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Discussion

Magnesium supplementation is found to support cardiovascular, neurological, musculoskeletal, metabolic, and immunological health. Magnesium bisglycinate chelate is a well-tolerated buffered form of magnesium that reduces the gastrointestinal discomfort associated with some forms of magnesium supplementation. Magnesium lysinate glycinate chelate offers support for the cardiovascular, nervous, and immune systems. Magnesium also supports anabolic recovery of muscular tissue from injury or athletic performance.

MAGNESIUM THE MAGNIFICENT MINERAL

Magnesium is a magnificent mineral, essential for physiological function and for optimal health. It is one of the most abundant cations in the body, second only to potassium. As a cofactor for enzymes, magnesium is involved in over 300 metabolic, cellular, and neurological processes.¹⁻⁵

At the cellular level, magnesium is a key initiator in the creation of ATP (adenosine triphosphate) in the energy production cycle; it is essential for synthesis of protein, RNA and DNA, and for cellular reproduction. This mineral also plays a key role in the stabilization of mitochondrial membranes and in cellular signaling. ^{2,6-8}

Crucial for healthy function of the nerves and muscles, magnesium influences nerve signal transmission, neuromuscular signaling, and helps regulate heart muscle activity and vasomotor tone.^{3,9}

MAGNESIUM DEFICIENCY OFTEN GOES UNDIAGNOSED

About 99% of the body's magnesium stores are in cation form within the intracellular spaces.⁵ Over half of the body's magnesium is found in bone with the remainder found in heart muscle tissue, skeletal muscle, and in the liver.^{4,5}

Only about 1% of the body's total magnesium circulates in the blood.^{3,10} Serum levels of magnesium are regulated through the interaction of intestinal absorption and renal excretion.²

Therapeutic Actions of Magnesium:

- Promotes cardiovascular, neurological, and immune health
- Encourages healthy inflammatory response
- Supports metabolic health
- Promotes a healthy musculoskeletal system
- Supports cellular energy production
- Enhances relaxation, restful sleep, and positive mood

Because of this, serum magnesium is not an accurate diagnostic marker of magnesium deficiency, and subclinical magnesium deficiency most often goes undiagnosed.¹ A possible indicator of magnesium deficiency is low potassium and calcium levels.¹

MAGNESIUM DEFICIENCY PANDEMIC

Estimates find that at least half the adult American population have inadequate magnesium intake to support health. Even a subclinical deficiency is correlated with increased incidence of chronic disease conditions.^{4,11,12}

Multiple factors contribute to low dietary magnesium levels.^{4,12} Since the 1940s, micronutrient depletion in soil and plants has been well-documented as a significant contributor.^{1,11} Moreover, poor nutrient intake, diets low in green leafy vegetables, and diets high in processed and refined foods often leave patients lacking or low in magnesium.^{1,11}

Even organically-grown food, which is high in micronutrients, has to have magnesium-rich fertilizers applied to crops consistently to increase magnesium. And while whole grains are especially abundant in magnesium - as are dark green leafy vegetables, nuts, legumes, and potatoes^{3,13} - there are a



number of environmental and nutritional obstacles to patients achieving optimal magnesium levels. For instance, high sodium diets contribute to magnesium deficiency.⁵

Certain drugs, such as diuretics and proton-pump inhibitors, are known to induce low magnesium levels.^{2,5} Aluminum (found in cookware, deodorant, some medications, baking powder, and elsewhere) is found to dramatically reduce absorption and retention of magnesium.¹ Additionally, high intake of vitamin D, calcium, and phosphorus increases the need for magnesium and can result in magnesium deficiency.¹

Aging in and of itself affects the body's ability to absorb nutrients like zinc and magnesium. In fact, humans in their 70s are found to have about two-thirds of the magnesium levels of 30 year-olds.¹³

Internal mechanisms can also dysregulate magnesium metabolism, including intestinal absorption, bone storage, and kidney filtration. Stress alone has been found to induce neuroendocrine alterations and lower magnesium levels. ¹³

