

Two Remarkable Stress Relief Supplements; Take Them Together

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STORY AT-A-GLANCE

- › Vitamin B6 escorts magnesium to the cells that need it most, thus ensuring that the magnesium you're getting, whether from foods or supplements, is being used as efficiently as possible. Vitamin B6 thus helps augment the many benefits of magnesium
- › Research shows a combination of magnesium and vitamin B6 can lower perceived stress to a greater degree than magnesium alone in those with severe or extremely severe stress. Those taking magnesium and B6 in combination also experienced fewer side effects
- › Magnesium and vitamin B6 are two nutrients commonly recommended for women with premenstrual syndrome. Magnesium deficiency may cause and intensify PMS symptoms, and magnesium appears to work because it has a calming effect on the neuromuscular system
- › Researchers have found vitamin B6 and magnesium are most effective for lowering rates of depression, water retention and anxiety in women with PMS
- › The recommended dietary allowance for magnesium ranges from 310 mg to 420 mg for adults over the age of 19, depending on age, gender and pregnancy status, and the adult RDA for vitamin B6 is between 1.2 mg and 2 mg per day, depending on age and gender; both nutrients are abundant in whole foods

This article was previously published June 10, 2019, and has been updated with new information.

You may be familiar with the connection between magnesium, calcium and vitamins K2 and D and how they work in tandem. But are you aware of the crucial link between magnesium and vitamin B6 (pyridoxine)? Individually, magnesium and vitamin B6 are both essential for heart and brain health. Both also play roles in the regulation of your blood sugar level.^{1,2}

When you get insufficient amounts of magnesium from your diet, your body will leach magnesium from your bones, muscles and internal organs, which can lead to osteoporosis, kidney problems and liver damage.

Vitamin B6 can help ameliorate this by escorting magnesium to the cells that need it most, thus ensuring that the magnesium you're getting, whether from foods or supplements, is being used as efficiently as possible. In so doing, vitamin B6 also helps augment the many benefits of magnesium.

Magnesium-B6 Combo Is Superior for Severe Stress

The importance of magnesium in combination with vitamin B6 was presented in a 2018 study³ in the journal PLOS ONE. Taken together, these two nutrients have been shown to have a complementary effect on stress reduction in animal studies.

In this randomized trial, they evaluated whether the combination of magnesium and B6 would improve perceived stress levels in 264 human subjects who also had low magnesium to start. Healthy adults with a depression anxiety stress scale score above 18 and a serum level of magnesium between 0.45 nanomoles per liter (nmol/L) and 0.85 mmol/L were randomized to receive either:

1. 300 milligrams (mg) of magnesium in combination with 30 mg of vitamin B6
2. 300 mg of magnesium only

The primary endpoint was a reduction in stress score from baseline to Week 8. While both treatment groups experienced similar reductions in their stress scores – the magnesium-B6 combo group reporting a 44.9% reduction in perceived stress and the

magnesium-only group a 42.4% reduction – a more significant impact was shown in those with severe and/or extremely severe stress.

According to the authors, adults with a stress score at or above 25 had a 24% greater improvement with magnesium-vitamin B6 versus magnesium only at Week 8. Those taking magnesium and B6 in combination also experienced fewer side effects: 12.1% of those taking magnesium-vitamin B6 versus 17.4% of those taking magnesium only experienced some form of adverse event. As noted by the authors:⁴

"These findings suggest oral Mg supplementation alleviated stress in healthy adults with low magnesemia and the addition of vitamin B6 to Mg was not superior to Mg supplementation alone. With regard to subjects with severe/extremely severe stress, this study provides clinical support for greater benefit of Mg combined with vitamin B6."

Magnesium and B6 May Ease Premenstrual Syndrome

Magnesium and vitamin B6 are two nutrients commonly recommended for women struggling with premenstrual syndrome. According to a research paper⁵ published in the Journal of Caring Sciences, magnesium deficiency has been proposed "as one of the factors causing and intensifying premenstrual syndrome symptoms," and magnesium appears to work because it has a calming effect on the neuromuscular system.

"Vitamin B6 is another proposed treatment for this syndrome," the paper notes.⁶ "On the one hand vitamin B6 increases serotonin and dopamine levels and improves premenstrual syndrome symptoms, and on the other, it has an essential role in the synthesis of prostaglandin and fatty acids, which are reduced in etiologies causing premenstrual syndrome.

Moreover, researchers believe that vitamin B6 deficiency decreases dopamine in the kidneys and therefore increase sodium excretion, which in turn causes water accumulation in the body and induces symptoms such as swelling in

extremities, edema, and abdominal and chest discomfort. The administration of vitamin B6 can thus decrease these symptoms and improve premenstrual acne."

