Boosting mitochondrial biogenesis for healthy ageing

Supplement ingredient options provide varying degrees of safety and efficacy

SHOJI MATSUKAWA

Vice President
Mitsubishi Gas Chemical America
655 Third Avenue 19th Floor
New York, NY 10017, USA

matsukawa@mg-a.com

Healthy ageing is the process of optimizing opportunities for physical, social and mental health to enable older people to take an active part in society without discrimination and to enjoy an independent and good quality of life, according to AGE Platform Europe. Healthy ageing essentially enhances the later years in life, enabling seniors to continue being who they aspire to be and doing what they desire.

The United States National Institute of Health research has identified action steps that can be taken to maintain health and function as people get older. They suggest improving diet and levels of physical activity, getting health screenings, and managing risk factors for disease to help an individual in the healthy ageing process. Decades of research and studies indicate mitochondrial-targeted therapies, such as nutraceuticals and dietary supplements, may contribute to healthy ageing. Nutraceuticals are gaining importance and recognition across Europe as they become part of the consumer's daily diet. According to Mordor Intelligence, the European nutraceutical market is expected to register a CAGR of 7.5 percent over the next five years. (1)

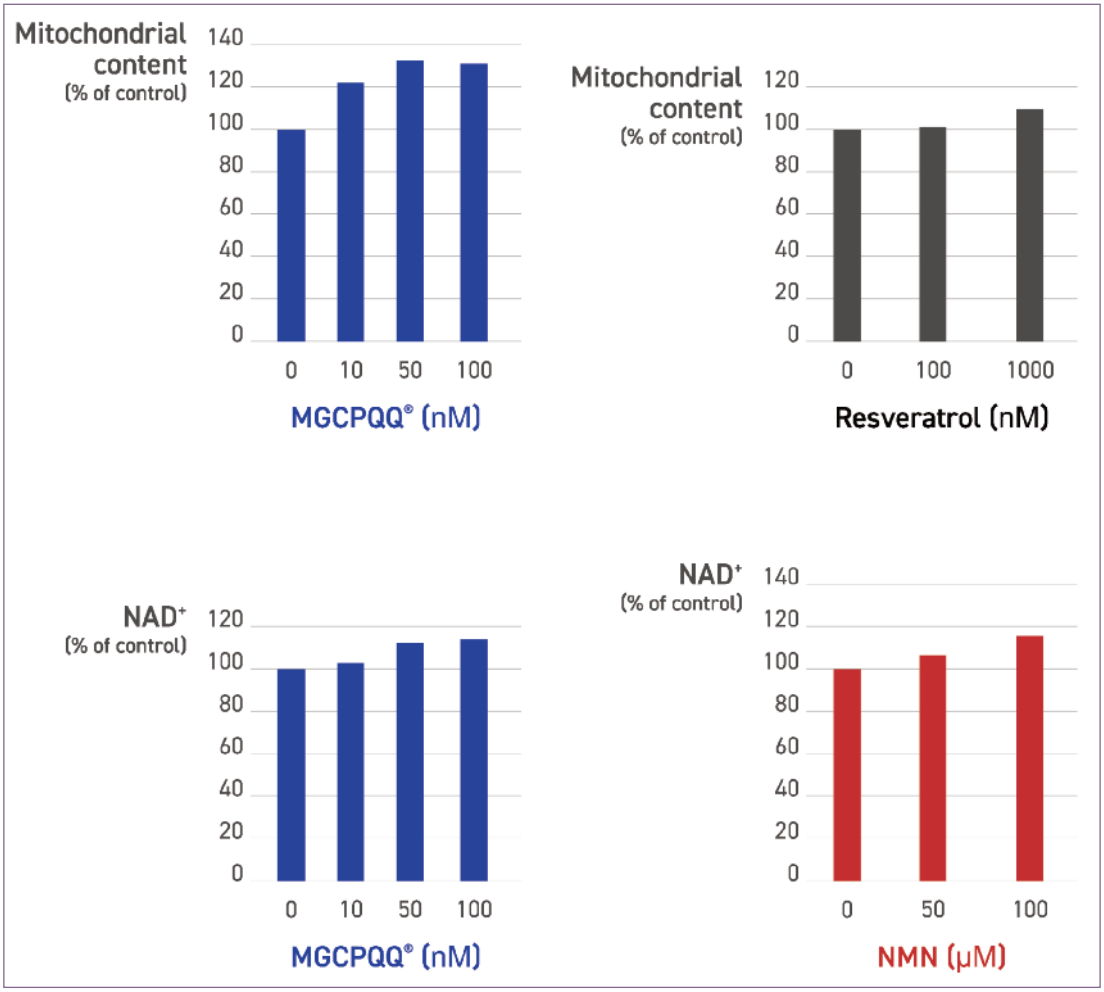
Over the last few decades, science and research have made significant developments in the understanding of the ageing process. Ageing can be broadly described as the progressive, time-dependent deterioration of cellular function caused by the accumulation of cellular damage, including genomic instability, deregulated nutrient-sensing, cellular senescence, stem cell exhaustion, altered intercellular communication, and mitochondrial dysfunction. (2) So one way to mitigate the risks associated with growing old is to target the double-membraned organelles with

