramunt N, et al. *Alzheimer's research & therapy*. 2017 Dec;9(1):71.
Kalaria RN, Maestre GE, Arizaga R et al. *Lancet Neurol* 2008; 7(9): 812–826

9

Proposed Risk Factors & Associations

- Metabolic syndrome and insulin resistance^{1,2}
- Non-alcoholic fatty liver disease³
- Glymphatic system dysfunction⁴
- Air pollution^{5,12}
- Metal toxicity (i.e. aluminium exposure and heavy metal)⁶

References following

10

Proposed Risk Factors & Associations

- Olfactory dysfunction⁷
- Infection (esp. herpes family viruses and periodontal bacteria)⁸
- Inflammatory bowel disease⁹
- Loss of vision¹⁰ or hearing¹¹

References next slide

11

References Previous Slide

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4. Boespflug EL, Iliff JJ. Biological psychiatry. 2018 Feb 15;83(4):328–336.
5. Chen H, Kwong JC, Copes R, et al. Environment international. 2017 Nov 1;108:271–7.
6. Adlard PA, Bush AI. Journal of Alzheimer's Disease. 2018 Jan 1;62(3):1369–79.
7. Kotecha AM, Corrêa AD, Fisher KM, Rushworth JV. Biosensors. 2018 Apr 13;8(2):41.
8. Sochocka M, Zwolinska K, Leszek J. Current neuropharmacology. 2017 Oct 1;15(7):996–1009.
9. Zhang B et al. Gut. 2021 Jan; 70(1): 85–91.
10. Ehrlich JR et al. JAMA Neurol. 2022 Jun 1; 79(6): 623–626.
11. Stevenson JS et al. Alzheimers Dement. 2022 Mar; 18(3): 445–456.
12. Iaccarino L et al. JAMA Neurol. 2021 Feb 1; 78(2): 197–207.

12

Emerging and Controversial Risk factors

- Vitamin D deficiency¹
- Dysbiosis: gut and oral^{2,3,4}
- Acetaminophen (Tylenol)⁵

13

References Previous Slide

1. Jones A et al. Dement Geriatr Cogn Disord. 2024 Feb 12. PMID: 38346414.
2. Jemimah S et al. PLoS One. 2023 May 24;18(5):e0285346. PMID: 37224131;
3. Parra-Torres V, et al. Oral Dis. 2023 Jan;29(1):21–28. PMID: 34698406.
4. Anand N, Gorantla VR, Chidambaram SB. The Role of Gut Dysbiosis in the Pathophysiology of Neuropsychiatric Disorders. Cells. 2022 Dec 23;12(1):54. PMID: 36611848.
5. Zhang Y, et al. Association of regular use of ibuprofen and paracetamol, genetic susceptibility, and new-onset dementia in the older population. Gen Hosp Psychiatry. 2023 Sep-Oct;84:226–233. PMID: 37633120.

14

Protective Factors in AD

- The Mediterranean diet is highly protective¹
- Regular intake of fruit and vegetable juices²
- Regular exercise³



1. Luchsinger JA, Noble JM, Scarmeas N. Current neurology and neuroscience reports. 2007 Sep 1;7(5):366–72.
2. Dai Q, Borenstein AR, Wu Y, et al. The American journal of medicine. 2006 Sep 1;119(9):751–9.
3. Lange-Asschenfeldt C, Kojda G. Experimental gerontology. 2008 Jun 1;43(6):499–504.

15

The FINGER Study of Cognitive Decline

- Diet, exercise, cognitive training and monitoring vascular risk found to improve or maintain cognitive functioning
- Those with the ApoE4 gene responded more favourably
- Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) study: a large, long-term, RCT
- Aimed to assess multidomain intervention in older people to reduce the risk of cognitive decline
- 1,260 participants (aged 60-77 years)

Crous-Bou M, Minguillón C, Gramunt N, et al. Alzheimer's research & therapy. 2017 Dec;9(1):71.

16

Causes of Cognitive Decline & Dementia

- Mitochondrial dysfunction
- Microglia-induced neuroinflammation
- Microvascular pathology
- Trophic alterations
- Immune dysfunction
- Vascular health: ischemia, arterial stiffness
- White matter hyperintensities
- Disrupted glymphatics

17



**Reversal
of
Cognitive
Decline**

Rao RV, Subramaniam KG, Gregory J, et al.
Int J Mol Sci. 2023 Jan 14;24(2):1659.

18

Key Herbs for Improving Cognition

- Ginkgo
- Saffron
- Spearmint
- Lemon Balm
- Turmeric (Curcumin)
- Lion's Mane
- Resveratrol
- Bacopa
- Korean Ginseng
- Withania
- Holy Basil
- Gotu Kola
- Rosemary
- Schisandra
- Eleuthero
- Green Tea



19

Saffron



20

10

Saffron

Crocus sativus

- Analgesic
- Anti-inflammatory
- Antioxidant
- Cytoprotective
- Anti-apoptotic
- Antidepressant
- Neuroprotective, Nootropic



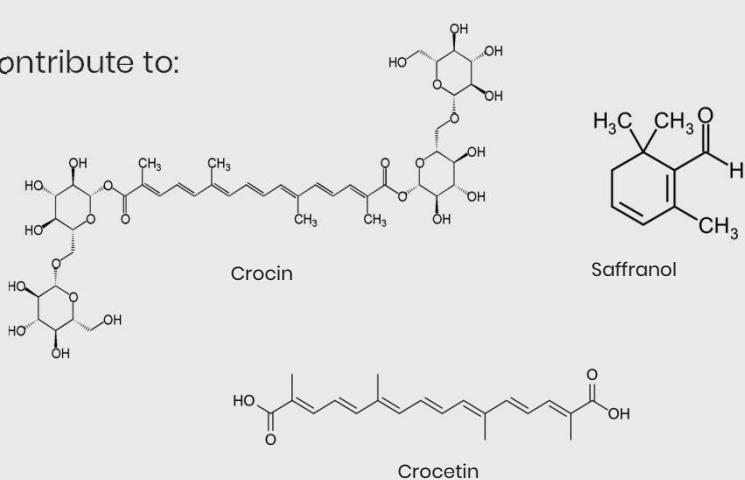
Golpour-Hamedani S, Pourmasoumi M, Zarifi SH, et al. *Helijon*. 2024;10(2):e24334. Published 2024 Jan 10.
doi:10.1016/j.heliyon.2024.e24334

21

Saffron Against Neurodegeneration

Crocin, crocetin and safranal contribute to:

- ↓ DNA damage
- ↓ Protein damage
- ↓ Apoptosis
- ↓ Lipid peroxidation
- ↓ Neuroinflammation
- ↓ Mitochondrial dysfunction