While there is discussion that phytate-rich foods inhibit magnesium absorption, some research dismisses this idea, especially since many high-phytate foods, such as grains and beans, are also among the richest sources of magnesium.¹ Generally, the body compensates for low bioavailable magnesium through decreasing urinary magnesium excretion. Notably, a diet deficient in vitamin B6 is problematic because it contributes to increased excretion of magnesium.¹

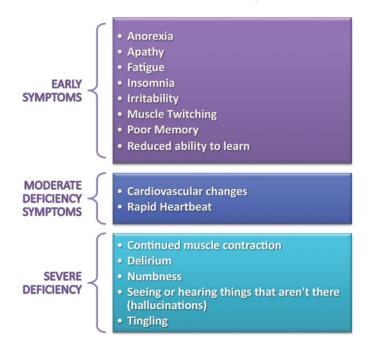


Image Source: see reference #7

MAGNESIUM SUPPLEMENTATION

Because of the prevalence of low dietary magnesium, supplementation can help promote well-being as part of a holistic program. Studies find magnesium especially beneficial for those dealing with chronic health issues, inflammatory conditions, and cardiovascular health challenges. Magnesium supplementation is also found to support neurological, musculoskeletal, and immunological health.

Magnesium is absorbed in the small intestines and colon through both active and passive transport. Magnesium levels are regulated and excreted through the kidneys.⁵

Studies find that human metabolism functions optimally with about 600 mg magnesium per day.¹ Modern dietary intake is much lower, and studies estimate that daily intake over the last one hundred years has fallen from about 500 mg per day to 200 mg per day.¹¹ Recommended dosage for those with health challenges is assessed by the practitioner, but standard dosing for healthy individuals is generally considered to be around 300 mg to 400 mg per day.⁸

MAGNESIUM MODULATES INFLAMMATION AND HEALTH

Magnesium plays a key role in modulating inflammatory processes.¹⁴ Research finds that even sub-clinically low levels of magnesium are associated with increased inflammatory processes and implicated in the increased risk and development of multiple neurological, musculoskeletal, metabolic, and inflammatory conditions. This includes osteoporosis, metabolic syndrome, type-2 diabetes, hypertension, cardiovascular disease, artherosclerosis, and obesity.^{1,3,4,11} Furthermore, about 84% of postmenopausal women with osteoporosis are found to be magnesium deficient.¹

Conversely, increased magnesium intake is correlated with reduced risk of these disorders.¹¹ Studies report that supplemental magnesium is correlated with a decrease in elevated C-reactive protein, an inflammatory marker related to cardiovascular health.¹⁵⁻¹⁸ Increased levels of intracellular and serum magnesium are also correlated with a decrease in oxidative stress markers and inflammatory markers including TNF-a.¹⁹

MAGNESIUM SUPPORTS METABOLIC HEALTH

Notably, fatigue, muscle weakness, and metabolic conditions are associated with sub-clinical to serious magnesium deficiency.^{1,5} Magnesium helps maintain the balance of the intracellular ions, calcium, and potassium, and supports the integrity of cells and tissues.¹



Some research correlates increased incidence of type-2 diabetes in the United States with a change in the dietary ratio of calcium to magnesium and concurrent decrease in dietary magnesium.¹ These studies report the optimal dietary calcium-to-magnesium ratio to be around 2:1.¹

MAGNESIUM'S CARDIOVASCULAR INFLUENCE

Since magnesium exerts a direct relaxatory action on vascular smooth muscle cells, it plays a key role in regulating blood pressure²⁰ while also regulating cations that modulate blood pressure (ratios of cellular sodium/potassium and intracellular calcium). Endothelial cells are adversely affected by low magnesium as the deficiency disrupts the release of the vasodilator nitric oxide.^{1,21} When sufficient magnesium increases prostaglandin production in the endothelium, it contributes to decreased platelet aggregation.²¹

