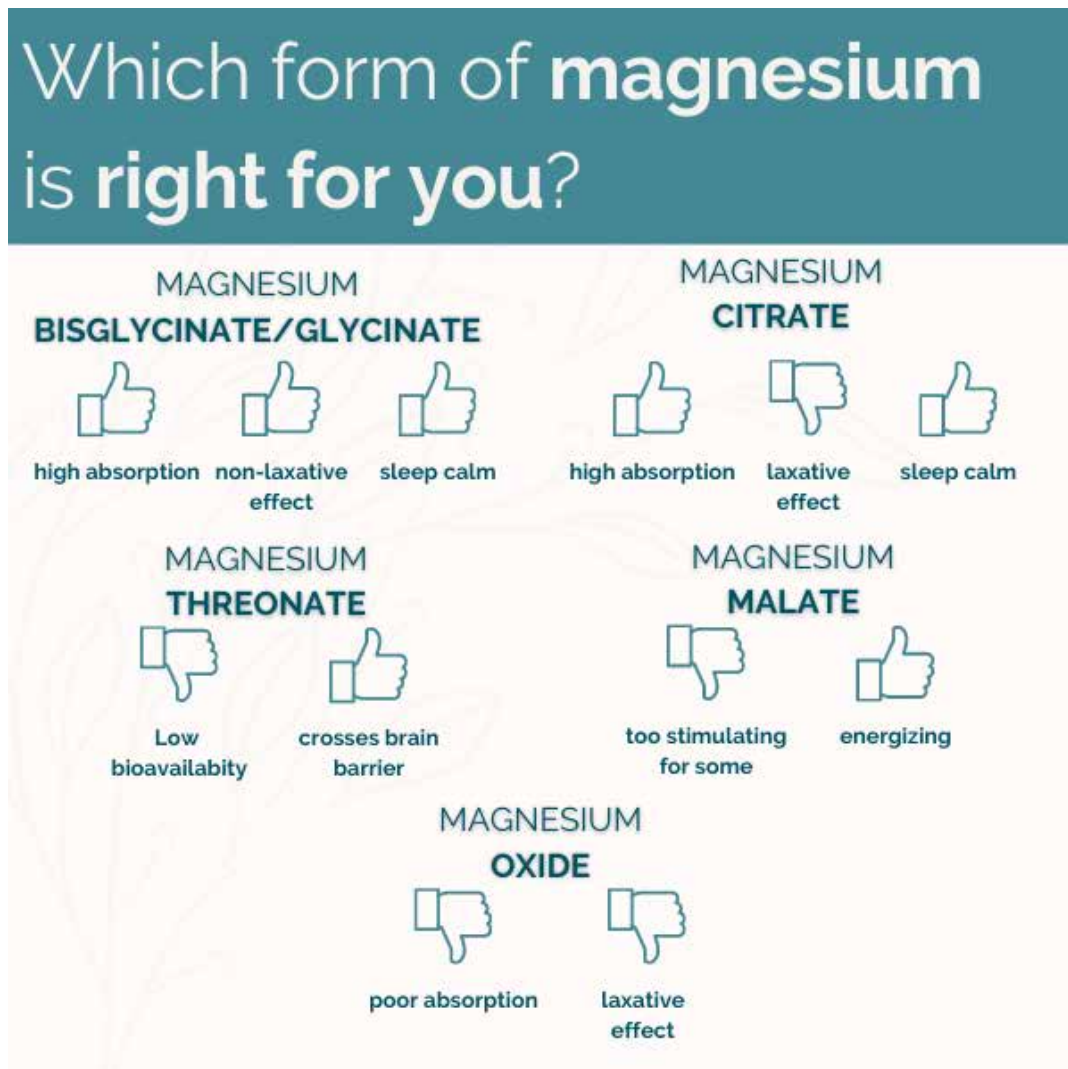


Understanding Magnesium and its potential as the perfect ‘Chill Pill’

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What are the roles of Magnesium in the body?