Golpour-Hamedani S, Pourmasoumi M, Zarifi SH, et al. *Helijon*. 2024;10(2):e24334. Published 2024 Jan 10.
doi:10.1016/j.heliyon.2024.e24334

22

Saffron for Mental Health

- Meta-analysis (2024): Saffron for neurological/psychiatric disorders
- 46 RCTs (4-48 weeks)
 - Cognition enhancement & cognitive diseases
 - Depression
 - Anxiety
 - Sleep
 - ADHD
 - OCD

Han S, Cao Y, Wu X, *Phytther Res*. Published online February 29, 2024. doi:10.1002/ptr.8110

23

Saffron & MCI

- Improves MMSE in MCI after 1 year intake and MRI, EEG and ERP showed significant improvement in specific domains (no dose) (SBCT)¹
- Improves visual short-term memory (30 mg/day) (DBRPCT)²
- Improves cognitive function and activities of daily living in patients with AD or MCI (30 mg/day) (meta-analysis of 4 RCTs, 2020)³

1. Tsolaki M, Karathanasi E, Lazarou I, et al. J Alzheimers Dis. 2016;54(1):129-133. doi:10.3233/JAD-160304

2. Ghodrat, M., Sahraei, H., Razjouyan, J., & Meftahi, G. H. Neurophysiology. 2014;46, 247-253.

3. Ayati Z, Yang G, Ayati MH, et al. *BMC Complement Med Ther*. 2020;20(1):333. Published 2020 Nov 9. doi:10.1186/s12906-020-03102-3

24

Saffron for Metabolic Health

- Meta-analysis (2022)
- 11 DBPCTs (8-12 weeks)
- Populations with diabetes, metabolic syndrome or schizophrenia
- Dose: 30-100 mg/day
- Improves lipid profile: TC, TG, LDL-C, HDL-C
- RCTs demonstrate hypoglycemic activity too

Roshanravan B, Samarghandian S, Ashrafizadeh M, et al. *Arch Physiol Biochem*. 2022;128(3):666-678.
doi:10.1080/13813455.2020.1716020

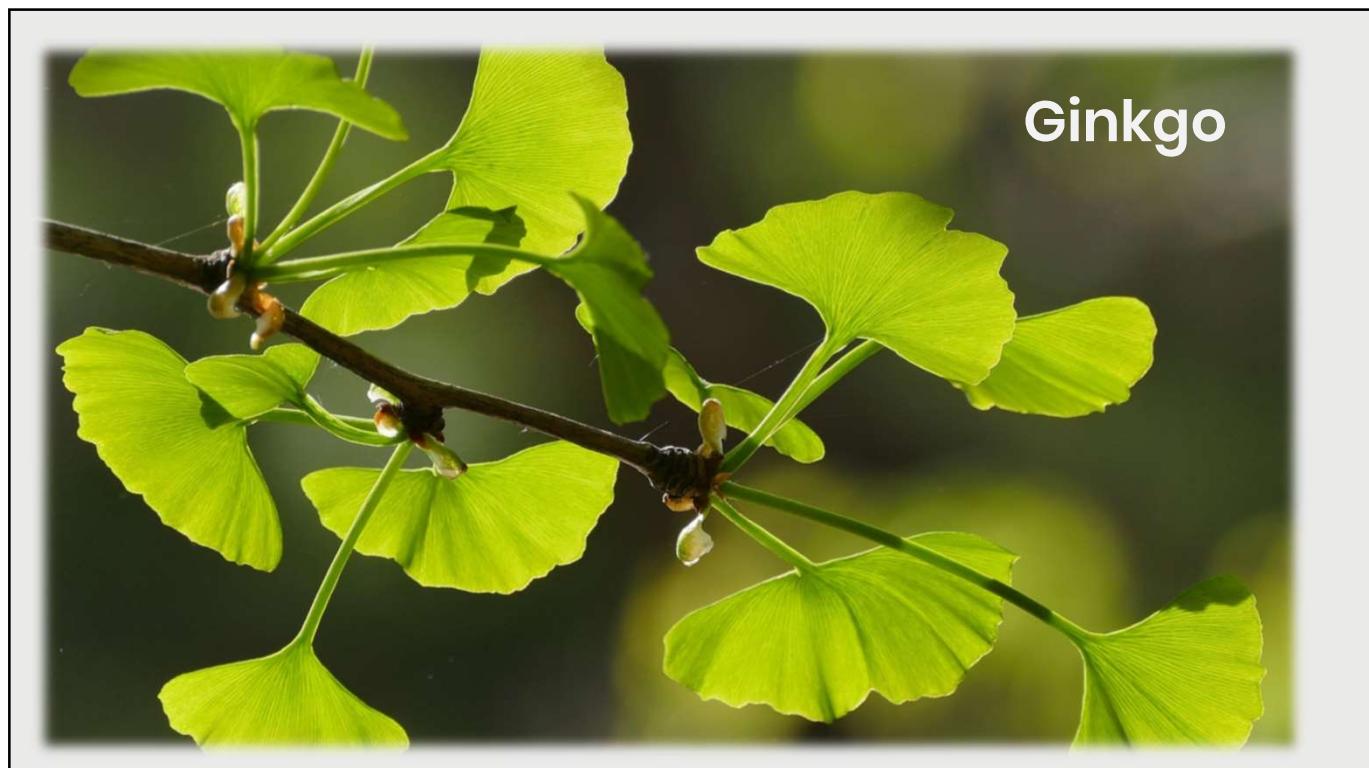
25

Saffron Cardiovascular Disease

- Dose: 30-50 mg extract daily
 - Reduces diastolic blood pressure¹
 - Fasting plasma glucose¹
 - Lowers LDL and reduces oxidized LDL¹
 - Lowers triglycerides¹
 - Increases HDL¹
 - Body weight and waist circumference¹

¹. Roshanravan N, Ghaffari S. The therapeutic potential of Crocus sativus Linn: A comprehensive narrative review of clinical trials. *Phytother Res*. 2022 Jan;36(1):98-111.

