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Higher Levels of These Antioxidants Linked to Lower Dementia

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STORY AT-A-GLANCE

- People with higher levels of lutein, zeaxanthin and beta-cryptoxanthin had a lower risk of developing dementia as measured in 7,283 people over 16 years
- Lutein and zeaxanthin have long been prized for their ability to protect the eyes; when combined with vitamin E they appear to improve lung function and when combined with beta-cryptoxanthin and vitamin E they are inversely correlated with congestive heart failure
- Astaxanthin is another antioxidant associated with slowing brain aging; it plays a role in protecting the skin from the inside out and against dementia, heart disease and Parkinson's disease
- Sulforaphane is an organosulfur compound that fights against Alzheimer's Disease and activates the antioxidant and anti-inflammatory responses in the body, including augmenting the role of glutathione, the "master antioxidant"

A study supported by the National Institute on Aging and published in the journal Neurology demonstrates that people who have higher levels of specific antioxidants in their blood could reduce their potential risk of developing dementia.[1,2]

Antioxidants are substances that help protect the body against cell damage from free radicals. The body produces free radicals as a part of normal metabolism, after

exposure to some environmental pollutants and exercise.[3] At high levels they can damage cells and genetic material.

Free radicals have one less electron, which makes them unstable. The free radical seeks to steal the necessary electron from any nearby substance, thus turning that substance into a free radical. Free radical damage can also change how a cell functions, which leads to oxidative stress and chronic diseases.[4]

The body uses antioxidants to fight against free radicals because they donate an extra electron to the free radical without turning into a free radical themselves. Some of the antioxidants you are likely familiar with include carotenoids, manganese, selenium, vitamin E, vitamin C and beta-carotene.

While antioxidants all have similar functions, they are not all interchangeable, which means they have unique properties and no one single substance can do all the work. In the past decade, researchers have discovered that many of the chronic diseases and disorders in modern day society are linked to an increase in inflammation.

An imbalance of natural antioxidants to free radical production can increase the inflammatory response that's associated with diabetes, cardiovascular disease, inflammatory bowel disease, obesity and arthritis.[5]

Researchers have long known that antioxidants play a role in the prevention of dementia.[6,7,8] The featured study has identified three specific antioxidants that may play a role in reducing the risk of dementia.[9]

Lutein, Zeaxanthin and Beta-Cryptoxanthin Lower Dementia Risk

Researchers were interested in how antioxidants may affect the development of dementia. One study author, May A. Beydoun, Ph.D., MPH, of the National Institutes of Health's National Institute on Aging in Baltimore, Maryland, commented on the need to address cognitive functioning in an aging population:[10]

> *"Extending people's cognitive functioning is an important public health challenge. Antioxidants may help protect the brain from oxidative stress, which can cause cell damage. Further studies are needed to test whether adding these antioxidants can help protect the brain from dementia."*

According to the Alzheimer's Association,[11] by 2050, there will be nearly 13 million people living with Alzheimer's disease. Currently, it kills more people than breast cancer and prostate cancer combined and, in 2020, COVID contributed to a 17% rise in the deaths of people with dementia and Alzheimer's.

In 2022, the Alzheimer's Association estimated that dementia costs $321 billion, which could rise to nearly $1 trillion by 2050. An estimate published in 2022 in the Lancet[12] and funded by the Bill & Melinda Gates Foundation, estimated the global number of people with all forms of dementia would rise from 57.4 million to 152.8 million in 2050.

The writers of the study then noted that the "growth and number underscores the need for public health planning efforts and policy to address the needs of this group."[13] The study supports the Foundation's investment in dementia,[14] including interest in vaccines[15] with a partnership with the pharmaceutical industry.[16]

A systematic review and meta-analysis published in 2020[17] found that the number of people with dementia nearly doubles every five years and the prevalence is greater in women than in men. These numbers underscore the importance of finding strategies that can help reduce the potential risk of Alzheimer's and other dementias.

