



The New New Magnesium

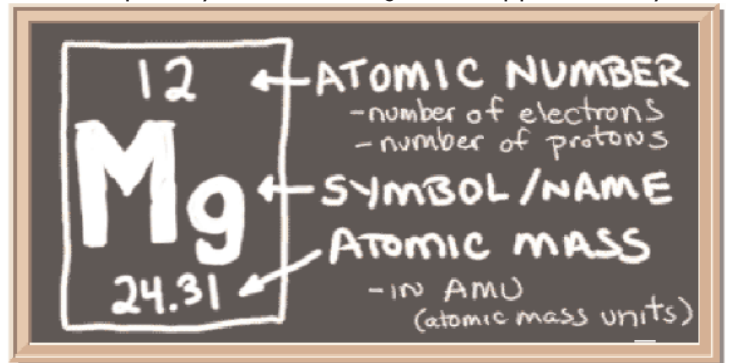
True Magnesium Orotate for Cardiovascular Health

Ask health-conscious people about the mineral most important to their heart health, and most will hit on **magnesium** right away. Studies in large populations have shown that higher intake of this mineral is associated with lower risk of high blood pressure, stroke, and ischemic heart disease.¹ Long known as "**nature's calcium-channel blocker**,"¹ a recent meta-analysis² has cut through the mixed results of different clinical trials to prove that **magnesium supplements lower blood pressure**. In experimental animals, low-magnesium diets worsen the impact of an atherosclerosis-producing diet, while supplemental magnesium slows the development of the disease.¹ Low magnesium also puts a person at risk for **insulin resistance** (the process through which the body's cells stop responding to the hormonal command to take up blood sugar)¹ and of progressing from there to "**Syndrome X**" and **non-insulin-dependent ("type-2") diabetes**³ - which are themselves major risk factors for heart disease.⁴ (Recent studies are also confirming that magnesium supplementation can actually treat the metabolic disturbances of diabetes).⁵

With huge swaths of the population suffering marginal magnesium status or even frank deficiency,^{6,7} many people could benefit from a couple of hundred milligrams of extra magnesium to supplement what's in their diet, bringing it up to the requirement of 420 mg for men and 320 mg for women, as established by the Institute of Medicine.⁸ As the studies show, people with vulnerable heart health may have especially good reasons to ensure that they're getting

adequate intakes of this mineral.

So it's no surprise that magnesium is one of the most popular mineral supplements amongst health-conscious people. Unfortunately, few people look beyond the amount of elemental magnesium in their supplements to consider the importance of the other half of their magnesium supplement - the chelating amino acid or anion to which it's bound. People do sometimes pay attention to this, but usually only to think about the effect it will have on the bioavailability of the magnesium itself. There's a good reason for this: absorption is important for all supplements, but it's especially critical for magnesium supplements if you



want to avoid a common and really unpleasant side-effect, since unabsorbed magnesium causes loose, watery stools. The widely-used **magnesium oxide has "extremely low" bioavailability (22.8%),⁹** making it more likely to cause diarrhea. On top of this embarrassing side-effect, **magnesium oxide is an antacid**, which can impair digestion and nutrient absorption. This is an especial concern in many older people, whose low stomach acid may even trigger pernicious anemia (flat-out B₁₂ deficiency).

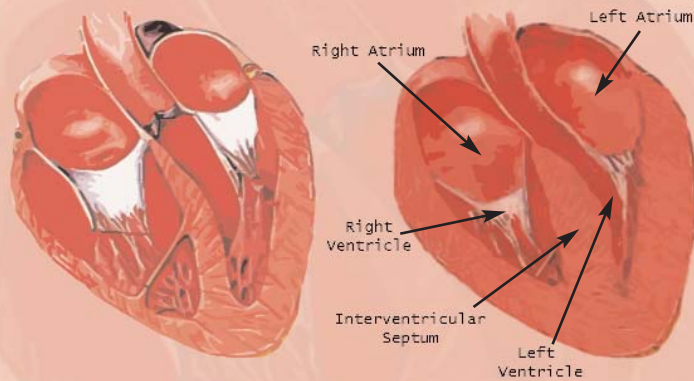
Magnesium citrate is certainly somewhat better, at 29.64% absorption,⁹ but much of the supposed "magnesium citrate" on health-food store shelves is not true, fully-reacted magnesium citrate, but "blends" of magnesium citrate with magnesium oxide. Indeed, much better absorption is available from other forms of magnesium, such as **magnesium monoaspartate.⁹**

Yet there's more to the effects of a magnesium supplement than its bioavailability, because **the "other half" of one magnesium supplement is extensively documented to have profound effects on cardiovascular health.** That supplement is true, fully-reacted **Magnesium Orotate**.