26



27

Ginkgo for Cognitive Decline

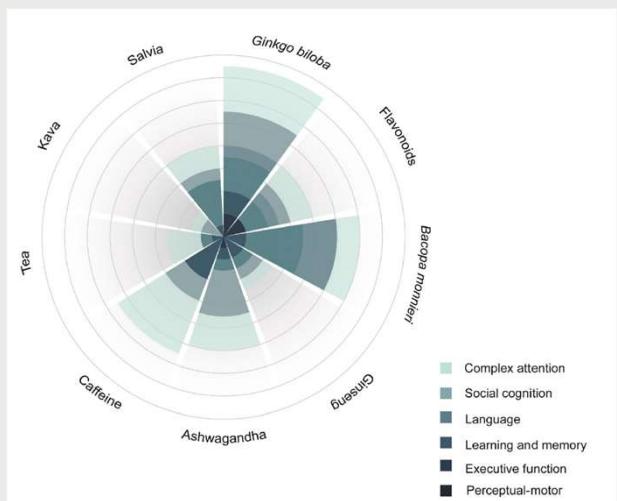
- Ginkgo is ideally suited for prevention
- Numerous studies demonstrate neuroprotective effects 1,2,3
- Protects against ischemia and improves brain energy metabolism
- Antioxidant and anti-inflammatory4

1. Bastianetto S, Quirion R. Cellular and molecular biology (Noisy-le-Grand, France). 2002 Sep;48(6):693-7.
2. Zimmermann M, Colciaghi F, Cattabeni F, et al. Cellular and molecular biology (Noisy-le-Grand, France). 2002 Sep;48(6):613-23.
3. Ahlemeyer B, Kriegstein J. Pharmacopsychiatry. 2003 Jun;36(S 1):8-14.
4. Smith JV, Luo Y. Journal of Alzheimer's Disease. 2003 Jan 1;5(4):287-300.

28

Ginkgo & Cognitive Function

1. Complex attention
2. Social cognition
3. Learning & memory
4. Executive function
5. Perceptual-motor functions
6. Language



Lorca C, Mulet M, Arévalo-Caro C, et al. *Crit Rev Food Sci Nutr.* 2023;63(22):5521-5545.

29

Ginkgo for Cognition

- Healthy volunteers (aged 50–65) with subjective memory impairment (RDBPCT pilot)
 - Improved cognitive flexibility (processing efficiency)
 - Accelerated endocrine stress recovery (speed-accuracy trade-off task)
 - Enhancement of prefrontal dopaminergic system thought to be key

Beck SM, Ruge H, Schindler C, et al. *Human Psychopharmacology: Clinical and Experimental.* 2016 May 1;31(3):227-42.

30

Ginkgo & Mild NCD – Systematic Review

- 9 clinical trials involving 946 patients with mild NCD
- Dose: 120 mg (3), 160 mg (3), 240 mg (4) *Ginkgo biloba* extract EGb 761
- Duration: 8 to 52 weeks
- Significant improvements:
 - Memory, Speed of Processing
 - Attention, Executive Functioning
- Depression (2 of 3 studies) and Anxiety (1 of 1 study) were also significantly improved

Hort J, Duning T, Hoerr R. Ginkgo biloba Extract EGb 761 in the Treatment of Patients with Mild Neurocognitive Impairment: A Systematic Review. *Neuropsychiatr Dis Treat.* 2023 Mar 23;19:647–660. doi:10.2147/NDT.S401231. PMID: 36994422.

31

Received: 23 October 2018 | Revised: 27 November 2018 | Accepted: 28 November 2018
DOI: 10.1111/cns.13095

CLINICAL GUIDELINES

WILEY CNS Neuroscience & Therapeutics

Treatment of dementia and mild cognitive impairment with or without cerebrovascular disease: Expert consensus on the use of *Ginkgo biloba* extract, EGb 761®

Nagaendran Kandiah¹  | Paulus Anam Ong² | Turana Yuda³ | Li-Ling Ng⁴ |
Kaysar Mamun⁵ | Reshma Aziz Merchant⁶  | Christopher Chen⁷ | Jacqueline Dominguez⁸ |
Simeon Marasigan⁹ | Encarnita Ampil⁹ | Van Thong Nguyen¹⁰ | Suraya Yusoff¹¹ |
Yee Fai Chan¹² | Fee Mann Yong¹³ | Orapitchaya Krairit¹⁴ | Chuthamanee Suthisisang¹⁵ |
Vorapun Senanarong¹⁶ | Yong Ji¹⁷ | Ramesh Thukral¹⁸ | Ralf Ihl¹⁹

- Ginkgo biloba extract EGb 761® is current best practice

Kandiah N, Ong PA, Yuda T, et al. Treatment of dementia and mild cognitive impairment with or without cerebrovascular disease: Expert consensus on the use of Ginkgo biloba extract, EGb 761®. *CNS Neurosci Ther.* 2019 Feb;25(2):288–298. PMID: 30648358.

32

Asian Expert Consensus on Ginkgo

- Ginkgo + conventional therapy recommended for management of:
 - Alzheimer's disease
 - Vascular dementia
 - Behavioural and psychological symptoms of dementia
 - Mixed dementia (AD + CVD)
- Ginkgo only recommended for management of:
 - Mild cognitive impairment
- Recommended dose 240 mg/day

Kandiah N, Ong PA, Yuda T, et al. *CNS Neurosci Ther.* 2019;25(2):288–298. doi:10.1111/cns.13095

33

Expert Consensus on the Use of Ginkgo

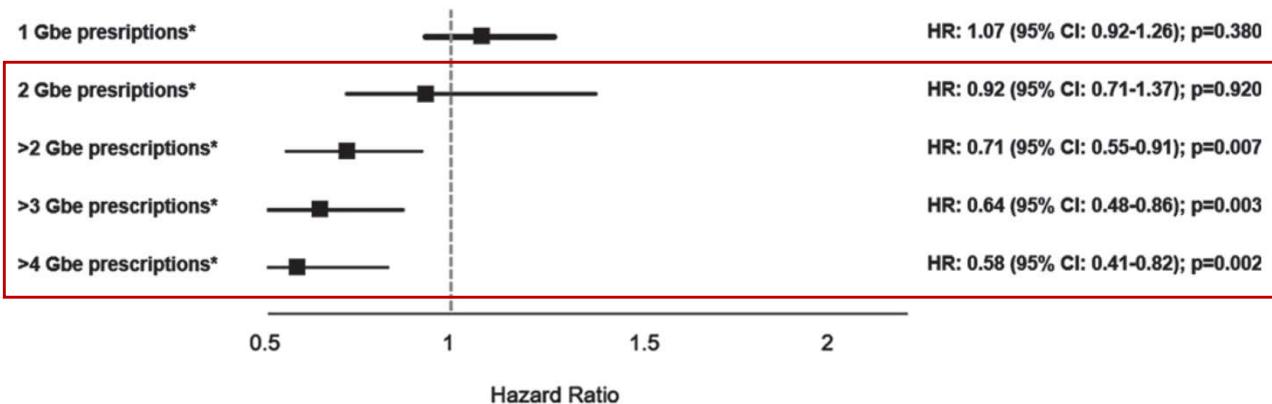
Evidence suggests that 240 mg/day Ginkgo extract has comparable efficacy to all current drugs

Kandiah N, Ong PA, Yuda T, et al. Treatment of dementia and mild cognitive impairment with or without cerebrovascular disease: Expert consensus on the use of Ginkgo biloba extract, EGb 761®. *CNS Neurosci Ther.* 2019 Feb;25(2):288–298. PMID: 30648358.

