Mito SAP

*Science-based formulation for mitochondrial support**

Mito SAP is a synergistic formulation containing key nutraceuticals that helps improve mitochondrial health.* **Mito SAP** can be used in combination with **L-Taurine SAP** to support optimal mitochondrial energy metabolism.* Mitochondria, the "powerhouse of the cell," are crucial organelles for cell survival and death, involved in important functions including oxidative phosphorylation, ATP synthesis, signalling, and proliferation. Mitochondrial dysfunction caused by oxidative stress and aging has been implicated in a variety of diseases such as CVD, neurodegenerative diseases, and cancers.* **Mito SAP** contains a combination of active ingredients, namely *N*-acetyl-L-carnitine, quercetin, *R-alpha*-lipoic acid, grapeseed extract, thiamine, and coenzyme Q_{10} (as PQ_{10}; pea-emulsified coenzyme Q_{10} for enhanced absorption) of the highest quality and efficacy for optimal mitochondrial support.* **Mito SAP** can help promote mitochondrial biogenesis, assist in the protection of mitochondria against oxidative damage, and enhance exercise endurance.* In addition, **Mito SAP** can help ameliorate mitochondrial abnormalities by maintaining mitochondrial pH-buffering capacity, electron-transport chain activity, and ATP generation.* Therefore, **Mito SAP**, through the regulation of mitochondrial function and energy metabolism, can be very useful to promote cardiovascular, neurological, and retinal health.*

SUPPLEMENT FACTS

Serving Size: 1 Capsule

	Amount Per Serving	% Daily Value
Thiamin (Vitamin B1; from thiamin hydrochloride)	33.33 mg	2778%
Acetyl-L-carnitine hydrochloride	333.33 mg	**
Quercetin	166.67 mg	**
R-alpha-Lipoic acid	100 mg	**
Grape seed (*Vitis vinifera*) extract, 95% proanthocyanidins	83.33 mg	**
PQ_{10} (emulsified coenzyme Q_{10})	20 mg	**

**Daily Value not established

Other ingredients: Vegetable hypromellose, purified water, magnesium stearate, silicon dioxide, and pea protein.

This product is non-GMO and vegan friendly.

Contains no: Gluten, soy, wheat, eggs, dairy, citrus, preservatives, artificial flavor or color, starch, or sugar.

Mito SAP contains 90 capsules per bottle.

DIRECTIONS FOR USE

Adults: Take 1 capsule each of **Mito SAP** and **L-Taurine SAP** three times daily with food or as directed by your healthcare practitioner.

INDICATIONS

Mito SAP:

- Provides a source of coenzyme Q10, an antioxidant involved in supporting cellular energy production and mitochondrial synthesis of ATP.*
- May help promote mitochondrial biogenesis and assist in the protection of mitochondria against oxidative damage.*

and can:

- Be useful to improve exercise endurance.*
- Help ameliorate mitochondrial abnormalities by maintaining mitochondrial pH buffering capacity, electron transport chain activity, and ATP generation.*
- Be used to enhance healthy inflammatory responses and antioxidant status.*

CAUTIONS AND WARNINGS

Consult a healthcare practitioner prior to use if you are pregnant or breast-feeding; if you have liver disease, kidney disease, and/or a seizure disorder; if you are taking blood-pressure medication; or if you have diabetes. May cause digestive problems. Discontinue use and consult a healthcare practitioner if you experience sweating, paleness, chills, headache, dizziness, and/or confusion.

PURITY, CLEANLINESS AND STABILITY

All ingredients listed for each **Mito SAP** lot number have been tested by an ISO 17025–accredited third-party laboratory for identity, potency, and purity.