Magnesium Orotate is magnesium bound to **orotic acid**, a key intermediate in the biosynthesis of **pyrimidine nucleotides** (a building block of the "letters" of your DNA

a recent meta-analysis has cut through the mixed results of different clinical trials to prove that magnesium supplements lower blood pressure.

Hypertrophic Cardiomyopathy



Normal Heart

Hypertrophied Heart

code, and of **RNA**, the messenger that delivers the instructions from the DNA to the cellular machinery that assembles cellular proteins based on DNA's commands). Although little known and underappreciated, **decades of research and clinical trials have documented the powerful benefits of Magnesium Orotate to the weakened heart.**

Russian Research

The use of orotic acid and its mineral forms as metabolic therapy for cardiovascular patients began in the early 1960s in the former Soviet Union.^{10,11} Where it was primarily used to provide support to patients with **heart failure**, particularly in cases of **cardiomyopathy** - the degeneration of the heart muscle that causes maladaptive enlargement of the chambers of the heart and the thinning and weakening of the wall of the heart's crucial **left ventricle** (the main pumping chamber, which receives oxygen-rich (red) blood fresh from the lungs and sends it on to the rest of the body).

Cardiomyopathy was an especially widespread health threat in the USSR at the time, primarily because of alcohol abuse, so the need for a solution was high on the minds of Soviet scientists. Animal models had shown that heart failure increases the demand for RNA for the biosynthesis of proteins needed to repair the heart. Soviet cardiologists reasoned that since orotate is needed for the biosynthesis of RNA precursors, supplemental orotate might speed the recovery of heart muscle function by facilitating the recovery of function in damaged heart cells. It would also enhance the ability of healthy cells to meet the challenges of having the entire burden of cardiac function suddenly shifted onto the reduced mass of surviving heart tissue, increasing its metabolic needs.

Animal models provided early evidence to support the Russian scientists' expectations. In experimental heart

failure, cardiomyopathy, heart attack and stroke, studies demonstrated that **supplemental orotate increases cardiac glycogen, protein synthesis, and ATP levels (all depressed by infarction or heart failure), and improves cardiac contractile function** following damage to the heart, without interfering with normal baseline function in healthy hearts.^{10,12,13,14,15} Especially exciting was the finding that orotate not only provides benefits when given via infusion during a model heart attack, but also when administered some days after infarction¹³ and when given orally in models of chronic, hereditary cardiomyopathy.¹²

This evidence was enough to get Russian cardiologists going on clinical trials of mineral orotates in the 1960s. In one randomized, controlled trial,¹⁶ a group of 83 people suffering with **cardiac decompensation** (the most common form of heart failure) supplementing with mineral orotates were compared with two other experimental protocols and a 250-person control group, with all groups prescribed diuretics and cardiac glycosides (standard drugs for heart failure in those days and not uncommonly used today). **The group supplementing with orotate experienced much higher rates of "excellent" clinical results** (seen in 97%, 68%, and 19% of people with Russian heart failure classes IIA, IIB, and III, respectively, as compared with 47%, 16%, and 4% of people in the respective control groups), and much lower rates of non-improvement (just 3%, 0%, and 0% of the orotate users in these classes failed to improve, versus 1%, 9%, and 34% of control patients, respectively). Patients taking mineral orotates also appear to have fared slightly better than the other active groups, although a careful statistical analysis was not performed.

Orotate treatment also reduced the incidence of pronounced bradycardia (abnormally slow heartbeat) and bigeminy (an abnormal pulse pattern in which two beats in rapid succession are followed by a pause).¹⁶ Orotate users also saw greater improvements in their blood pressure and in the proper timing of the opening

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and closing of their aortic valve (particularly in subjects in classes IIB and III) than did the control group.¹⁶

