

Natural Products **Insider**[®]

Vol. 12, No. 8 August 2022

naturalproductsinsider.com US\$20.75

Healthy aging

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The longevity paradigm



Ingredients for improved longevity

by Joanna Cosgrove



Aging is unavoidable. However, improving one's healthy longevity is entirely attainable with a balanced lifestyle plus a spectrum of ingredients that strategically target oxidative stress, inflammation, cognitive function, muscular/skeletal issues and other concerns that can potentially undermine long-term health.

"The quality of your aging is something you can tilt in your favor," commented Lindsay Cole, brand manager, Natures Crops International, a producer of Ahiflower oil. "If addressed thoughtfully and consistently through a healthy diet and active lifestyle, many of the outward signs of unhealthy aging can be mitigated or reversed."

Thwarting inflammation

Inflammation contributes to a variety of conditions that can be detrimental to healthy aging. Cole asserted that the typical Western diet of saturated fats, industrial cooking oils, refined sugars and grains, and salt adds to the pro-inflammatory aging burden and as result, many people struggle with cascading conditions like weight gain, blood pressure/glycemic challenges, fatigue, joint and skin issues.

Omega fatty acids can provide broad-spectrum help. "Taking in rich omega-3 sources helps the body balance out excessive pro-inflammatory influences in our diets and environments; omega-3s are critical for maintaining cell membrane permeability, porosity, integrity and inflammation-resolving functions which cumulatively drive how the body ages and how well we respond to all of life's stressors," she said. "Omega-3s are now known to potentiate and balance the gut microbiome and its ability to digest and assimilate the foods we eat, [having] major effects on the gut-brain axis and therefore on our daily mood, outlook, energy levels and overall mental well-being."

Fatty acids, in the form of omega-6 and omega-3, are important structural components of cell membranes and serve as [precursors](#) to bioactive lipid mediators. Long-chain omega-3 polyunsaturated fatty acids ([PUFAs](#)) also exert anti-inflammatory effects.¹

Ahiflower oil—while not a direct source of omega-3 EPA (eicosapentaenoic acid) or DHA (docosahexaenoic acid)—converts to circulating EPA. Emerging science is showing how dietary intakes



of precursor plant-based omega-3 results in similar tissue DHA maintenance in the brain as from supplemental DHA.²

Research has also confirmed a link between oxidative stress and cellular signaling proteins called sirtuins, chiefly the “longevity gene” known as sirtuin 1 (Sirt1). “Sirt1 in humans is believed to improve healthy aging and longevity through a variety of biological pathways related to oxidative stress, inflammation, metabolism, immune health and cognition,”³ explained James Roza, chief scientific officer, Layn Natural Ingredients. “Studies involving calorie restriction, exercise, resveratrol and urolithin A—which is formed from ellagic acid in the microbiome—have all been shown to activate Sirt1.⁴ By increasing Sirt1 expression, mitochondrial function is improved, autophagy (the ability for cells to remove waste) is more efficient, and oxidative stress is reduced.”^{5,6}

Roza pointed to the root of *Polygonum cuspidatum* (Japanese knotweed) as a source of both the antioxidants resveratrol and ellagic acid, which is converted to urolithin A in the microbiome.^{5,6} Urolithin A has been shown to improve mitochondrial function, and reduce inflammation and glycation associated with a few age-related conditions such as muscle dysfunction and cardiovascular disease.^{5,7,8,9}

Layn also markets SophorOx, a quercetin ingredient that promotes mitochondrial biogenesis, wellness and efficiency through the attenuation of reactive oxygen species (ROS) produced by oxidative stress.⁹ Initial research confirming SophorOx’s role in the improvement of several key biomarkers measuring oxidative stress have even given rise to a human study.

Bioenergy Life Science (BLS) has used mitochondria as a springboard for its line of branded ingredients. “Scientists have started to realize that the common cause behind both aging and disease is mitochondrial dysfunction, which is another way of saying that both aging and disease are driven by low metabolism,” commented the company’s Marianne McDonagh, VP of sales.

BLS’ RiaGev is a patented bioenergy ribose and nicotinamide formula for increasing NAD (nicotinamide adenine dinucleotide), ATP (adenosine triphosphate) and GSH (glutathione) simultaneously.¹⁰ Test subjects showed less fatigue, improved mental concentration and motivation.