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

NFH®

351, Rue Joseph-Carrier, Vaudreuil-Dorion, Quebec, J7V 5V5
T 1 866 510 3123 • F 1 866 510 3130 • nfh.ca

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MITOCHONDRIAL METABOLISM AND ITS HEALTH IMPLICATIONS

Mitochondria, often referred to as the "powerhouse of the cell," are complex cell organelles that exist as a tubular network, and are the most active and important organelle in defining continued cell survival and death.[1] Mitochondria consume nearly 90% of the total oxygen content in the cell to enable oxidative phosphorylation and adenosine triphosphate (ATP) synthesis.[1] Cells contain ~ 1000 to 2500 mitochondria, with an average cell using 10 billion ATP molecules per day, translating to a requirement of 3.0×10^{25} ATP molecules in a typical adult. The initial presumption for the role of mitochondria in the cell was solely limited to energy generation in the form of ATP. However, research in the past few decades has shed light on the versatile roles of mitochondria in cellular activities including signalling, proliferation, and death.[1][2] Notably the size, number, and location of mitochondria in a cell is dependent on the cellular requirements. Given the increased realization of the crucial role of mitochondria in a plethora of cellular processes, it becomes quite apparent that mitochondrial dysfunction is related to the pathogenesis in a variety of diseases.[1] For instance, mitochondrial dysfunction has been implicated in coronary heart disease (CHD) and diabetes.[3]

Oxidative Stress and Mitochondrial Damage

Various compartments of mitochondria work together in concert to generate ATP in a complex multistep process involving electron transport chain complex (ETC) and oxidative phosphorylation (OXPHOS).[2] Nutrient deficiencies, environmental toxins, and oxidative damage affect the normal functioning of mitochondria. Besides, the primary source of oxidative stress in cells is leakage of oxygen and high-energy electrons from the mitochondria under conditions when key nutrients or protective antioxidant defense molecules are missing.[2] The mitochondrial respiratory chain is also a powerful source of reactive oxygen species (ROS), primarily the superoxide radical and hydrogen peroxide. Due to such ROS production, biological damage to cellular lipids, proteins, and DNA may occur. Particularly, mitochondrial DNA (mtDNA) is extremely sensitive to ROS damage due to its close proximity to the region of ROS production.[4] Mitochondria therefore become both the important sources and targets of oxidative damage.[4]

Mitochondria Dysfunction in Neurodegeneration

The strong relation between mitochondrial dysfunction and neurodegeneration is explained by the fact that the brain uses 70% of ATP.[1] In neuronal cells, mitochondria accumulate predominantly at high energy, demanding sites such as presynaptic terminals, nodes of Ranvier, and active growth cones and branches.[3]

Mitochondria and Aging

One of the causes of mitochondrial dysfunction is aging, which is characterized by a decline in mitochondrial respiration and oxidative capacity, an increase in oxidative stress, reduced mitochondrial mass, and morphological changes of mitochondria.[3] These are signs of unhealthy aging, and hence maintenance of mitochondrial health is of utmost importance during aging for healthy living.[3]

Mitochondria Dysfunction in Ischaemia/Reperfusion Injury

Ischaemia/reperfusion (I/R) injury of the heart represents a major health burden, mainly associated with acute coronary syndromes.[5] Mitochondria occupy a fixed fractional volume (≈ 21% of the total heart mass) in mammalians and are strategically placed in the vicinity of myofibrils to ensure the delivery of a huge amount of ATP. The disrupted mitochondrial electron system is a potential source of oxyradicals leading to I/R injury. Mitochondrial dysfunction resulting in cardiomyocyte death during I/R injury is mainly caused by a number of mechanisms such as calcium dysregulation, ATP depletion, release of proapoptotic proteins, and oxidative stress.[5]

NUTRACEUTICALS FOR MITOCHONDRIAL HEALTH

α-Lipoic Acid

α-Lipoic acid (ALA) is an endogenous disulfide compound synthesized de novo in mitochondria. Apart from its well-established role in mitochondrial energy metabolism and antioxidant effects, various studies have shown that ALA also exerts other beneficial effects including attenuation of mitochondrial decay during aging, and mitochondrial-targeted antitumour effect.[6] Maximal absorption and plasma concentration levels are ~ 50% higher for the *R*-isomer (naturally synthesized and used in biological systems) versus the *S*-isomer of ALA.[7] ALA is also extensively recommended for treatment of diabetic neuropathy. ALA treatment for 24 h improved insulin sensitivity, restored expression levels of mitochondrial OXPHOS complexes, and increased intracellular ATP production in an endoplasmic reticulum stress cell model.[8] In addition, ALA enhanced the β-oxidation capacity of the mitochondria and abated oligomycin-induced mitochondrial dysfunction.[8]

In one study, ALA administration was found to promote mitochondrial biogenesis and brown fat–like remodelling in cultured white subcutaneous adipocytes from overweight/obese donors.[9]