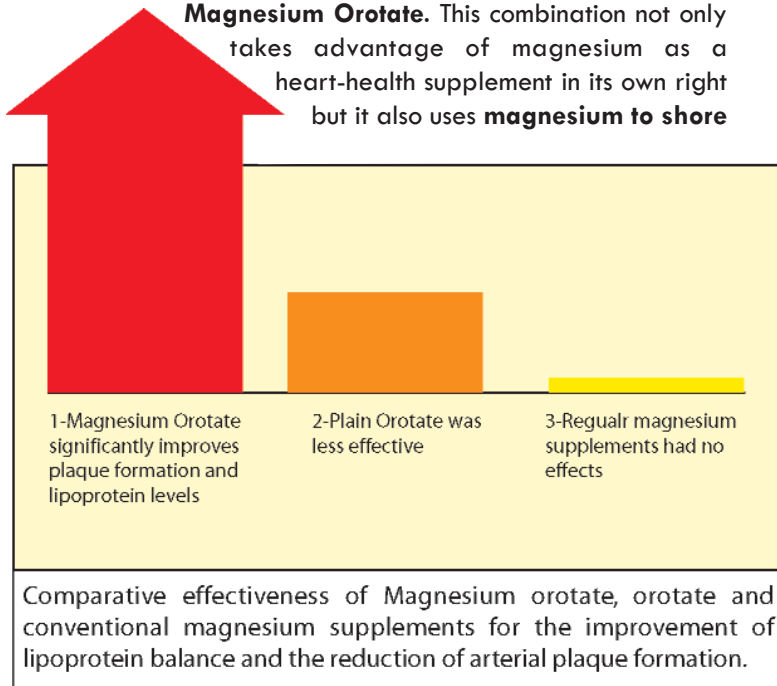
In another of the Russian orotate trials,¹⁷ 80 people who had just suffered a heart attack received, at random, either a cocktail of 1500 mg of orotic acid, along with folic acid and vitamin B₁₂ (which are also involved in nucleic acid synthesis) for 8 weeks. At the end of the trial, **one quarter of the people in the control group had died of the aftermath of their heart attacks, versus only 3 deaths out**

of 40 orotate-supplementing patients. This was connected with the fact that none of the heart attack patients who had taken orotate supplements developed heart failure following their heart attack, while 7 out of 40 people in the control group had suffered this fate.¹⁷

Magnesium Orotate: the Synergistic Cardiovascular Supplement

In the early days, research was conducted on a variety of mineral orotates, such as calcium orotate and potassium orotate. It was only later that researchers picked up on the unique advantage of combining orotate with magnesium to create one unique cardiovascular health supplement:

Magnesium Orotate. This combination not only takes advantage of magnesium as a heart-health supplement in its own right but it also uses magnesium to shore



up a potential weakness in the ability of orotate to work its cardiovascular wonders. For in addition to its many other cardioprotective mechanisms of action,¹ magnesium is a key cofactor for the very enzyme that uses orotate to biosynthesize the RNA precursors (pyrimidine nucleotides) through which orotate strengthens and restores heart cells under stress.¹⁸ This means that the central cardiovascular benefit of orotate depends on having sufficient magnesium available.

Unlike many supplements that are claimed to have special additive or synergistic interactions on the basis of nothing but a theoretical, biochemical "just so" story, the superior effects of combining these two nutrients have been demonstrated in real-world, living organisms. One study in cholesterol-fed rabbits¹⁵ compared the effects of **Magnesium Orotate** with a conventional magnesium

supplement and with stand-alone orotate. The results showed that **Magnesium Orotate improves the levels and/or balance of lipoproteins, reduces the plaque-forming burrowing of immune cells into the blood vessel walls, and actually reduces plaque formation** to a clinically relevant degree. **Plain orotate was shown to be less effective, and the other magnesium supplement was not reported to have any effect.**

More Trials Confirm the Power of Magnesium Orotate

So in later trials, scientists began to deliver orotate as the specific compound, **Magnesium Orotate**. Recently, Gaita and coworkers performed a randomized, controlled trial in 32 congestive heart patients who had recently undergone **coronary artery bypass grafting (CABG)** surgery.¹⁹ Within two days of surgery, each subject received either a 2000 mg **Magnesium Orotate** supplement (providing 130 mg of magnesium and 1870 mg of orotate) or a placebo dummy pill as an add-on to their standard heart medication. Eight weeks later, **Magnesium Orotate users experienced functional improvements on a wide range of heart function parameters** in comparison with those taking the placebo: their exercise times were 11% longer; they were able to walk 6.8% further without angina pains; their VO₂max (the maximum amount of oxygen the body can process in a given time) was 21% higher; and they enjoyed a 63% lower risk of suffering **extrasystoles** ("extra" heartbeats, felt as "missed" beats or "flip-flops" in the chest).