The study[18] engaged 7,283 people who were given blood tests and a physical exam and then followed for an average of 16 years. All participants were at least 45 years old at the start. The researchers measured levels of three antioxidants — lutein, zeaxanthin and beta-cryptoxanthin.

The researchers[19] split the participants into three groups and found those whose blood levels were highest for lutein and zeaxanthin had a lower risk of developing dementia than those who had the lowest levels. For every standard deviation of increase in these two antioxidants, the participants had a 7% reduction in risk.

They also found that for every standard deviation increase in beta-cryptoxanthin, the participants had a 14% reduced risk of dementia. Beydoun pointed out there were several limitations to the study, including that when other factors were considered in the analysis, such as education and physical activity, the risk of dementia was lowered.

The writers also noted that antioxidants were measured at the start and end of the study. However, this may not reflect the level of antioxidants that a person had throughout their lifetime. Foods high in lutein and zeaxanthin[20] include dark leafy greens like spinach, peas, summer squash, pumpkin and broccoli. Foods high in beta-cryptoxanthin include peppers, pumpkin, squash, oranges and persimmons.[21]

Lutein and Zeaxanthin Important for Eye Health

Lutein and zeaxanthin have long been prized for their vision enhancing properties as they are the only two antioxidants that reach the retina.[22] Researchers write they are "uniquely concentrated in the retina and lens, indicating that each has a possible specific function in these two vital ocular tissues."[23]

Animal studies have shown that diets that are less than optimal in primates trigger pathological problems in the macula. Researchers believe these antioxidants are "conditionally essential nutrients."[24]

Both are carotenoids that are major contributors to the yellow and red pigments found in vegetables. There is mounting evidence that lutein can improve or prevent age-related macular disease and has a positive effect on other health conditions, such as cognitive function, cancer and heart health.[25]

High levels of these carotenoids help stave off age-related eye diseases such as cataracts and macular degeneration. Diet influences your risk for healthy vision. According to Loren Cordain, an evolutionary biologist at the Colorado State University in Fort Collins, elevated insulin levels affect the development of your eyeball, making it abnormally long, thereby causing near-sightedness.[26]

High insulin levels from excess carbohydrates can increase insulin resistance and disturb the delicate choreography that normally coordinates eyeball lengthening and lens growth. When your eyeball elongates, the lens can no longer flatten itself enough to focus a sharp image on your retina.

This theory is consistent with observations that you're more likely to develop myopia if you are overweight[27] or have Type 2 diabetes,[28] both of which raise insulin levels. Lutein has also been found to promote health in other ways, including:

- Diets rich in the carotenoids beta-carotene, lutein and lycopene confer greater resistance against oxidation of low-density lipoprotein (LDL) cholesterol,[29] which plays a role in the development of atherosclerosis. Higher plasma concentration of carotenoids was also associated with lower DNA damage.[30]
- Lutein and zeaxanthin in combination with vitamin E appear to improve lung function.[31]
- Plasma levels of antioxidants such as lutein, zeaxanthin, vitamin E, beta-cryptoxanthin, lycopene and alpha- and beta-carotene are inversely correlated with congestive heart failure severity.[32]
- Plasma carotenoid levels are also inversely correlated with prostate cancer.[33]

Astaxanthin Slows Brain Aging

Astaxanthin is another carotenoid, which is responsible for the pink or red color of wild-caught Alaskan salmon. According to Science Direct,[34] “when compared to other antioxidants such as lycopene, vitamin E and vitamin A,” astaxanthin comes out on top and is often referred to as the “king of antioxidants.”

It is derived from Haematococcus microalgae, which produce astaxanthin as a protective mechanism to shield from harsh ultraviolet (UV) light.[35] Data demonstrates how astaxanthin helps protect your skin from the inside out.[36]

Your body uses astaxanthin to protect against reactive oxygen species (ROS) and oxidation, which plays a role in protection against dementia, heart disease, aging and Parkinson's disease.[37] Antioxidant supplementation helps when you don't get enough from your diet, which helps alleviate oxidative damage.