Quercetin has been studied for its anti-inflammatory effects and impact on areas such as immune, cardiovascular, bone and joint health.¹¹ NutriScience Innovations, supplier of SunActive IsoQ, a highly bioavailable quercetin precursor, is both soluble and bioavailable for a high absorption at a low dose—ideal for formats like beverages.¹²

The ingredient’s bioavailability, explained Michael Lelah, Ph.D., NutriScience’s chief science officer, was achieved in partnership with Taiyo International. In a clinical study comparing intake of the branded and regular quercetin, he noted, “At six hours, blood quercetin levels were 25 times higher in study participants taking SunActive IsoQ.”¹³

Supporting mental acuity

Staying mentally sharp is another age-related challenge. BacoMind, a branded *Bacopa monnieri* from Natural Remedies, is marketed to support cognitive functions like memory, attention, learning and focus. According to Laurentia Guesman, business manager, food and supplement ingredients at AIDP, the exclusive North American distributor of BacoMind, the product has three modes of action: neuroprotection, dopamine preservation and serotonin preservation.¹⁴

A randomized clinical trial affirmed BacoMind's ability to enhance both long- and short-term memory recall, as well as promote memory acquisition and retention in middle-aged and senior adults.¹³ Another placebo-controlled study divided 65 healthy adults ages 50-75 into two groups, one of which took BacoMind (450 mg/d) while the other took a placebo.¹⁴ Compared to the placebo, BacoMind enabled participants to achieve several statistically significant improvements, including improved attention and verbal memory.

According to Guesman, AIDP's No. 1 cognitive support ingredient, Magtein, also supports cognitive health across myriad conditions. One of the ingredient's most recent published studies highlights the benefits of Magtein for stress and anxiety—a bonus for the broader cognitive market.¹⁵

Improving mobility



Aches and pains are another unwelcome reminder of advancing age.

Mark LeDoux, CEO and chairman of Natural Alternatives International (NAI), is an advocate of early-in-life nutrient intervention to ensure the adequate intake of key nutrients such as fatty acids and specific vitamins such as B12 and folate (B9) to thwart issues that crop up later in life. "[Age-related] weight loss and loss of muscle mass have been shown to precede cognitive decline, taking us full circle back to nutritional interventions and supplements to ensure adequate nutrient intake and a focus on maintenance of the musculoskeletal system," he said. "Specific nutrients, such as NAD+ and carnosine, have been examined for their impacts on the aging process in the past, and research continues to demonstrate their importance."^{16,17}

He noted that NAD+ is essential for metabolic function and has also been shown to protect against DNA damage and support muscle function.¹⁸ NAD+ levels decline with age, he said, and impacts are seen across muscle, neurologic and overall cellular health.

SR CarnoSyn, a patented, sustained release format of beta-alanine from NAI, was developed in response to a need for a scientifically validated means of reducing sarcopenia, a condition of muscle wasting associated with aging.¹⁹

Easier nutrient delivery with dissolvable oral films

Age-related dysphagia makes it difficult to swallow multiple pills, which can compromise compliance. That's why Aavishkar Oral Strips Pvt. Ltd. developed ThinSol oral thin films (OTFs), a pill alternative that dissolves on the tongue to potentially deliver a higher-than-average amount of active ingredients.

"Seniors want the benefits of supplements and are willing to commit to long-term consumption; however, the idea of a handful of pills to swallow is often daunting," said Dinesh Reddy, company co-founder and CEO. "Gummies help, but seniors tend to avoid excess sugars and sugar substitutes, and denture wearers will abstain from this form as well."

ThinSol OTFs are compatible with a variety of supplement ingredients, and the company offers a nutraceutical product portfolio of approximately 100 plant-based, natural flavor and color options spanning more than 100 ingredients and over 320 SKUs.

Editor note: FDA has maintained only orally digested forms can be considered dietary supplements, so it is important for brands using dissolvable films to consider the marketing and product instructions around how these ingredients are absorbed.

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- Lindsay Cole, brand manager, Natures Crops International



LeDoux reported, "Beta-alanine supplementation enhances cellular (and extracellular) carnosine levels in different tissues, providing benefits via multiple mechanisms of action [including] impact on cognition and mood via beta-alanine's supportive role in neurotrophin levels in the brain [and] immune health through antioxidant action and balance of inflammatory pathways."²⁰ He pointed to clinical studies supporting muscle strength and function in older adults and master athletes, stating, "This is what we see in healthy aging—you live actively with a balanced, healthy and clear mind."