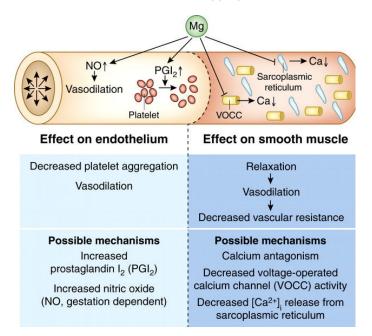


Image Source: see reference #40

Magnesium deficiency is correlated with the development of atherosclerosis¹ and with increased incidence of hypertension and thrombosis.^{19,22-24} A study with over a thousand human subjects reported a 16% reduction in coronary artery calcification for every 0.17 mg/dL increase in serum magnesium levels,²⁵ indicating that magnesium intake is shown to exert a beneficial influence in preventing coronary artery calcification and in helping maintain healthy cholesterol levels.¹⁹ In addition, magnesium aids in modulating collagen and elastin turnover in the vascular wall and regulating matrix metalloproteinase activity, encouraging vascular health.²⁶

Magnesium deficiency is correlated with heart irregularities such as arrhythmias.^{1,19,22,23,27} A study done in 2016 gave 400 mg of magnesium daily to high-stress patients and measured their heart rate variability (HRV) as a parameter. The subsequent increase in HRV suggested that parasympathetic activity was enhanced by the magnesium supplementation.²⁰

Because of its influence on the cardiovascular system and anabolic recovery, magnesium can also benefit athletic performance and recovery time. At the end of a 12-week study, healthy women who received 300 mg of magnesium daily were found to significantly improve in physical performance tests.²⁸

Eclampsia/pre-eclampsia	Arrhythmia
 Reduced risk of eclampsia 	Torsade de pointes in patients with long
in pre-eclamptic women	QT-Syndrome
	 Digoxin induced arrhythmia
	MAGNESIUM AND EFFECTS ON RENT DISEASES
Type 2 diabetes mellitus	Hypertension
 Improved glycemic control 	 Enhancing effect of antihypertensive therapy
Atherosclerosis	Acute myocardial infarction
 Increased HDL-concentration Lower blood triglycerides 	No consistent effect
 Reduced systemic inflammation 	Muscle cramps
Reduced endothelial dysfunction	Reducing frequency of events (?)
	NESAEMIA AND LOW DIETARY INTAK PMENT OF DIFFERENT DISEASES
Coronary artery disease	Metabolic syndrome
Hypertension	Type 2 diabetes mellitus

Image Source: see reference #43

MAGNESIUM PLAYS A KEY ROLE IN NEUROLOGICAL AND BRAIN HEALTH

Magnesium is well-known for its essential role in brain and neurological health, playing a key role in neuroplasticity. Because of this, it is being explored for its possible role in helping prevent dementia.²⁹⁻³¹

Magnesium is of special interest to Alzheimer's researchers due to its antioxidant and neuroprotective properties.³¹ The concentration of magnesium in the cerebrospinal fluid is slightly higher than that in the blood, and the body's homeostatic mechanisms work to keep these levels stable. In some studies, people with Alzheimer's are found to have



significantly lower levels of magnesium in their cerebrospinal fluid than healthy control subjects.^{29,31}

Additionally, magnesium is found to help improve cerebral blood flow partially through its effects in contributing to vascular relaxation.³³ In fact, in animal models, elevated brain magnesium is found to exert significant synaptoprotective effects.^{29,32}

MAGNESIUM BENEFITS RELIEF FROM PAIN AND ENHANCES RELAXATION

Magnesium is found beneficial in alleviating pain associated with neuropathy, dysmennorhea, headache, and acute migraine headache, ^{34,35} and is well-known for helping to alleviate stress and enhance relaxation by modulating catecholamine response in acute and chronic stress.^{26,36} In addition, magnesium is well-known for its potential in alleviating insomnia, supporting relaxation, and encouraging a deep restorative sleep. Studies show that it does so by enhancing healthy levels of GABA, a key neurotransmitter influencing relaxation and sleep.³⁷ Another study found that magnesium encourages beneficial changes in sleep markers such as melatonin and serum cortisol.³⁸

Magnesium also plays a key role in the biological and neuroendocrine systems involved with depression, anxiety, and mood.³⁸⁻⁴² Its activity is particularly associated with the limbic-hypothalamic-pituitary-adrenocortical axis, which modulates emotional and stress responses.⁴¹ Magnesium is found to have the capacity to relieve anxiety caused by a number of factors such as mild anxiety experienced during postpartum or premenstrual phase or anxiety due to hypertension.⁴²