the body's cells that provide critical and necessary functions – the mitochondria.

THE IMPORTANCE OF POWERHOUSE OF THE CELL

Mitochondria, the powerhouse of the cell, are vital to cell survival. Present in nearly all types of human cells, they take in nutrients and break them down into cellular energy, known as adenosine triphosphate (ATP). This metabolic conversion provides the energy to drive many of the processes in cells. As the body ages, mitochondria are among the first part of the cell to become dysfunctional, especially where high amounts of energy are needed like the brain, heart, and muscles. (3) Because of this, mitochondria has been identified as a key indicator in the ageing process. Healthy mitochondria play an essential role in supporting important markers of ageing, cognition and physical performance.

There are many ways to improve mitochondrial health: sleep, exercise and proper diet, just to name a few. Fortunately, there are also supplements available that safely stimulate mitochondrial biogenesis, the growth and division of pre-existing mitochondria and increase the number of mitochondria in the body. Mitochondrial biogenesis is influenced by environmental activity such as exercise, caloric restriction, low temperature, oxidative stress, cell division and renewal and differentiation and is accompanied by variations in number, size and mass. (4)



MGCPQQ has been shown to help activate mitochondrial biogenesis and work up to 100 to 1,000 times better than ingredients known to support mitochondria production.

Recent research suggests mitochondrial dysfunction is connected to the manifestation of

depression. The new data increasingly indicates the capacity of the nervous system can modify itself. Mitochondria are the powerhouse of eukaryotic cells, and they also regulate brain function through oxidative stress and apoptosis. (5)

SYMPTOMS OF MITOCHONDRIAL DISORDER

A healthy body continually creates new mitochondria. However, over time, the body's mitochondrial function declines and regeneration slows. Mitochondrial biogenesis is a physiological response to increased energy demand, and lead to an overall increase in the ATP production and improvement in the clinical status. (6) As the body ages, mitochondrial function declines, much like overall energy levels, which leads to impaired functioning of the brain and other vital organs. Damage to mitochondria can lead to a host of health issues, including sarcopenia, infections, diabetes, dementia and other neurodegenerative diseases.

Damaged mitochondria, the degradation of function and quality of mitochondria, have been known to contribute to the decrease of muscle mass, declined heart function, and the decline in pancreas B cells, which can often lead to diabetes. For these reasons, it's important to maintain healthy mitochondria for as long as one is able.

HOW MITOCHONDRIA WORK

Nicotinamide adenine dinucleotide (NAD) is a vital coenzyme that is present in every cell. It is an essential reduction-oxidation (redox) cofactor as well as a cosubstrate for many enzymes. Within the mitochondria, NAD+ accepts electrons from a variety of sources and transfers them to complex I of the electron transport chain, resulting in the generation of ATP.