From the botanical arsenal, turmeric/curcumin has enjoyed a swell of consumer interest thanks to its association with easing mobility-related inflammation.²¹

During one study, a turmeric extract standardized not to curcuminoids but to

Broad-spectrum brand solutions



Lack of quality sleep can have a profound impact on quality of life, taking a bite out of energy, contributing to brain fog, inhibiting creativity and adversely affecting cellular regeneration.^a

"Experts agree that how well we sleep depends on a few factors: latency (the time it takes you to fall asleep), duration (the length of time you stay asleep) and restfulness (tossing and turning versus peacefully/soundly)," remarked Angelo Keely, Kion CEO and co-founder.^b

Kion Sleep is formulated with gamma-aminobutyric acid (as PharmaGABA) in an attempt to reduce stress, promote relaxation and improve sleep quality;^c L-theanine to elevate levels of the GABA, serotonin and dopamine neurotransmitters;^d and L-tryptophan to increase levels of serotonin and melatonin.^d

CELLF from Mikra combines bioactive glutathione (GSH), coenzyme (Co)Q10 and PQQ (pyrroloquinoline quinone) compounds to address inflammation^{e,f} and oxidative stress while boosting energy levels,^g enhancing cognitive function and promoting healthy sleep.^h The product is packaged in convenient 10 ml sachets that contain a vanilla-flavored liposomal liquid gel.

"It's not meant to target one specific part of your health, it's designed to impact all of your biological systems by rebuilding your cellular system from the ground up," said Faraaz Jamal, Mikra's CEO and founder. "CELLF is meant to restore and protect [and] results are tangible in a variety of different ways, like reduced recovery times after exercise, enhanced focus, better mood and sleep."^{e-h}

References

- a Harvey AG et al. "The subjective meaning of sleep quality: a comparison of individuals with and without insomnia." *Sleep*. 2008;31(3):383-393.
- b Voderholzer U et al. "Impact of experimentally induced serotonin deficiency by tryptophan depletion on sleep EEG in healthy subjects." *Neuropsychopharmacol*. 1998;18(2):112-124.
- c Yoto A et al. "Oral intake of γ -aminobutyric acid affects mood and activities of central nervous system during stressed condition induced by mental task." *Amino Acids*. 2012;43(3):1331-1337.
- d Hartmann E and Spinweber CL. "Sleep induced by L-tryptophan. Effect of dosages within the normal dietary intake." *J Nerv Ment Dis*. 1979;167(8):497-499.
- e Farsi F et al. "Can coenzyme Q10 supplementation effectively reduce human tumor necrosis factor- α and interleukin-6 levels in chronic inflammatory diseases? A systematic review and meta-analysis of randomized controlled trials." *Pharma Research*. 2019;148:104290.
- f Joraj MV et al. "The effects of coenzyme Q10 supplementation on biomarkers of inflammation and oxidative stress in among coronary artery disease: a systematic review and meta-analysis of randomized controlled trials." *Inflammopharmacol*. 2019;27(2):233-248.
- g Mehrabani S et al. "Effect of coenzyme Q10 supplementation on fatigue: A systematic review of interventional studies." *Comp Ther Med*. 2019;43:181-187.
- h Qu H et al. "Effects of Coenzyme Q10 on Statin-induced Myopathy: An Updated Meta-Analysis of Randomized Controlled Trials." *J Am Heart Assoc*. 2018;7(19).

tumerosaccharides (as Turmacin from Natural Remedies) was shown to substantially decrease pain and stiffness, improve physical function, and reduce reliance on rescue medication to relieve pain.²² Further, significant decreases in joint tenderness and related joint issues were also documented.

In another study, 70 subjects with knee osteoarthritis (OA) took 800 mg Turmacin plus 200 mg curcuminoids or placebo daily for 12 weeks.²³ Compared to placebo, the supplement combo significantly reduced knee pain and improved function.