34

17

Ginkgo Dosing for Seniors with MCI



Bohlken J, Peters O, Kostev K. *J Alzheimers Dis*. 2022;86(2):703-709. doi:10.3233/JAD-215348

35

Lemon Balm



36

18

Lemon Balm

Melissa officinalis

- Antioxidant
- Mild sedative
- Anxiolytic
- Nervine
- Thymoleptic

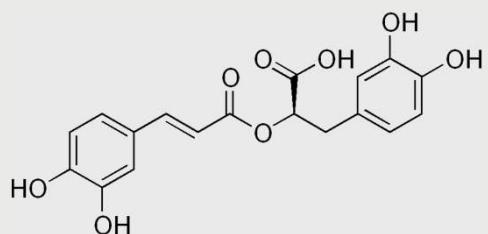


Noguchi-Shinohara M, Ono K, Hamaguchi T, et al. *Sci Rep.* 2020;10(1):18627. Published 2020 Oct 29. doi:10.1038/s41598-020-73729-2

37

Rosmarinic Acid

- Antioxidant
- Antiinflammatory
- Antimutagenic
- Antibacterial
- Antiviral
- Anti-amyloidogenic & anti-Alzheimer's



Noguchi-Shinohara M, Ono K, Hamaguchi T, et al. *Sci Rep.* 2020;10(1):18627. Published 2020 Oct 29. doi:10.1038/s41598-020-73729-2

38

Lemon Balm & RA for Cognitive Decline

Lemon Balm extract containing rosmarinic acid 500 mg /day:

Subjects with mild dementia due to AD (DBRPCT):

- Improves dementia symptom frequency/severity¹

Subjects with subjective or mild cognitive impairment (DBRPCT):

- Improves dementia severity scale²

1. Noguchi-Shinohara M, Ono K, Hamaguchi T, et al. *Sci Rep.* 2020;10(1):18627. Published 2020 Oct 29. doi:10.1038/s41598-020-73729-2

2. Noguchi-Shinohara M, Hamaguchi T, Sakai K, et al. Effects of *Melissa officinalis* Extract Containing Rosmarinic Acid on Cognition in Older Adults Without Dementia: A Randomized Controlled Trial. *J Alzheimers Dis.* 2023;91(2):805–814. PMID: 36502333.

39



40

Spearmint For Memory Impairment

Spearmint extract containing min. 14.5% rosmarinic acid:

Subjects with age-associated memory impairment had the following significant improvements compared to placebo after 3 months (DBRPCT):

- Quality of working memory & spatial working memory accuracy:
 - 900 mg/day = 15% improvement
 - 600 mg/day = 9% improvement
- Sleep onset (900 mg/day)
- Vigor-activity, mood disturbance, & alertness/behaviour after waking

Herrlinger KA, Nieman KM, Sanoshy KD, et al. *J Altern Complement Med.* 2018;24(1):37-47. doi:10.1089/acm.2016.0379

41

Spearmint Improves Cognitive Function

Spearmint extract containing min. 14.5% rosmarinic acid: 900 mg/day

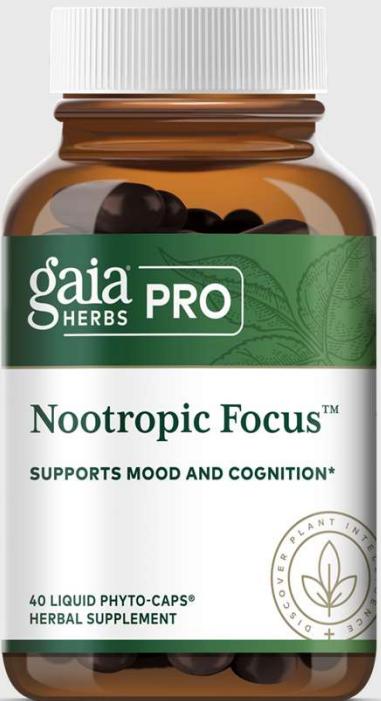
In healthy active adults (aged 18-50)

- Improves attention (sustained and complex)¹
- Improves measures of reactive agility²

1. Falcone PH, Nieman KM, Tribby AC, et al. *Nutr Res.* 2019;64:24-38. doi:10.1016/j.nutres.2018.11.012

2. Falcone PH, Tribby AC, Vogel RM, et al. *J Int Soc Sports Nutr.* 2018;15(1):58. Published 2018 Dec 12. doi:10.1186/s12970-018-0264-5

42



Supplement Facts

Serving Size 2 Capsules
Servings Per Container 20

	Amount Per Serving	% Daily Value
Calories	5	
Total Carbohydrate	1 g	<1%*
Saffron (<i>Crocus sativus</i>) stigma extract	32 mg	†
Ginkgo (<i>Ginkgo biloba</i>) leaf extract	120 mg	†
Proprietary Extract Blend	800 mg	†
Organic Spearmint (<i>Mentha spicata</i>) leaf, Organic Lemon Balm (<i>Melissa officinalis</i>) aerial parts		

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Other ingredients: Vegetable glycerin, water and vegan capsule (hypromellose, chlorophyll).

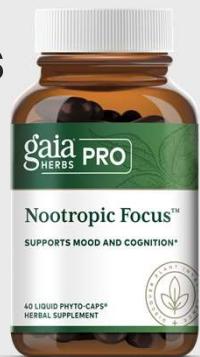
Gaia Herbs, Inc., 101 Gaia Herbs Drive, Brevard, NC 28712

[102]

43

Nootropic Focus Dosing Suggestions

- Label – Adults take 2 caps 1-2 times daily between meals
- 1-2 capsules twice daily, in the morning and evening
- At the low dose of 1 cap twice daily add at least 2 Gaia Ginkgo caps (next slide)
- Long term use will give best results



44



Supplement Facts

Serving Size 2 Capsules
Servings Per Container 30

	Amount Per Serving	% Daily Value
Calories	5	
Total Carbohydrate	1g	<1%*
Proprietary Extract Blend	1,430 mg	†
Organic Ginkgo (<i>Ginkgo biloba</i>) leaf, Ginkgo (<i>Ginkgo biloba</i>) leaf extract		
Flavonoid glycosides	20 mg	†

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Other ingredients: Vegetable glycerin, water and vegan capsule (hypromellose, chlorophyll).