BENEFITS OF CHELATED MAGNESIUM

Glycinate and lysinate forms of magnesium optimize magnesium absorption. Mineral chelates are well-tolerated in the gut, resilient to stomach acids, and are very well absorbed in the intestines, increasing the amount of magnesium taken up into the bloodstream. Unlike mineral salts that must be digested by stomach acid before the desired mineral portion can be released and absorbed, mineral chelates are primarily absorbed in the intestines and therefore avoid competing with other minerals for absorption.

Through a special process, manufacturers complex the mineral within a glycine amino acid ring which helps increase bioavailability. Chelating magnesium with glycine molecules discourages it from being bound by dietary compounds and encourages enhanced absorption in the intestinal tract. The glycine molecules that occupy active sites on each magnesium molecule reduce magnesium's tendency to complex with

phytates and other substances that could otherwise inhibit absorption.

Glycinate chelate forms of magnesium improve absorption and reduce gastric distress. Glycine bonds with the mineral ions in two locations to stabilize and chelate the mineral.

This advanced form of magnesium is well-tolerated and does not cause the loose stools or stomach upset that can sometime occur with magnesium supplementation. This stable chelated mineral is formed by a magnesium ion bound between two glycine amino acids. The glycine takes up active binding sites on the magnesium molecule so less water can attach to the magnesium. This action mitigates the laxative effect typically associated with magnesium supplementation. The ability of glycine to decrease small intestine pH improves the solubility of magnesium bisglycinate, enhancing its absorption.

About 15% of magnesium bisgycinate chelate is comprised of magnesium oxide, the gold-standard elemental form of magnesium. By itself, magnesium oxide is not always welltolerated, but when the load is limited, it is kept soluble and buffered, reducing the alkalinizing effect on the small intestines and eliminates its side effects. The combination allows for high assimilation through the intestinal wall and into the bloodstream.

Magnesium bisglycinate offers synergistic benefits for the nervous, cardiovascular, and metabolic systems. Glycine binds easily to magnesium and both compounds are known to play a role in circadian rhythm regulation and to support sleep quality^{43,44}

Glycine is found to support cardiovascular and metabolic health, with circulating levels of glycine being correlated with lower incidence of coronary heart disease and type-2 diabetes.^{45,46} Additionally, glycine modulates inflammatory processes, ^{45,46} and as a precursor to the cellular antioxidant glutathione, glycine plays a key role in cellular and hepatic processes.^{47,48}

MAGNESIUM LYSINATE GLYCINATE CHELATE

The magnesium lysinate glycinate chelate brings additional cardiovascular, nervous system, and immune system support. It also offers anabolic support for muscle recovery after intense workouts or injury.

Lysine, an essential amino acid, is the precursor for carnitine, a building block for protein. Oral supplementation of lysine is noted to produce a significant increase in plasma carnitine levels.⁴⁹ Lysine is found to modulate the bone-vascular axis and to be bone-protective.⁵⁰



The magnesium lysinate complex can also calm stressinduced anxiety responses, including helping reduce herpes viral outbreaks.^{51,52} Moreover, lysine is found to temper stressinduced anxiety and to help reduce stress-related diarrhea. ^{53,54}

Both glycine and lysine work together with magnesium in helping with diabetes and metabolic disorders,^{55,56} with lysine being found to inhibit protein glycation and to help prevent increases in the adverse markers of diabetes.⁵⁷

Lysine is absorbed in the small intestine through active transport into the enterocytes where it is metabolized. From there, any lysine not metabolized enters the liver where it is involved in protein synthesis.^{58,59} Lysine is both glycogenic and ketogenic, and some lysine in the body is metabolized to acetoacetyl-CoA, which is active in the energy cycle. Lysine is also found to be part of the cellular energy production process.⁵⁹

For more information on any of the ingredients listed here, including extensive research or individual monographs compiled by Donnie Yance, please email info@naturaedu. com.



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