Two AIDP offerings also support bone health and mobility. KoAct, a patented combination of collagen and calcium, is positioned as ideal for older women who pursue active lifestyles and has been “clinically proven superior to traditional bone health ingredients in improving bone mineral density.”²⁴ KollaGen-II xs supports healthy, flexible joints via a combination of type II collagen from avian sternum, chondroitin and hyaluronic acid.²⁵

Eric Ciappio, Ph.D., is a registered dietitian and the strategic development manager of nutrition science at Balchem, supplier of Creatine MagnaPower, a blend of creatine and magnesium. He mentioned creatine is typically associated with sports nutrition among younger adults, but it’s increasingly being investigated for its ability to support muscle health and performance in older adults. In fact, a meta-analysis concluded creatine improves lean muscle mass and increases strength during resistance training in adults ages 50 and older. Advancements in creatine’s older adult benefits prompted the European Food Safety Authority (EFSA) to release a health claim on creatine for adults ages 55 and above in 2016.^{26,27}

Safeguarding vision

Diminished visual acuity can be another casualty of aging. In June, the National Institutes of Health (NIH) published AREDS (Age-Related Eye Disease Study) Report, a follow-up on the efficacy and safety of the landmark 2018 AREDS 2 data, which advocated for the intake of certain nutrients to potentially help reduce the risk of severe macular degeneration.²⁸

“The [study found the] probability of progressing to late advanced macular degeneration by 10 years was 47.9% for those taking lutein/zeaxanthin and 49.0% for those not taking lutein/zeaxanthin,” said Tyler Holstein, global product manager, Kemin Industries, supplier of FloraGLO Lutein and ZeaONE/Optisharp Natural Zeaxanthin, which were used in the AREDS 2 study. “By 10 years [it] was ... 49.5% for lutein/zeaxanthin.”²⁸

A recent meta-analysis examined the overall health benefits of carotenoids, specifically related to eye disorders.²⁹ Specifically, zeaxanthin and lutein were designated “eyesight protecting agents.” As retinal carotenoid macular pigments, the high-powered duo exerted beneficial antioxidant properties capable of “absorb[ing] short wavelengths and high-energy blue lights,” subsequently protecting the retina from phytochemical damage and ultraviolet (UV)-induced peroxidation.

As science continues to keep pace with the aging population, supplements will remain a helpful resource for aging gracefully. LeDoux concluded, “It’s exciting that organizations such as the NIH are encouraging researchers to look at nutrients—including traditional herbs—and identify/further clarify their mechanisms of action and key constituents that play a role in overall health, as well as their potential roles in maintaining optimal health with age.” ♦



Joanna Cosgrove is a Pennsylvania-based writer who has covered the healthy food, beverage and dietary supplement markets for more than 20 years.