A second controlled trial²⁰ compared the effects of 3000 mg **Magnesium Orotate** (providing 195 mg magnesium and 2805 mg orotate) with standard control treatment in 84 people suffering with **mitral valve prolapse**, a condition in which one of the main valves of the heart bulges into one of the heart chambers during its contraction, with the result that blood leaks backwards into the wrong chamber of the heart. The results: a "6-month therapy with

Magnesium Orotate users experienced functional improvements on a wide range of heart function parameters in comparison

[Magnesium Orotate] completely or partially reduced the symptoms in more than half the patients. Positive changes were registered primarily in clinicofunctional manifestations."²⁰

In a third study,²¹ fourteen coronary heart disease patients with **left ventricular dysfunction** (problems with the pumping chamber of the heart that delivers fresh, oxygen-rich blood to the rest of the body) who were undergoing an exercise therapy program, took either **Magnesium Orotate** (3000 mg) or placebo pills as an add-on to their existing medications for

four weeks. Compared with the placebo group, **users of Magnesium Orotate enjoyed greater improvements in exercise times and in the emptying and filling of the left ventricle**, indicating "favorable effects of oral Magnesium Orotate to left ventricular function and exercise tolerance in patients with CHD."

In the most recent study,²² Australian cardiologists have used **Magnesium Orotate** as a central part of their "**Metabolic Physical and Mental (MPM) Program**," a whole-lifestyle intervention involving an exercise (Physical) component, stress reduction (Mental), and Metabolic supplement use (1200 mg **Magnesium Orotate** (providing



78 mg of magnesium and 1122 mg of orotate) along with **coenzyme Q10** (300 mg), **lipoic acid** (150 mg), and **omega-3 fatty acids** (3 g). In this historically significant controlled trial, the MPM program was compared to previous cases given standard care at the same clinical center in 11 elderly people scheduled for **cardiac surgery**. Even in the two week period between starting the trial and going under the knife, **Magnesium Orotate** users undergoing the MPM improved their overall quality of life, with both physical and mental quality-of-life scores increasing by 22%. One month after surgery the benefits became striking. As part of the MPM, **using Magnesium Orotate led to a full 50% jump in physical quality of life, while mental quality of life also got 24% better**. By contrast, scores on all of these parameters had gotten worse during the same periods in the control group. Meanwhile, **malondialdehyde** (a marker of lipid peroxidation and thus of **free radical stress**) **plunged 45% after the Magnesium Orotate-based intervention**. Excited by their preliminary results, the Australian team has launched a randomised prospective controlled trial of the full MPM.²³

Other clinical trials have documented the effectiveness of **Magnesium Orotate** supplements in delivering improved

quality of life and psychoemotional status in elderly patients with **stable angina**;²⁴ in supporting exercise and a salt-restricted diet to reduce blood pressure, eliminate heart palpitations, and improve sleep quality in **child hypertensives**;²⁵ and in improving the flexibility of blood vessels and reducing anginal pains in patients with **arteriosclerosis or inflammatory vessel disorders**.²⁶ In a recent double-blind, randomized controlled trial, **Magnesium Orotate supplementation has also been found to simultaneously improve physical performance and reduce some of the punishing negative impacts of extreme physical exercise in triathletes**. Compared to the placebo group, **Magnesium Orotate** users enjoyed faster times on the course, better mitochondrial energy metabolism, reduced overactivation of the immune response, a less extreme cortisol (stress hormone) spike, decreased muscle damage as measured by the enzyme **creatin kinase**, and greater reductions in insulin levels.²⁷

A Remarkable Safety Record

Magnesium Orotate has been documented to be an extremely safe supplement. A 1998 review of studies on **Magnesium Orotate**¹³ states that "No adverse effects arising from [orotic acid] administration in humans have been reported". Even diarrhea - the most commonly-reported side effect of magnesium supplements - appears to be extremely rare in **Magnesium Orotate** users: the only trial reporting any diarrhea was a recent study,²⁸ published after the 1998 review, exploring whether **Magnesium Orotate** would improve sperm characteristics in men with idiopathic infertility (it doesn't). One patient in this trial got a case of bad diarrhea while using **Magnesium Orotate**, and brief, mild diarrhoea was also seen in two others in the **Magnesium Orotate** group and in one person taking the placebo. However, none of these episodes lasted more than two days or led to anyone quitting their **Magnesium Orotate** use.²⁸

While animal experiments once suggested that high-dose orotate supplements might harm the liver, this turned out to be a quirk of the unusual metabolism of the rat, which doesn't apply to other species.^{29,30,31} Quite the contrary, in fact: **orotate and its salts have been used as a treatment for a variety of liver disorders in humans**.^{32,33,36,37}

