**What is Mild Cognitive Impairment?**

Mild cognitive impairment (MCI) refers to patients who have a degree of cognitive impairment that causes complaints from the patient and/or family members without affecting the patient’s ability to function normally. This differs from Alzheimer’s disease or dementia, which do impact a patient’s ability to function at a normal level or live safely at home and are more severe than MCI. The risk of developing MCI increases with age. Only about 5% of patients ages 65 to 69 have some form of memory impairment, whereas nearly 35% of patients experience memory impairment by ages 85 and older. MCI can be classified as either amnesic or non-amnesic, meaning it affects either memory or cognitive skills other than memory, respectively.

**The History of Cognitive Enhancement Supplements**

The idea of preventing cognitive decline is not a new one. In fact, ancient remedies from India and China have been used for memory improvement for about 5,000 years. In Indian culture, Ayurvedic medicine was an approach to natural and holistic medicine that focuses on three aspects of mental health: memory, learning and understanding, and retention. Supplements used in this culture include *Bacopa monnieri*, winter cherry, aloeweed, and pennywort. In traditional Chinese medicine (TCM), various supplements were used for improving memory and cognition as well, including *Ginkgo biloba*, ginseng, goji berries, reishi mushrooms, and danggui-shaoyao-san (DSS).
<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Where it’s found</th>
<th>Theories on how it works</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apoaequorin</td>
<td>Jellyfish species <em>Aequorea victoria</em></td>
<td>Binds calcium in neuronal cells to mitigate cell death caused by excess calcium</td>
</tr>
<tr>
<td><em>Coffee arabica</em> fruit extract</td>
<td>Fleshy fruit surrounding coffee beans on coffee plant</td>
<td>Increases brain-derived neurotrophic factor and reduces reactive oxygen species</td>
</tr>
<tr>
<td>Phosphatidylserine</td>
<td>Human cell membranes and myelin of brain tissue; egg and soybean</td>
<td>Improves neurotransmission, receptor sensitivity, enzyme function; prevents neuronal cell membrane remodeling</td>
</tr>
<tr>
<td>Omega-3-fatty acids</td>
<td>Fish, other marine animals, humans</td>
<td>Patients with cognitive dysfunction potentially have lower levels of omega-3-fatty acids</td>
</tr>
<tr>
<td>Vitamin B6 (pyridoxine)</td>
<td>Foods such as grains, flour, eggs, vegetables, legumes, and meats</td>
<td>Prevents gray matter atrophy by increasing homocysteine metabolism</td>
</tr>
<tr>
<td>Vitamin B9 (folic acid)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B12 (cyanocobalamin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Citrus fruits</td>
<td>Prevents cellular damage from oxidative stress via antioxidant properties</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Made by the skin when exposed to sunlight; milk, eggs, fish</td>
<td>Potential link between low vitamin D levels and poor cognitive function</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Various foods, including oils, nuts, and vegetables</td>
<td>Prevents cellular damage from oxidative stress via antioxidant properties</td>
</tr>
<tr>
<td><em>Ginkgo biloba</em></td>
<td>Leaf extract of a tree native to Asia, but also found in Europe and the United States</td>
<td>Prevents cellular damage from oxidative stress via antioxidant properties</td>
</tr>
<tr>
<td>Medium chain triglycerides (MCTs)</td>
<td>Dairy fat, various oils</td>
<td>Induces ketosis which could improve energy metabolism in the brain; prevents amyloid plaque damage</td>
</tr>
<tr>
<td>Citicoline</td>
<td>Human and animal cells</td>
<td>Reduces free radicals in the brain, improves cell membrane stability, stimulates dopamine release</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Extract from <em>Panax ginseng</em> plant</td>
<td>Increases hippocampus acetylcholine levels and inhibits acetylcholinesterase in the CNS</td>
</tr>
<tr>
<td>Soy</td>
<td>Soybean plant</td>
<td>Up-regulates nerve growth factor and choline acetyltransferase; decreases phosphorylation of protein tau</td>
</tr>
<tr>
<td>Resveratrol</td>
<td>Grapes, red wine, some berries, eucalyptus, spruce, and peanuts</td>
<td>Inhibits beta-amyloid buildup and improves connectivity in the hippocampus</td>
</tr>
</tbody>
</table>
Common Products Today\textsuperscript{26-31}

Today, there are a variety of different OTC cognitive function supplements that use a variety of different combinations of the above ingredients. Branded over the counter products are rated on safety and efficacy from the Natural Medicines Database on a scale named the Natural Medicines Brand Evidence-based Rating (NMBER). These combinations have limited evidence of their use, but some of the most common products can be seen in the chart below.