Coenzyme Q_{10} (PQ_{10})

Coenzyme Q_{10} (CoQ_{10}) is the predominant form of ubiquinone in humans, serving as an electron carrier in the mitochondrial respiratory chain (MRC), and is a lipid-soluble antioxidant.[10] CoQ_{10} deficiency has been reported to be associated with a variety of MRC disorders. The therapeutic potential of CoQ_{10} in the treatment of MRC disorders has been evaluated in several studies.[10] Some of the beneficial effects observed in MRC patients in these studies include improvement in neurological function tremor and ataxia, exercise intolerance, cramps, and muscle stiffness.[10] Especially, in one study, 30 patients with mitochondrial cytopathy receiving 1200 mg/d CoQ_{10} for 60 days showed moderate improvements in cycle-exercise capacity.[11] Using a neuronal cell model of CoQ_{10} deficiency, researchers established that CoQ_{10} treatment significantly decreased the level of mitochondrial superoxide and restored mitochondrial membrane potential to 90% of the control level in the CoQ_{10}-deficient neurons.[12]

Thiamine

Pyruvate oxidation defects due to reduction in pyruvate dehydrogenase (PDH) activity affect mitochondrial energy metabolism, leading to mitochondrial diseases.[13] Thiamine is an essential cofactor of PDH. Animal studies lend evidence showing the neuroprotective ability of thiamine supplementation in improving neurological function and oxygen consumption in mitochondria, restoring thiamine pyrophosphate levels, and increasing PDH activity in the brain.[13]

Thiamine treatment at 300 mg three times per day in patients with Kearns-Sayre syndrome normalized abnormal lactate and pyruvate levels.[14] In another study with a patient with mitochondrial myopathy, cardiomyopathy, and lactic acidosis, thiamine treatment (100 mg two times per day) in combination with prednisone improved overall strength and reduced lactic acidosis.[15]

Quercetin

Quercetin is an important dietary polyphenol and, apart from its antioxidant and anti-inflammatory properties, has been shown to modulate mitochondrial function, by altering mitochondrial biogenesis, influencing the membrane potential, and regulating ETC activity and ATP generation.[16] In an animal study, quercetin administration improved markers of mitochondrial biogenesis in skeletal muscle and brain, and enhanced exercise tolerance.[17] In a human clinical study, healthy but untrained participants given 1000 mg/d of quercetin showed enhanced maximal aerobic capacity and delayed fatigue during prolonged exercise.[18]

Grapeseed Extract (*Vitis vinifera*)

Grape seed proanthocyanidin extract (GSPE) has been suggested to modulate energy metabolism and mitochondrial function. In an animal study, acute administration of GSPE increased key genes involved in energy metabolism and ETC activity, and profoundly increased the oxidative capacity of skeletal and brown adipose tissue mitochondria.[19] Also, chronic administration of GSPE in a cell-culture study using Human Head and Neck Cancer Cells (HNSCC) has shown the ETC complex III targeted function and apoptotic death–induction ability of GSPE.[20]

N-Acetyl-L-Carnitine

Acetylcarnitine (ALC) is a derivative of L-carnitine which is a conditionally essential amino acid crucial for transporting long-chain fatty acids across the inner mitochondrial membrane for the process of β-oxidation. ALC is better absorbed and more efficiently transported than L-carnitine.[21] ALC supplementation significantly reverses the age-associated decline of mitochondrial membrane potential.[21] ALC supplementation can ameliorate oxidative mitochondrial decay, a major contributor to aging. Coadministration of ALC with ALA has been reported to improve mitochondrial abnormalities.[22]

Taurine

Taurine deficiency is thought to profoundly reduce the respiratory chain complex activity, accompanied by a 30% reduction in oxygen consumption.[23] Taurine plays a significant role in maintaining electron transport chain health. In a recent in vitro study, taurine supplementation was found to alleviate mitochondrial dysfunction in patient-derived pathogenic cells and prevented stroke-like episodes in MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes) patients.[24] Taurine helps prevent the damaging oxidative burst frequently observed during reperfusion, and also aids in mitochondrial pH-buffering capacity.[23][25] Taurine also regulates mitochondrial permeability by blocking calcium overload–mediated apoptosis and protecting against glutamate induced toxicity.[23]

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