NAD+ plays a key role in mitochondrial function via participation in pyruvate dehydrogenase, tricarboxylic acid cycle, and oxidative phosphorylation chemistries. As the body ages, NAD+ levels diminish, which are implicated in mitochondrial deterioration.

Proper sleep, diet and exercise are good for your general health and have been known to improve mitochondria. Exercise can increase NAD+ levels as it causes the body to burn NADH, thus generating more NAD+ along the way.

In addition to what people eat and the activities they take part in, vitamin-like supplements such as MGCPQQ®, Resveratrol and NMN, can increase mitochondria and activate mitochondrial biogenesis. However, what makes these ingredients different are the varying degrees of scientific research and clinical studies that validates their safety and efficacy.

MGCPQQ

Extensive research into the compound pyrroloquinoline quinone (PQQ) has found it may stimulate mitochondria and help support cognitive performance, including boost memory and attention. The ingredient is found in trace amounts in vegetables, fruits, meat, and in human breast milk, and it has been commercialized as a nutraceutical. Research suggests that the PQQ compound may play a role in preserving and

improving cognitive function, in both humans and animals, and help delay the effects of aging. Some early findings show that it may also support heart health.

Research showed that PQQ treatment induces increased activity of the NAD+-dependent protein deacetylase sirtuin 1 (SIRT1) and caused a concentration-dependent increase in the cellular NAD+ levels, suggesting that PQQ-inducible mitochondrial biogenesis can be attributed to activation of the SIRT1/PGC-1α signaling pathway by enhancing cellular NAD+ formation.

MGCPQQ®, a specific brand of PQQ manufactured by Mitsubishi Gas Chemical, is a safe, all-natural ingredient added to many supplements sold throughout Europe. It is the most studied and researched ingredient of its kind. Studies suggest MGCPQQ can help to increase mitochondria and activate mitochondrial biogenesis, which results in the growth of mitochondria clusters in cells. (7)

MGCPQQ has also been shown it can promote the production of a protein called Nerve Growth Factor (NGF), which is composed of 118 amino acid residues. NGF is important because it helps develop and maintain peripheral sympathetic and sensory neurons that are susceptible to damage from oxidative stress. Neuronal death is considered a causal factor in some cognitive disorders. MGCPQQ may stimulate NGF synthesis and NGF receptor synthesis, and as an antioxidant ingredient, MGCPQQ can help to protect neurons in the brain that are susceptible to cell damage. In addition to its antioxidant characteristics, the ingredient may inhibit neurotoxicity and play a role in the growth and recovery of damaged nerves and organs like the brain.

In a study, (8) MGCPQQ also showed positive effects on stress, fatigue and sleep. The results demonstrated that all six measures of vigor, fatigue, tension-anxiety, depression, anger-hostility and confusion improved significantly after the test subjects took 20 mg of MGCPQQ daily for eight weeks. Additionally, measures for quality of life, appetite, sleep, obsession and pain also improved considerably among both male and female subjects during this same time period.

MGCPQQ is manufactured in Japan through a proprietary fermentation process. While there are other naturally fermented PQQ ingredients on the market, MGCPQQ remains the most researched and studied for its safety, efficacy and quality. In fact, MGCPQQ has the most regulatory approval of all the PQQ brands. For the consumer, this is critical information.

A safety evaluation was conducted on MGCPQQ by the European Food Safety Authority (EFSA). After completing and publishing its evaluation, MCGPQQ became the only ingredient of its kind to appear on the European Union's approved list of Novel Food Ingredients. In Japan, it is certified by the Ministry of Health, Labour and Welfare as a food ingredient and is the only permissible PQQ

brand available. For athletes seeking to safely increase stamina and physical performance, MGCPQQ has certifications from the Informed-Choice and Informed-Sport quality assurance programs, ensuring every batch of the ingredient has been tested for substances banned by the World Anti-Doping Agency (WADA). This provides an additional level of assurance for consumers that MGCPQQ is well-tolerated and safe to use for athletic competition. The company has marketed the ingredient under the brand name BioPQQ® in the United States, Canada and Japan. In the US, BioPQQ is the only compound of its kind with a New Dietary Ingredient with the US Food and Drug Administration (FDA).