<table>
<thead>
<tr>
<th>Product</th>
<th>Image of product</th>
<th>Ingredients</th>
<th>Safety/Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevagen\textsuperscript{®}</td>
<td><img src="https://www.prevagen.com/shop/prevagen-regular-strength/" alt="Prevagen Image" /></td>
<td>Apoaequorin</td>
<td>Safety: Prevagen\textsuperscript{®} has been shown to be safe over a period of 90 days, and there have been only non serious ADRs reported in post market surveillance.  Efficacy: There is insufficient data to support the efficacy of this product for decreasing age related cognitive decline.</td>
</tr>
</tbody>
</table>

Acetyl-L-carnitine

- Human liver, kidney, and brain; foods such as red meat and dairy
- Decreases oxidative stress and prevents acetylcholine depletion

*Bacopa monnieri*

- Herb from India
- Enhances acetylcholine release, inhibits acetylcholinesterase activity, reduces beta-amyloid levels

*Rhodiola rosea*

- Plant found at cold climates in Asia and Europe
- Provides antioxidant activity and inhibits monoamine oxidase
<table>
<thead>
<tr>
<th>Product</th>
<th>Safety:</th>
<th>Efficacy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuriva (Original)®</td>
<td>Both the Original and Plus products have been shown to be safe.</td>
<td>The ingredients caffeine and phosphatidylserine have been shown to have possible efficacy in reducing age related cognitive decline, other ingredients have limited data or are likely ineffective.</td>
</tr>
<tr>
<td>Neuriva (Plus)®</td>
<td>Safety:</td>
<td>Efficacy:</td>
</tr>
<tr>
<td></td>
<td>There is a lack of safety data for many of the ingredients.</td>
<td>There is some data supporting the use of Acetyl-L-Carnitine for reducing age related cognitive decline, but the other ingredients included do not have the data supporting their use.</td>
</tr>
<tr>
<td>Irwin Natural® Brain Awake®</td>
<td>Safety:</td>
<td>Efficacy:</td>
</tr>
</tbody>
</table>

Image available from https://www.schiffvitamins.com/
The most well-known out of the three brands is Prevagen® and has a rating of 6 out of 10 (1 being the lowest recommendation, 10 being the highest) on the NMBER scale for safety and efficacy. The evidence behind the use of this product comes from a study conducted by the parent company, Quincy Bioscience, LLC, and was not reviewed by the FDA. Prevagen® recently settled a class action lawsuit for misrepresenting claims that their product helped prevent memory loss.

Also rated as a 6 on the NMBER scale are the Neuriva® products, both original and plus. The Irwin Naturals product has been rated as a 2 on the NMBER scale and cannot be recommended due to the lack of evidence of the ingredients included in the product.

The last “dose” ...

“I am starting to think that maybe memories are like this dessert. I eat it, and it becomes a part of me, whether I remember it later or not.” -Erica Bauermeister, New York Times bestselling author

“Why is it I can remember the lyrics to my favorite song in high school 20 years later, but I can’t remember why I came into the kitchen?” -Someecards®

Health Professional with a Question? Drugs – Therapeutics – Pharmacy Practice?
Please contact us. We can help resolve your issue.

Please call 344-844-4400 Monday-Friday 8:00 to 5:00 pm (some holidays excepted)
or visit our website, 24/7 at: http://www.auburn.edu/academic/pharmacy/dilrc/overview.html

An electronic bulletin of drug and health-related news highlights, a service of ...
Auburn University, Harrison School of Pharmacy, Drug Information Center
• Phone 334-844-4400 • http://www.auburn.edu/academic/pharmacy/dilrc/overview.html
Bernie R. Olin, Pharm.D., Director
Archived issues are available at: http://www.auburn.edu/academic/pharmacy/dilrc/au-informed.html
Resources:


42

AU InforMed, vol.18, no. 6, Wednesday, December 16, 2020