To evaluate the effects of these two nutrients on premenstrual syndrome, 126 women diagnosed with premenstrual syndrome, based on American Psychiatric Association criteria, were divided into three groups, which received either 250 mg of magnesium oxide, 250 mg of vitamin B6, or a placebo, taken from the first day of the menstrual cycle until the beginning of the next cycle.

Magnesium and B6 Have Similar Rates of Effectiveness

Overall, magnesium and B6 had similar rates of effectiveness for premenstrual syndrome in this Journal of Caring Sciences study. Mean scores of premenstrual syndrome before and after intervention in the three groups were as follows:

	Magnesium	Vitamin B6	Placebo
Before intervention	36.89%	36.51%	35.8%
After intervention	22.22%	22.84%	28.41%

As you can see, while the placebo also helped reduce premenstrual syndrome symptoms, magnesium and B6 did so more effectively, and at similar rates. When looking at specific symptoms, B6 and magnesium were found to be the most effective for lowering rates of depression, water retention and anxiety. In conclusion, the authors noted:⁷

"Considering the importance of premenstrual syndrome and the numerous effects it has on society and the lives of women, health groups should prioritize the diagnosis and treatment of this syndrome. Since there is no definitive etiology and treatment for this syndrome, many researchers have tried to find

the best and most effective drug with the least side effects to prevent the occurrence of the syndrome ...

The current study was also undertaken with the goal of finding an effective compound with no side effects to reduce the symptoms of this syndrome and its direct and indirect economic and social effects. All compounds used in the current study had no side effects, were effective, non-chemical, and acceptable by most groups of women in the society.

Hence, health groups, especially midwives, can compare the effectiveness the compound on their specific patients and select the most appropriate treatment for each individual. Moreover, in cases where the patient is prohibited from using chemical drugs to treat premenstrual syndrome, such as oral contraceptive pills and gonadotropin releasing hormone (GnRH) agonists, the use of these compounds seems effective ..."

Unfortunately, a combination of magnesium and B6 was not evaluated in this study. It would have been interesting to see what their combined effect would have been. Considering the importance of both of these nutrients for health, I see no risk in combining them, though, should you struggle with premenstrual syndrome.

The Importance of Magnesium for Optimal Health

Magnesium⁸ is the fourth most abundant mineral in your body and the second most common intracellular cation⁹ (positively charged ion) after potassium. It's required for the healthy function of most cells in your body, but is especially important for your heart, kidneys and muscles.

Low magnesium will impede your cellular metabolic function and deteriorate mitochondrial function, which can have far-reaching health consequences, seeing how loss of mitochondrial function is a foundational factor in most chronic diseases, including heart disease and cancer.

According to one scientific review,¹⁰ which included studies dating as far back as 1937, low magnesium actually appears to be the greatest predictor of heart disease, and other recent research shows even subclinical magnesium deficiency can compromise your cardiovascular health.¹¹

Being one of the most abundant minerals in the human body, it's not surprising that it has several hundred biological functions. To list just a few, magnesium helps:

- Relax your muscles as well as your blood vessels – Being deficient in it can cause muscle cramps and weakness
- Promote mental and physical relaxation – It's a stress antidote that works by boosting GABA, an inhibitory neurotransmitter that relaxes your nervous system. Magnesium also helps boost your melatonin production
- Detoxification and reduces damage from electromagnetic fields
- Regulate blood sugar and improve insulin sensitivity, potentially protecting against Type 2 diabetes

Magnesium Is Required for Activation of Vitamin D

Magnesium is also a component necessary for the activation of vitamin D,^{12,13,14} and deficiency may hamper your ability to convert vitamin D from sun exposure and/or oral supplementation.

According to Mohammed Razzaque, professor of pathology at Lake Erie College of Osteopathic Medicine in Pennsylvania, coauthor of a study published in The Journal of the American Osteopathic Association (JAOA) in March 2018,¹⁵ "By consuming an optimal amount of magnesium, one may be able to lower the risks of vitamin D deficiency, and reduce the dependency on vitamin D supplements."

Interestingly, the first paper I ever had published, back in 1985, was also in the JAOA. My paper was about the use of calcium to control hypertension, but if I had written the

paper this century, it most certainly would have been about the use of magnesium for that purpose.¹⁶

A second study,¹⁷ published in The American Journal of Clinical Nutrition in December 2018 also concluded that your magnesium status plays an important role in your vitamin D status. Overall, people with high magnesium intake were less likely to have low vitamin D. They also had a lower mortality risk from cardiovascular disease and bowel cancer.

As explained by Dr. Qi Dai, professor of medicine at Vanderbilt University Medical Center and the lead author of this study, "Magnesium deficiency shuts down the vitamin D synthesis and metabolism pathway." What's more, magnesium was found to have a regulating effect, raising and lowering vitamin D based on baseline levels.