RESVERATROL

Resveratrol is a plant compound that acts like an antioxidant and is found in grapes, berries, peanuts, and red wine and is believed to protect a cell's DNA. It is also thought to promote longevity by activating the NAD+-dependent protein SIRT1. The compound has been shown to increase the lifespan of fruit flies, yeasts, and nematodes. (9) However, research on resveratrol has primarily been done in animals and test tubes using high amounts of the plant compound.

Resveratrol has been promoted to have many health benefits such as protecting the heart and circulatory system and protecting against clots which can cause heart attacks and stroke. Resveratrol supplements may help lower blood pressure by increasing the production of nitric oxide as well as benefit blood fats in animals. As an antioxidant, resveratrol may also decrease LDL cholesterol oxidation. Animal studies have suggested it can lower blood sugar levels.

Resveratrol is also available in solution form and as a transdermal patch and is considered a dietary supplement. In the United States, while its safety and effectiveness have not been approved by the US FDA (10) some brands of resveratrol can claim self-affirmed GRAS.

NICOTINAMIDE MONONUCLEOTIDE (NMN)

NMN is another compound believed to generate NAD+. It is derived from ribose, a sugar, and vitamin B3. It is reported that NMN is a precursor to NAD+. Animal studies have shown that using NMN restores NAD+ levels and it may help to prevent age-related physical decline. For example, a study in aging mice demonstrated that supplementing orally with NMN prevented age-associated genetic changes and improved energy metabolism, physical activity, and insulin sensitivity. (11)

Additional animal studies report that NMN may increase insulin sensitivity, lengthen the lifespan in certain animals, ease joint pain, and suppress cancer cells. Earlier this month, the first clinical study was published on NMN but did not adequately assess the effect of NMN supplementation on NAD+ levels in humans. Like Resveratrol, NMN has not been approved by the US FDA for its safety and effectiveness.

While there are many supplements on the market that claim to help decrease the acceleration of aging, MGCPQQ has more than 40 years of research to back it up. To date, more than 1,000 animal and human tests have been conducted using Mitsubishi's PQQ molecule, demonstrating that it is a safe and powerful ingredient with various health benefits. In fact, when compared among Resveratrol and NMN, MGCPQQ has shown to outperform these well-known mitochondria enhancers at a rate of 100 to 1,000 times higher.

From well-controlled studies, to safety evaluations by third-party regulators, consumers interested in safely stimulating mitochondrial biogenesis and maintaining their overall health as their body ages have a safe and effective option in MGCPQQ. To learn more about the research and studies behind MGCPQQ, visit mgcpqq.eu.

REFERENCES

1. S. Banerjee, A. Pal, "Likely to be liked? A study of Facebook images," 2018, https://ieeexplore.ieee.org/abstract/document/8392808?reload=true
2. J. Morton, "Why Color Matters," https://www.mordorintelligence.com/industry-reports/europe-nutraceutical-market
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3836174/
4. https://www.ncbi.nlm.nih.gov/books/NBK22436/
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3883043/
6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5997778/
7. https://www.sciencedirect.com/book/9780128170069/mitochondrial-medicine
8. https://pubmed.ncbi.nlm.nih.gov/29185343/ Nakano, Masahiko & Yamamoto, Tetsuro & Okamura, Hisayoshi & Tsuda, Akira & Kowatari, Yasuyuki. (2012). Effects of Oral Supplementation with Pyrroloquinoline Quinone on Stress, Fatigue, and Sleep. Funct. Foods Health Dis. 2. 307-324. 10.31989/ffhd.v2i8.81.
9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5630366/
10. https://www.drugs.com/resveratrol.html
11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5668137/