References

- 1 Troesch B et al. "Expert Opinion on Benefits of Long-Chain Omega-3 Fatty Acids (DHA and EPA) in Aging and Clinical Nutrition." *Nutrients*. 2020;12(9):2555.
- 2 Lefort N et al. "Consumption of Buglossoides arvensis seed oil is safe and increases tissue long-chain n-3 fatty acid content more than flax seed oil – results of a phase I randomised clinical trial." *J Nutr Sci*. 2016;5:e2.
- 3 Salminen A and Kaamiranta K. "SIRT1: regulation of longevity via autophagy." *Cell Signal*. 2009;21(9):1356-1360.
- 4 Chung KW and Chung HY. "The Effects of Calorie Restriction on Autophagy: Role on Aging Intervention." *Nutrients*. 2019;11(12):2923.
- 5 Andreux PA et al. "The mitophagy activator urolithin A is safe and induces a molecular signature of improved mitochondrial and cellular health in humans." *Nat Metab*. 2019;1(6):595-603.
- 6 Yang X and Jiang T. "The Role and Mechanism of SIRT1 in Resveratrol-regulated Osteoblast Autophagy in Osteoporosis Rats." *Sci Rep*. 2019;9(1):18424.
- 7 Ghosh N et al. "Urolithin A augments angiogenic pathways in skeletal muscle by bolstering NAD+ and SIRT1." *Sci Rep*. 2020;10(1):20184.
- 8 Kujawska M and Jodynis-Liebert J. "Potential of the ellagic acid-derived gut microbiota metabolite - Urolithin A in gastrointestinal protection." *World J Gastroenterol*. 2020;26(23):3170-3181.
- 9 Shanmugasundaram D and Roza JM. "Assessment of anti-inflammatory and antioxidant activity of quercetin-rutin blend (SopHox) – an invitro cell-based assay." *J Complement Integr Med*. 2022; Online ahead of print.
- 10 Xue Y et al. "A Combination of Nicotinamide and D-Ribose (RiaGev) Is Safe and Effective to Increase NAD+ Metabolome in Healthy Middle-Aged Adults: A Randomized, Triple-Blind, Placebo-Controlled, Cross-Over Pilot Clinical Trial." *Nutrients*. 2022;14(11):2219.
- 11 Li Y et al. "Quercetin, inflammation and immunity." *Nutrients*. 2016;8(3):167.
- 12 Kapoor MP et al. "Bioavailability of dietary isocoumaritrin- β -cyclodextrin molecular inclusion complex in Sprague-Dawley rats and healthy humans." *J Funct Foods*. 2021;85:104663.
- 13 Morgan AK and Stevens J. "Does Bacopa monnieri Improve Memory Performance in Older Persons? Results of a Randomized, Placebo-Controlled, Double-Blind Trial." *J Altern Complement Med*. 2010;16(7):753-759.
- 14 Barbhaiya HC et al. "Efficacy and Tolerability of BacoMind on Memory Improvement in Elderly Participants -- A Double-Blind Placebo Controlled Study." *J Pharmacol Toxicol*. 2008;3(6):425-434.
- 15 Hewlings S and Kalman D. "A Randomized, Double-Blind, Placebo-Controlled, Comparator Trial Evaluating Magtein Magnesium Supplement on Quality of Life as Related to Levels of Stress, Anxiety, Fear and Other Indicators." *EC Nutrition*. 2022;17(3):7-14.
- 16 Shlisky J et al. "Nutritional Considerations for Healthy Aging and Reduction in Age-Related Chronic Disease." *Adv Nutr*. 2017;8(1):17-26.
- 17 Hipléss AR. "Aging, Proteotoxicity, Mitochondria, Glycation, NAD and Carnosine: Possible Inter-Relationships and Resolution of the Oxygen Paradox." *Front Aging Neurosci*. 2010;2:10.
- 18 Chu X, Raju RP. "Regulation of NAD+ metabolism in aging and disease." *Metabolism*. 2022;126:154923.
- 19 Furst T et al. "Alanine supplementation increased physical performance and improved executive function following endurance exercise in middle aged individual." *J Int Soc Sports Nutr*. 2018;15:32.
- 20 Murakami T and Furuse M. "The impact of taurine- and beta-alanine-supplemented diets on behavioral and neurochemical parameters in mice: antidepressant versus anxiolytic-like effects." *Amino Acids*. 2010;39(2):427-434.
- 21 Madhu K et al. "Safety and efficacy of Curcuma longa extract in the treatment of painful knee osteoarthritis: a randomized placebo-controlled trial." *Inflammopharmacology*. 2013;21(2):129-136.
- 22 Dally JW et al. "Efficacy of Turmeric Extracts and Curcumin for Alleviating the Symptoms of Joint Arthritis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials." *J Med Food*. 2016;19(8):717-729.
- 23 Wang Z et al. "Effectiveness of Curcuma longa Extract for the Treatment of Symptoms and Effusion-Synovitis of Knee Osteoarthritis: A Randomized Trial." *Ann Intern Med*. 2020;173(11):861-869.
- 24 Elam ML et al. "A calcium-collagen chelate dietary supplement attenuates bone loss in postmenopausal women with osteopenia: a randomized controlled trial." *J Med Food*. 2015;18(3):324-331.
- 25 Lopes AP et al. "A 30-day clinical investigation of the safety and efficacy of KollaGen II-xS, a new avian sternal collagen type II hydrolysate." *HealthMED*. 2016;10(2).
- 26 Forbes SC et al. "Meta-Analysis Examining the Importance of Creatine Ingestion Strategies on Lean Tissue Mass and Strength in Older Adults." *Nutrients*. 2021;13(8):1912.
- 27 "Creatine in combination with resistance training and improvement in muscle strength: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006." *EFSA J*. 2016;14(2):4400.
- 28 Chew EY et al. "AREDS2 Research Group. Long-term Outcomes of Adding Lutein/Zeaxanthin and -3 Fatty Acids to the AREDS Supplements on Age-Related Macular Degeneration Progression: AREDS2 Report 28." *JAMA Ophthalmol*. 2022:e221640.
- 29 Tan BL and Norhaizan ME. "Carotenoids: How Effective Are They to Prevent Age-Related Diseases?" *Molecules*. 2019;24(9):1801.



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