In people who had a baseline vitamin D level of 30 ng/mL (75 nmol/L) or below, magnesium supplementation raised their vitamin D level. However, in those who started out with higher vitamin D levels (50 ng/mL or 125 nmol/L), magnesium supplementation lowered their vitamin D.

Magnesium for Brain Health and Neurological Functioning

Magnesium is also crucial for optimal brain function, and is a common culprit in neurological ailments, including:

- **Migraines**^{18,19,20} — Researchers have noted that empiric treatment with a magnesium supplement is justified for all migraine sufferers.²¹
- **Depression** — Magnesium plays an important role in depression as it acts as a catalyst for mood-regulating neurotransmitters like serotonin. Research²² published in 2015 found a significant association between very low magnesium intake and depression, especially in younger adults.

Research²³ published in PLOS ONE demonstrated magnesium supplementation improved mild-to-moderate depression in adults, with beneficial effects occurring

within two weeks of treatment. In fact, the effects of magnesium were comparable to prescription SSRIs in terms of effectiveness, but without any of the side effects associated with these drugs.

Participants in the treatment group received a daily dose of 248 milligrams (mg) of elemental magnesium for six weeks, while controls received no treatment.

According to the authors, "It works quickly and is well tolerated without the need for close monitoring for toxicity."

- **Memory problems and loss of brain plasticity** – Memory impairment occurs when the connections (synapses) between brain cells diminish. While many factors can come into play, magnesium is an important one.

According to Dr. David Perlmutter, a neurologist and fellow of the American College of Nutrition, "magnesium is a critical player in the activation of nerve channels that are involved in synaptic plasticity."²⁴ Magnesium threonate, which most effectively permeates the blood-brain-barrier, is likely your best choice here.

The specific brain benefits of magnesium threonate were demonstrated in a 2010 study²⁵ published in the journal *Neuron*, which found this form of magnesium enhanced "learning abilities, working memory, and short- and long-term memory in rats."

Health Benefits of Vitamin B6

Like magnesium, vitamin B6 (as well as several other B vitamins) also plays an important role in heart and brain health. It is used in the creation of neurotransmitters, and is required for proper brain development during pregnancy and infancy.²⁶

Vitamins B6, B9 (folate, or folic acid in its synthetic form) and B12 may be particularly important for supporting cognitive function as you age, and have been shown to play a major role in the development of dementia, including Alzheimer's disease, which is the most serious and lethal form.

A primary mechanism of action here is the suppression of homocysteine,²⁷ which tends to be elevated when you have brain degeneration. High homocysteine has also been implicated in the development of atherosclerosis.^{28,29}

The good news is your body can eliminate homocysteine naturally, provided you're getting enough B9 (folate), B6 and B12. One study confirming this was published in 2010.³⁰ Participants received either a placebo or 800 micrograms (mcg) of folic acid (the synthetic form of B9), 500 mcg of B12 and 20 mg of B6.

The study was based on the presumption that by controlling homocysteine levels you might be able to reduce brain atrophy, thereby slowing the onset of Alzheimer's. Indeed, after two years those who received the vitamin-B regimen had significantly less brain shrinkage compared to the placebo group.

A 2013 study³¹ took this research a step further, showing that not only do B vitamins slow brain shrinkage, but they specifically slow shrinkage in brain regions known to be most severely impacted by Alzheimer's disease.

As in the previous study, participants taking high doses of folic acid and vitamins B6 and B12 lowered their blood levels of homocysteine, decreasing brain shrinkage by as much as 90%. High doses of vitamins B6, B8 (inositol) and B12 have also been shown to significantly reduce symptoms of schizophrenia, more so than standard drug treatments alone.³² Vitamin B6 is also important for healthy:

- **Metabolism**, by helping break down amino acids in the muscles to be used as energy and by converting lactic acid to glucose in your liver
- **Immune system**, as it helps create white blood cells that fight infections
- **Hair and skin health**, by reducing hair loss and alleviating dermatitis

How to Improve Your Magnesium and Vitamin B6 Status

The recommended dietary allowance (RDA) for magnesium ranges from 310 mg to 420 mg for adults over the age of 19, depending on age, gender and pregnancy status,³³ and

the adult RDA for vitamin B6 is between 1.2 mg and 2 mg per day, depending on age and gender.³⁴

Both magnesium and vitamin B6 are abundant in whole foods. Good sources of magnesium include leafy greens, berries, avocado, seeds, nuts and raw cacao nibs. Eating a primarily processed food diet is the primary culprit in magnesium deficiency, and if you fall into this group, you'd be wise to take a magnesium supplement.

Vitamin B6 is abundant in animal foods such as beef and wild-caught salmon, as well as dark leafy greens, papaya, oranges, cantaloupe, sweet potatoes, avocados, bananas, spinach, pistachios and sunflower seeds.³⁵ Nutritional yeast is another excellent source.

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