Magnesium is probably one of the most under-acknowledged of all nutrients, which seems bizarre when we learn of the plethora of biochemical functions affected by its presence or absence. It is an essential mineral involved in almost every system in our body and serves as a cofactor in over 300 enzyme reactions. Among the multitude of biochemical roles magnesium plays in human health are the following: i) energy production by converting food into energy, the main energy currency of the cell is complexed with magnesium as Mg-ATP and low magnesium levels are associated with conditions such as chronic fatigue, ii) neuromuscular and muscular regulation, thus affecting people with tremors, twitches, cramps, constipation, spasms etc., iii) blocking the NMDA receptor, which could be relevant for conditions such as migraines, Alzheimer’s disease, chronic pain, fibromyalgia etc., iv) synthesis of DNA, RNA, proteins and also the antioxidant Glutathione, v) vitamin D activation, magnesium-dependent enzymes are required for the hydroxylation of vitamin D3 into the active form calcitriol, therefore vitamin D could be co-supplemented with magnesium, vi) bone health, through modulating parathyroid hormone, vitamin D and osteoblast/osteoclast activity, vii) diabetes management, magnesium plays a role in insulin metabolism/resistance and glucose control, viii) cardiovascular health, magnesium controls the heartbeat and low magnesium has been linked to incidences of high blood pressure, stroke, arrhythmia and congestive heart failure, ix) female hormone balance, magnesium has been shown to relieve symptoms of PMS and menopause, x) inflammation and oxidative stress are controlled by magnesium, with chronic inflammation and markers such as CRPs and pro-inflammatory cytokines linked to magnesium status, xi) immune function regulation, magnesium influences cells of both the innate and adaptive immune systems, xii) fertility and pregnancy, magnesium deficiency has been linked to infertility and pregnancy complications such as miscarriage and pre-eclampsia, xiii) asthma, low magnesium is thought to



play a role in the constriction of airways, with magnesium inhalers being used to help alleviate symptoms, xiv) mental health relies on magnesium homeostasis to regulate many components of brain function and mood, low magnesium has been associated with conditions such as OCD, bipolar disorder, ADHD, autism and depression, xv) sleep and stress, are impacted by hormones and neurotransmitters both of which are modulated by magnesium.

How does Magnesium regulate Stress and Sleep?

This essential mineral has fondly been referred to as ‘the calming mineral’ as it not only

calms the body but also the mind and is gaining popularity as a powerful natural option when managing stress. Some of the most common symptoms experienced with psychological daily stress are fatigue, sleep issues and irritability, all of which are associated with a lack of magnesium. Sleep issues affect 35% of the adult population, reported by the Centers for Disease Control, CDC, who define short sleep duration as less than 7 hours per night, with 7-9 hours recommended for optimal health. A recent Global Emotions Survey reported on a study of global stress found that 40% of the 160,000 people surveyed confirmed they had

experienced stress. Another study found that 44% of patients screened for stress, had chronic latent magnesium deficiency. The regulation of sleep and stress involves certain pathways related to the HPA axis, cortisol, GABA, serotonin, melatonin, and NMDA receptors, and their relationship with magnesium needs to be discussed in more detail.

HPA axis and Cortisol: the hypothalamic-pituitary adrenal axis has been shown to be a mediator of neurobiological stress as it influences the production of stress hormones such as cortisol and adrenaline. Low magnesium causes an upregulation of the HPA axis which causes more of these stress hormones, leading



to feelings of increased stress. Magnesium supplementation has been shown to decrease stress hormones such as cortisol and help improve symptoms in people with HPA axis dysregulation.

GABA: gamma-aminobutyric acid is the body's most important inhibitory neurotransmitter and is known to reduce the activity of neurons in the brain and central nervous system, which subsequently induce feelings of calm, increased relaxation, sleepiness and balanced mood. Some call GABA the 'brakes' of the brain, which is exactly what you need when you want to stop overthinking and 'switch off'. Magnesium is involved in the production of GABA from glutamate, in the glutamine-glutamate- GABA pathway. Magnesium also activates the GABA receptors thus optimizing the beneficial effects of this powerful neurotransmitter in both stress and sleep management.