Gaia Herbs, Inc., 101 Gaia Herbs Drive, Brevard, NC 28712
[102]

45

Ginkgo Dosing Suggestions

- 1 capsule is equivalent to 80 mg Ginkgo extract used in CTs based on the ginkgo flavonoglycosides
- 2 capsules = 160 mg
- 3 capsules = 240 mg



46



47

Turmeric Fenugreek Soluble Fiber Complex

Curcuminoids + Fenugreek soluble fiber
=
Curcumagalactomannanosides
(CGM)



Kumar D, Jacob D, Subash PS, et al. Enhanced bioavailability and relative distribution of free (unconjugated) curcuminoids following the oral administration of a food-grade formulation with fenugreek dietary fibre: A randomised double-blind crossover study. *Journal of Functional Foods*. 2016 Apr 1;22:578-87

48

CGM Bioavailability Study Results

- CGM (compared to Standard Curcumin) enhances free curcuminoid oral bioavailability significantly:
 - >39.1-fold increase at a dose of 2 x 500 mg for 30 days¹
 - >30.7-fold increase at a single dose of 500 mg¹
- 74% (66–82%) free curcuminoids²
- 34% (18–34%) conjugated curcuminoids²

1. Matthewman C, et al. Review: Bioavailability and efficacy of 'free' curcuminoids from curcumagalactomannoside (CGM) curcumin formulation *Nutr Res Rev.* 2023 Jan; 1–18

2. Kumar D, Jacob D, Subash PS, et al. Enhanced bioavailability and relative distribution of free (unconjugated) curcuminoids following the oral administration of a food-grade formulation with fenugreek dietary fibre: A randomised double-blind crossover study. *Journal of Functional Foods.* 2016 Apr 1;22:578–87.

49

Bioavailable Curcumin Safety

- Curcumin-galactomannoside complex (CGM)
 - 1,000 mg/day (~380 mg curcuminoids)
 - 3 months
- No adverse effects or clinically relevant changes detected in healthy people, including liver function, renal function, lipid profile, haematological parameters and vital signs.

Pancholi V, Smina TP, Kunnumakkara AB, et al. *Toxicol Rep.* 2021;8:1255–1264. Published 2021 Jun 16. doi:10.1016/j.toxrep.2021.06.008

50

CGM and Occupational Stress

- 60 People under work stress randomized to 3 groups:
 1. CGM 2 x 500 mg/day (391 mg of total curcuminoids)
 2. Unenhanced curcuminoids 951 mg/day
 3. Placebo for 30 days
- Significant improvement in quality of life in CGM group ($p<0.05$)
- Reduced physical/mental fatigue and better concentration
- Improvements in overall stress, fatigue and anxiety ($p<0.001$) were significantly greater for CGM versus the unenhanced curcuminoids
- No changes in the placebo group

Pandaran Sudheeran S, Jacob D, Natinga Mulakal J et al. *J Clin Psychopharmacol*. 2016 Jun; **36**(3): 236–243. PMID: 27043120

51

51

CGM and Occupational Stress

- Significant increases in plasma antioxidant enzymes occurred in both curcuminoid groups including:
 - Superoxide dismutase 59.8%
 - Glutathione peroxidase 70%
 - Glutathione 77%

Pandaran Sudheeran S, Jacob D, Natinga Mulakal J et al. *J Clin Psychopharmacol*. 2016 Jun; **36**(3): 236–243. PMID: 27043120

52

52

CGM Alters Brain Waves

RDBPCT: 18 healthy volunteers (35–65 years)

1 g CGM/day (500 g BID), unformulated curcumin, or placebo for 1 month

- Increases α -waves: cognitive performance
- Increases β -waves: alertness, cognitive processing & reaction time
- Reduced α/β ratio: reduced fatigue
- Improved audio- and visual-reaction times

Khanna A, Das S S, Kannan R, et al. *Nutr Neurosci*. 2022;25(6):1240–1249. doi:10.1080/1028415X.2020.1853410

53

CGM and Alzheimer's Disease

- Changes from baseline

Test	Placebo	USC* 400 mg	CGM 400 mg
MMSE	16.09 → 13.81	15.69 → 16.15	16.07 → 19.21
MMSE % change	↓ 14.17 %	↑ 2.92 %	↑ 19.76 %
GLFS-25 % change	↑ 6.79 %	↑ 2.82 %	↓ 25.17 %

CGM group compared to placebo:

- MMSE improved 39.53%
- GLFS-25 (Geriatric Locomotive Function Scale) improved 31.39%

*USC = Unformulated standard curcumin complex

Das, S S, Gopal, P M, Thomas, J V et al. *Frontiers in Dementia*. 2023;2:1222708. doi:10.3389/frdem.2023.1222708

54

CGM and Alzheimer's Disease

The following are % change from baseline:

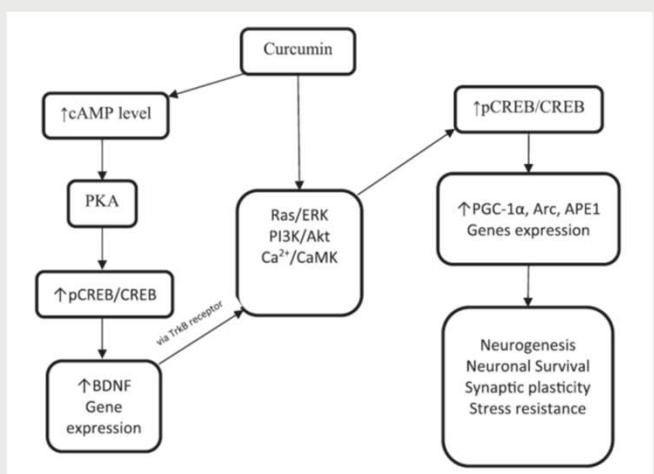
Test	Placebo	USC	CGM
BDNF	↓ 5.21	↑ 3.70	↑ 7.15
Tau	↑ 17.83	↓ 0.79	↓ 5.40
Aβ42	↑ 11.16	↓ 2.68	↓ 13.16
TNF-α	↑ 20.58	↓ 16.33	↓ 55.00

Das, S S, Gopal, P M, Thomas, J V et al. Frontiers in Dementia. 2023;2:1222708. doi: 10.3389/frdem.2023.1222708

55

Curcumin Enhances Serum BDNF

- A 2019 meta-analysis
- 4 RCT with 139 participants
- 200 to 1820 mg curcumin per day
- For 8 to 12 weeks
- Significantly increased serum BDNF levels $P < .01$