Researchers writing in the journal Marine Drugs,[38] recognized the challenge of maintaining brain function while human life expectancy lengthens. In their review of the literature, they identified several pathways astaxanthin could take in slowing brain aging. They found several studies where astaxanthin modulated biological mechanisms, one of the main factors which was the forkhead box 03 gene (FOXO3).

This is one of only two genes with a significant impact on human longevity. They also found that astaxanthin increases brain-derived neurotrophic factor (BDNF) in the brain and attenuates oxidative damage to DNA, lipids and protein. After reviewing the literature, they concluded it was possible astaxanthin could promote longevity and slow the rate of aging due to its neuroprotective properties.[39]

Slowing brain aging is significant since the neurological aging process is directly linked to cognitive function. Some cognitive changes that can occur with aging, but are not necessarily normal,[40] include finding it difficult to remember words, having difficulty with multitasking, recalling names, or having more difficulty paying attention.

Although astaxanthin is a carotenoid, the molecular structure is unique, and it is more potent than other carotenoids. One of the key differences is that it has a surplus of electrons to donate as it neutralizes free radicals.[41,42] Another unique factor is that it can protect both water- and fat-soluble parts of the cell.[43] This makes astaxanthin a powerful antioxidant, which data showed is greater than alpha lipoic acid, green tea catechins, CoQ10 and vitamin C.[44]

Most antioxidant carotenoids are either water-soluble or fat-soluble, but astaxanthin's effectiveness is due to the capability to interface between water and fat. It can also cross the blood-brain barrier, where it exerts a strong protective effect on neurological health.[45] While it is found in wild-caught salmon, you can purchase high-quality

astaxanthin supplements or consider krill oil supplements, which have the added benefit of omega-3 fatty acids.[46]

Sulforaphane Activates Antioxidant Responses

Sulforaphane is an organosulfur compound that researchers believe may prove useful to fight Alzheimer's Disease by altering the production of amyloid-beta and tau. These are two main factors known to contribute to the development of the disease.[47] Levels of amyloid-beta proteins may become abnormally high, clumping together to form plaques that disrupt neuron function.

Abnormal accumulation of the protein tau may also collect inside neurons, forming neurofibrillary tangles that disrupt communication. One animal study[48] of Alzheimer's disease showed that sulforaphane ameliorated amyloid-beta deposits and cognitive function. This hinted at a potential treatment that might also be useful in humans.

Sulforaphane is an Nrf2 activator that works in a dose-dependent fashion to halt dysregulation. An animal study[49] suggested that the dysregulation of Nrf2 may be attenuated through sulforaphane. Lab data[50] also show that sulforaphane "activates antioxidant and anti-inflammatory responses by inducing Nrf2 pathways" and has relevance to preventing neurodegeneration and signs of aging.

Eating more cruciferous vegetables high in sulforaphane or taking a high-quality supplement, is useful for far more than brain health. For instance, sulforaphane may be helpful in the treatment of diabetes as well as lowering blood glucose levels[51] and improving gene expression in your liver.[52]

Sulforaphane can also improve apoptosis in colon[53] and lung cancer cells.[54] It also can reduce damaging ROS by as much as 73%, which lowers your risk of inflammation.[55]

Sulforaphane plays a role in the augmentation of glutathione. Glutathione is commonly referred to as the master antioxidant,[56] since it is the most powerful antioxidant and is found inside every cell in the body. Glutathione is different from other antioxidants since

it works intracellularly[57] and has the unique ability to maximize the activity of other antioxidants.[58]

Excessive oxidative stress has a significant impact on the pathophysiology of brain disorders. One study[59] found a correlation between peripheral levels of glutathione and levels of glutathione found in the brain. They also discovered that sulforaphane raised blood levels of glutathione in humans after only seven days of oral supplementation.

The results of the pilot study have suggested there is a significant relationship between glutathione and sulforaphane that is worth exploring as it appeared to have an impact on neuropsychological measures that are altered in neuropsychiatric disorders.

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