Serotonin: The neurotransmitter serotonin, dubbed the 'feel-good hormone' is central to regulating our mood, but also learning and memory. The tryptophan-serotonin pathway is hugely influential in supporting sleep and calm. Serotonin is synthesized from tryptophan through the activity of tryptophan hydroxylase enzymes (TPH/TPH2), magnesium acts as a cofactor of TPH and can also affect TPH2 through its role in vitamin D metabolism,

allowing calcitriol to subsequently activate TPH2. Magnesium supplementation has been shown to raise serotonin levels and even to enhance the effects of SSRI medication.

Melatonin: the tryptophan-serotonin- melatonin pathway is completed in the pineal gland, where melatonin is synthesized from serotonin via activity of the serotonin-N-acetyltransferase enzyme (AANAT). This enzyme is triggered under conditions of darkness, and is suppressed by blue light, which is why too much bright light and screen-time before bedtime isn't recommended as our 'sleep-hormone' melatonin gets compromised. Melatonin helps regulate our sleep pattern and helps us stay asleep and prevent night-time wakening. Magnesium has been shown to be involved in AANAT activity, and low magnesium levels have been correlated with reduced AANAT activity. Research shows that magnesium supplementation helps with insomnia and has been shown to increase quality and duration of sleep.

Glutamate NMDA receptor: the glutamate receptor, N-methyl-D-aspartate, is an excitatory receptor and gets activated upon glutamate binding which causes brain activity to get stimulated, this equates to feeling 'switched-on' but sometimes this increased excitatory state causes hyperexcitability/excitotoxicity

of the neurons. Magnesium deficiency is linked to increased NMDA activity in the brain, which can cause anxiety and sleep disorders. Magnesium acts as a natural inhibitory modulator of the NMDA receptors, by blocking the calcium channel in the receptors thus calming them down. Through its role as NMDA antagonist, switching from 'on' to 'off' mode, oral magnesium has even been shown in animal studies to exert antidepressant-like effects.

What factors can affect Magnesium levels?

Magnesium is an essential nutrient for living organisms and must be obtained from our diet, however, reports show that between 48% and 69% of the population have inadequate intakes of magnesium, and while severe magnesium deficiency is uncommon this does suggest a high incidence of chronic latent magnesium deficiency. These percentages of intake may seem quite high, but there are a number of explanations for magnesium insufficiency in the general population: i) dietary factors, most people don't eat an assortment of whole real foods, fruit and vegetables which would contain magnesium, instead opting for highly processed and refined options, ii) depleted soils, after years of intense agriculture, there has been an estimated 30% reduction in magnesium content over the past 60 years, iii) certain

substances like alcohol, sugar and caffeine reduce our magnesium, iv) certain medications such as PPIs and loop diuretics compromise our magnesium status, v) being elderly has been linked to compromised magnesium status, though reduced absorption and increased excretion, vi) excess calcium intake impacts our magnesium levels, vii) digestive malabsorption issues such as Crohn's disease or coeliac disease, affect our ability to absorb magnesium, viii) conditions such as diabetes or kidney disease, can increase magnesium excretion, ix) low vitamin D levels affect our magnesium status, since active vitamin D stimulates magnesium absorption in the intestines, x) excessive exercise and perspiration puts us at risk of losing magnesium, xi) chronic stress is known to deplete our magnesium stores, which becomes a vicious cycle for those experiencing stress due to inadequate magnesium.

Should we take Magnesium supplements?

Supplementing with magnesium seems logical when we learn of the many factors compromising our ability to maintain adequate magnesium levels. There are a variety of magnesium supplement forms to choose from and while all forms give some benefit, not all are created equal. There is a consensus in the literature that the least bioavailable supplements are those in inorganic form, where magnesium is bound to mineral salts (oxide, sulfate, hydroxide, carbonate), whereas those bound to organic acids (citrate, chloride, aspartate, malate) are more bioavailable. Compounds bound to amino acids (bisglycinate/taurate) may have an absorption advantage as they can utilise different absorption pathways to other forms of magnesium. Sometimes, what magnesium is bound to can have additional benefits, for example, the bisglycinate form contains the amino acid glycine, which is also a neurotransmitter and shown in studies to improve mood and sleep quality. The evolution of the food supplement industry in recent years has provided us with a multitude of magnesium options, which alongside growing awareness and demand for OTC suggestions, makes this a great time to explore the use of magnesium as the perfect 'chill pill' for our stressed out and tired population.

References available upon request