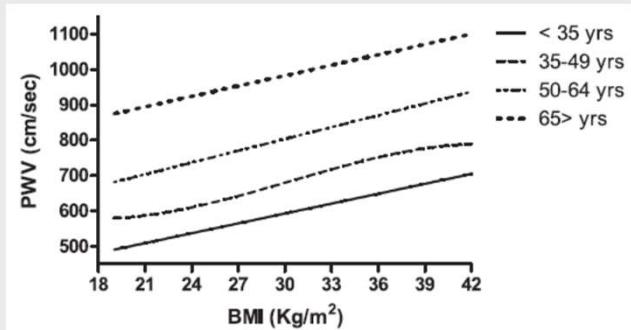


Sarraf P, et al. Short-term curcumin supplementation enhances serum brain-derived neurotrophic factor in adult men and women: a systematic review and dose-response meta-analysis of randomized controlled trials.. *Nutr Res* 2019 Sep;69:1-8

56

Curcumin & Cardiovascular Health

- In a double-blind, placebo-controlled pilot study of 22 obese young men, bioavailable curcumin reduces aortic stiffness¹
 - 500 mg/day bioavailable curcumin (CGM) over 12 weeks
 - Aortic stiffness reduced from 6.81 m/s to 5.84 m/s ($\downarrow 1$ m/s)
 - 1 m/s equivalent to preventing the normal amount of aortic stiffness accumulated across 10 years of life!²



Association between arterial stiffness (PWV) & BMI by age²

1. Campbell MS, Berrones AJ, Krishnakumar IM, et al. Journal of Functional Foods. 2017 Feb 1;29:154-60.
2. Scuteri A, Orru' M, Morrell CH, et al. Atherosclerosis. 2012;221(1):189-197.

57

57

Curcumin Positive Clinical Trials

- Depression
- Inflammation
- Microcirculation
- Non-alcoholic fatty liver disease
- Metabolic syndrome
- Pre-diabetes
- Type 2 Diabetes
- Cardiovascular disease
- Alzheimer's disease

58

29



Supplement Facts

Serving Size	1 Tablet	Servings Per Container	60
Amount Per Serving		% Daily Value	
Total Carbohydrate	<1g	<1%	*
Organic CurQfen® Organic Fenugreek (<i>Trigonella foenum-graecum</i>) seed 6:1 extract and Organic Turmeric (<i>Curcuma longa</i>) rhizome 45:1 extract	320 mg	†	
Curcuminoids	101.3 mg	†	

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Other ingredients: Organic acacia gum, organic oat fiber, organic psyllium husk, organic potato starch, and organic agave fiber.

Manufactured for: Gaia Herbs, Inc., 101 Gaia Herbs Dr., Brevard, NC 28712

Certified Organic by Oregon Tilth

CurQfen® is a registered trademark of Akay Flavours & Aromatics Pvt. Ltd.

[101]

59

Turmeric Fenugreek Complex Dosing Suggestions

- Label – Adults take 1 tablet twice daily
- 1 tablet 3 times daily
- 2 tablets twice daily



60

30

Lion's Mane



61

Lion's Mane Key Actions

Hericium erinaceus

- Antioxidant, anti-inflammatory
- Immunomodulatory
- Neuroprotective, neurotrophic
- Nootropic
- Prebiotic
- Gastrointestinoprotective
- Anti-hyperglycaemic



62

Lion's Mane Key Constituents

- Fungal beta-glucans & misc. polysaccharides
- Ergothioneine
- Hericenones (fruiting body)
- Erinacines (mycelium)

63

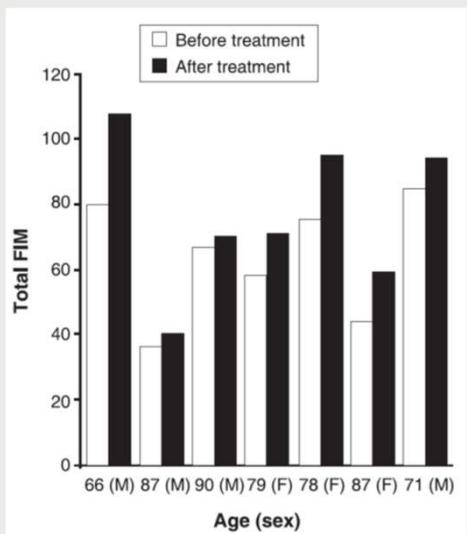
Lion's Mane Key Indications

- Anxiety ★
- Cognitive decline ★
- Dementia & Alzheimer's disease ★
- Depression ★
- Insomnia & sleep disorders ★
- Nerve damage/pain
- Cancer adjunct
- Diabetes & metabolic syndrome
- Dysbiosis ★
- Gastric & peptic ulceration
- Inflammatory bowel diseases

64

Lion's Mane for Mild Dementia

- 7 adults with mild dementia took 5g fruiting body daily in soup for 6 months
- Assessment with Functional Independence Measure (FIM)
- Improved perceptual capacity in 6/7 subjects
- Improved functional independence scores in 7/7 subjects



Kasahara, K., Kaneko, N., Shimizu, K. *Effects of Hericium erinaceum on aged patients with impairment*. Gunma Med Suppl 2001, 76: 77-8.

65

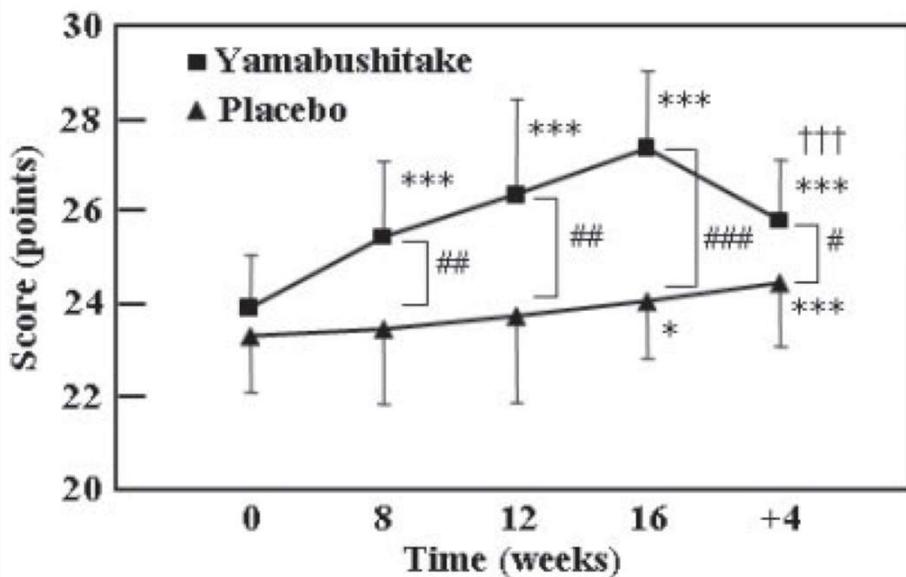
Lions Mane & Age-Related Cognitive Decline

Healthy senior populations (over 50 years of age): 3.2 g of fruiting body/day improves cognitive function^{1,2}

Senior populations with MCI: improvements can take about 8 weeks to detect, however improvements are accumulative over time²

1. Saitsu Y, Nishide A, Kikushima K, et al. *Biomed Res*. 2019;40(4):125–131. doi:10.2220/biomedres.40.125
2. Mori K, Inatomi S, Ouchi K, et al. *Phytother Res*. 2009;23(3):367–372. doi:10.1002/ptr.2634

66



Mori K, Inatomi S, Ouchi K, et al. *Phytother Res*. 2009;23(3):367-372. doi:10.1002/ptr.2634

67

Ergothioneine

- Antioxidant thiol molecule
- Protects the activity of glutathione
- Myriad other antioxidant mechanisms
- Sequestered into cells including neurons, long half-life
- Low levels in mushrooms but primary source

68

* $P < 0.05$
*** $p < 0.001$
$P < 0.05$
$P < 0.01$
$P < 0.001$
++ $P < 0.001$

Ergothioneine for Cognitive Decline

- Ergothioneine-rich lion's mane, without erinacines or hericenones, is also preventative of cognitive decline (mouse model of aging)

Roda E, De Luca F, Ratto D, et al. *Biology (Basel)*. 2023;12(2):196. Published 2023 Jan 28. doi:10.3390/biology12020196

69

Dietary Mushrooms

- Mushrooms modulate the microbiota
 - The microbiota contributes to the gut-brain axis
-
- 12-year prospective study (two nested cohorts, n=400 ea.)
 - 20 serum metabolites identified as markers of cognitive decline
 - Mushroom intake associated with protection against cognitive decline



González-Domínguez R, Castellano-Escuder P, Carmona F, et al. *Mol Nutr Food Res*. 2021;65(23):e2100606. doi:10.1002/mnfr.202100606

70



Supplement Facts

Serving Size	2 Capsules	Servings Per Container	30
Amount	Per Serving	% Daily Value	
Total Carbohydrate	<1 g	<1%*	
Organic Lion's Mane (<i>Hericium erinaceus</i>) fruiting body extracts	900 mg	†	
Beta Glucans	166 mg	†	

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Other ingredients: Organic vegan capsule (organic pullulan).

Manufactured for: Gaia Herbs, Inc.,
101 Gaia Herbs Dr., Brevard, NC 28712

Certified Organic by Oregon Tilth.

Each two capsule serving is equivalent to 5 g of dry mushrooms

Contains a blend of water and dual-extracted mushrooms

[101]

71

Lion's Mane Dosing Suggestions

- Label – Adults take 2 capsules twice daily
- Maintenance: 1 cap daily
- Treatment: 2 to 4 caps daily



72



73



Supplement Facts

Serving Size 2 Capsules
Servings Per Container 25

	Amount Per Serving	% Daily Value
Calories	5	
Total Carbohydrate	2 g	<1%*
Japanese Knotweed (<i>Polygonum cuspidatum</i>) root extracts	672 mg	†
Trans-Resveratrol	150 mg	†

* Percent Daily Values are based on a 2,000 calorie diet.

† Daily Value not established.

Other ingredients: Vegetable glycerin, vegan capsule (hypromellose) and water.

Gaia Herbs, Inc., 101 Gaia Herbs Drive, Brevard, NC 28712

Each 2 capsules provides 150 mg Trans-Resveratrol, the same amount found in 50 bottles of red wine. (Based on a mean calculation of one bottle of red wine containing 2.5 mg of Trans-Resveratrol).

[102]

74

Resveratrol Dosing Suggestions

- 1 capsule twice daily



75

Microcirculation is Paramount

- Green tea
- Garlic and spices
- Blueberries, blackberries, raspberries
- Pomegranate juice
- Cocoa
- Dietary nitrate (beets)
- Gotu Kola
- Ginkgo
- Resveratrol



76

38

Age-Related Cognitive Decline

Core Support

- Nootropic Focus: 2 to 4 caps/day
- Turmeric Fenugreek Complex: 2 to 4 tabs/day
- Resveratrol: 2 caps/day
- Address diet and physical activity

77

Age-Related Cognitive Decline

Additional Support

- Support the risk factors
- Select and appropriate adaptogen e.g. Daytime HPA 2-4/day
- Consider switching out Resveratrol for AMPK Activator 2/day
- Systolic Complex 2/day

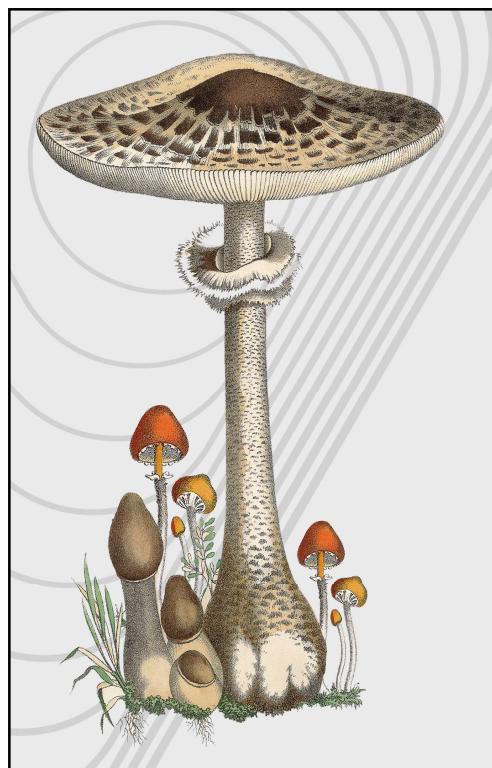
78

39



Thank You

79



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80



81

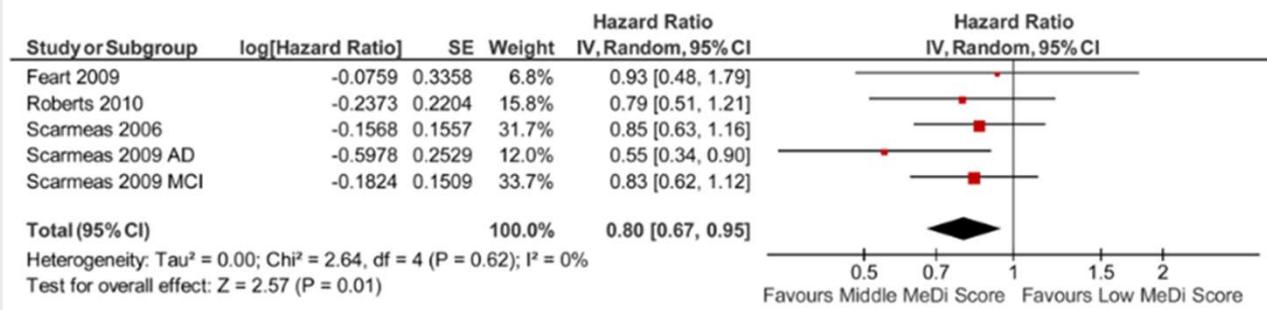
Additional Slides

82

Mediterranean Diet 33% Less Risk of MCI

4.3 Highest vs Lowest MeDi tertile

4.2 Middle vs Lowest MeDi tertile



Singh B, Parsaik AK, Mielke MM, et al. Association of mediterranean diet with mild cognitive impairment and Alzheimer's disease: a systematic review and meta-analysis. *J Alzheimers Dis.* 2014;39(2):271-82. PMID: 24164735

83

MIND Diet and Cognitive Decline

MIND Diet Component Servings and Scoring			
Diet Component	0	0.5	1
Green leafy vegetables	≤ 2 serving/wk	> 2 to < 6 /wk	≥ 6 servings/wk
Other vegetables	< 5 serving/wk	5 to < 7 wk	≥ 1 servings/d
Berries	< 1 serving/wk	1/wk	≥ 2 serving/wk
Nuts	< 1 /mo	< 1 /mo to < 5 /wk	≥ 5 servings/wk
Olive oil	Not primary oil		Primary oil used
Butter	> 2 T/d	1-2T/d	< 1 T/d
Cheese	7 + servings/wk	1-6/wk	< 1 serving/wk
Whole grains	< 1 serving/d	1-2serving/d	≥ 3 servings/d

Morris MC, Tangney CC, Wang Y, et al. *Alzheimer's & dementia.* 2015 Sep 1;11(9):1015-22.

84

MIND Diet and Cognitive Decline

MIND Diet Component Servings and Scoring			
Diet Component	0	0.5	1
Fish (not fried)	Rarely	1-3/mo	≥ 1 meals/wk
Beans	<1 meal/wk	1-3/wk	> 3 meals/wk
Poultry (not fried)	< 1 meal/wk	1/wk	≥ 2 meals/wk
Red Meat and products	7 + meals/wk	4-6/wk	< 4 meals/wk
Fast fried foods	4 + times/wk	1-3/wk	< 1 time/wk
Pastries and sweets	7 + servings/wk	5-6/wk	< 5 servings/wk
Wine	>1 glass/d	1/mo-6/wk	1 glass/d

MIND Diet score each row to get total score (Min 0, Max 15)

Morris MC, Tangney CC, Wang Y, et al. Alzheimer's & dementia. 2015 Sep 1;11(9):1015-22.

85



86

Bacopa

Bacopa monnieri

- Anti-inflammatory
- Antioxidant
- Neuroprotective
- Nootropic
- Antidepressant
- Anxiolytic
- Anti-hyperglycaemic



Fatima U, Roy S, Ahmad S, et al. *Front Nutr*. 2022;9:972379. Published 2022 Aug 18. doi:10.3389/fnut.2022.972379
Kongkeaw C, Dilokthornsakul P, Thanarangsarit P, et al. *Journal of ethnopharmacology*. 2014 Jan 10;151(1):528–35.

87

Bacopa & Cognitive Function

- Meta-analysis (9 RCTs, n=518):
 - Improves cognition, particularly speed of attention
- Open-label study (early-stage AD):
 - Improves cognition regarding times, places, persons
 - Better quality of life (reduced irritability and insomnia)
- Dose: 300 mg/day standardized to bacosides

Kongkeaw C, Dilokthornsakul P, Thanarangsarit P, et al. *Journal of ethnopharmacology*. 2014 Jan 10;151(1):528–35.

88

Bacopa for Learning & Memory

Improves free recall, immediate and working memory

Ongoing continuous intake can improve other aspects of memory including:

- Visual information processing,
- Learning rates,
- Memory consolidation

Effects witnessed in all age ranges including children and elderly, and across the spectrum of cognitive decline and dementia as well as in healthy cohorts.

Lorca C, Mulet M, Arévalo-Caro C, et al. *Crit Rev Food Sci Nutr.* 2023;63(22):5521-5545. doi:10.1080/10408398.2021.2021137

89

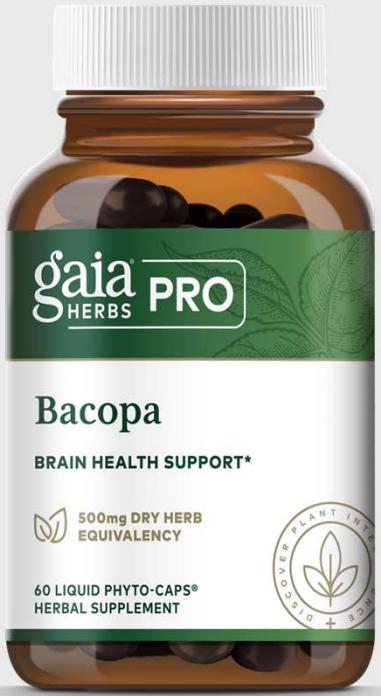
Bacopa in Healthy Seniors

DBRPCT (n=48 healthy seniors)

- Standardized bacopa extract 300 mg/day for 3 months
- Improvements:
 - Delayed recall ($p = 0.03$)
 - Cognitive processing & flexibility, and selective attention ($p = 0.003$)
 - Depression ($p = 0.05$)
 - Anxiety ($p = 0.04$)
 - Heart rate ($p = 0.01$)

Calabrese C, Gregory WL, Leo M, et al. *J Altern Complement Med.* 2008;14(6):707-713. doi:10.1089/acm.2008.0018

90



Supplement Facts

Serving Size 1 Capsule		
Servings Per Container 60		
Amount Per Serving	% Daily Value	
Total Carbohydrate Organic Bacopa (<i>Bacopa monnieri</i>) aerial parts extract	<1 g 350 mg	<1%* †

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Other ingredients: Vegetable glycerin, water, vegan capsule (hypromellose) and organic olive oil.

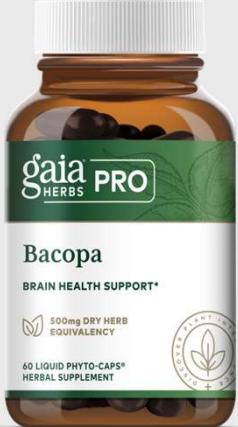
Gaia Herbs, Inc., 101 Gaia Herbs Drive, Brevard, NC 28712
Each serving contains 500 mg dry herb equivalent.

[103]

91

Bacopa Dosing Suggestions

- Label – 1 capsule 1–2 times daily
- Bacopa is a high-dose herb
- Clinical doses range from 2.5 g to 10 g daily
- I suggest a minimum of 4 capsules per day, 2 twice daily



92