Probably the best evidence of the safety of high-dose orotate supplements - including **Magnesium Orotate** - are the many trials in which they have been safely used without side effects in vulnerable population groups, such as children with hypertension²⁵ or liver and bile duct disorders,³³ as well as pregnant women,^{34,35} and even infants with jaundice.^{36,37}

What's Out There ... and Why

With all of the decades of research backing the benefits of **Magnesium Orotate**, why is it not more widely available? In part, it's because the research is so new to the West:

while many trials were carried out in former Soviet countries from the 1960s onward, these results have been buried in obscure Russian and Eastern European journals; it's only recently that the results of **Magnesium Orotate** supplementation have been reported in English-language scientific journals. If you don't know about the specific benefits of orotic acid, and think that the heart-health benefits of a magnesium supplement come entirely from the magnesium itself, then you might easily think that **Magnesium Orotate** is "just another magnesium supplement" on a shelf full of other, cheaper, and lower-pill-count alternatives.

Magnesium Orotate is also a bulky supplement. The orotic acid ligand in **Magnesium Orotate** is a big molecule, so when magnesium is bound to it, the final complex is only about 6.5% elemental magnesium by weight. So while companies using cheaper magnesium forms can cram a full day's magnesium into one tablet or two capsules, it takes several caps or tabs a day to get a proper dose of magnesium from this superior form. Supplement companies know that people don't like taking a lot of pills, so instead of educating people about the importance of choosing the right kind of magnesium in order to reap the full benefits of the mineral, most companies just pick a form of magnesium that makes their supplement look more convenient, because it uses fewer capsules.

However, to compare **Magnesium Orotate** to other magnesium supplements on a simple milligram-for-milligram basis is misleading, because **Magnesium Orotate** is not just a magnesium supplement: it's cardiovascular benefit derives from the orotic acid as much as it does from the magnesium itself. You don't need a whole RDA's worth of elemental magnesium to enjoy its effects: the many clinical trials on **Magnesium Orotate** clearly document that the cardiovascular benefits from **Magnesium Orotate** are achieved at effective doses.

Also, **Magnesium Orotate** is more expensive than other magnesium supplements, again on a milligram-of-magnesium basis - even though it is actually no more expensive than a variety of other heart health supplements at the dose actually needed to enjoy its benefits.

Once you know about the superior cardiovascular benefits of **Magnesium Orotate**, however, you still have the problem of locating the real thing. The fact is that the great majority of the "**Magnesium Orotate**" on the market is not *fully-reacted*, pure **Magnesium Orotate**, but a "*blend*" or "*complex*", mostly made up of **magnesium oxide**. For instance, we've seen one "magnesium orotate" product that claims to contain 500 mg of elemental magnesium per tablet - which is impossible, given the weight of the tablet itself. To deliver 500 mg of magnesium from **Magnesium Orotate**, the tablet would have to be a huge horse pill,

weighing almost *eight grams* (about the weight of two teaspoons of sugar); yet these are standard-sized tablets, weighing in at little more than a *gram and a half*.

These products look attractive, because they claim to provide this desirable form of the mineral, yet are cheap and contain a high amount of elemental magnesium per tablet - but that's only because the **Magnesium Orotate** in these supplements is "cut" with cheaper, denser forms of the mineral. That means that you not only wind up with a more

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poorly-absorbed form of magnesium which is more likely to cause diarrhea and inhibit your absorption of other nutrients. You also don't get the dose of orotic acid needed to enjoy **Magnesium Orotate**'s heart-healthy properties.

The labels of these products don't make this clear to consumers, of course. Many of them indicate that they are **Magnesium Orotate** even though they are really "complexes" or "blends" - and even when they do disclose this fact, most health-conscious people don't understand the euphemistic terminology. Reading a label that says the pills contain a **Magnesium Orotate** "complex," many people get the impression that they are getting a superior, more "natural" form of **Magnesium Orotate** that contains unspecified "cofactors"!

It may be fine to take one of these "blended" **Magnesium Orotate** "complex" products if all you need is a little extra insurance against frank magnesium deficiency. But if you need the full cardiovascular benefits of true **Magnesium Orotate**, you must be sure that you're getting the real thing. To do this, compare the amount of elemental magnesium listed on the label with the amount of orotic acid: **true, fully-reacted Magnesium Orotate contains nearly 15 times as much orotic acid as magnesium by weight.** If



the label isn't clear on this point, you can't be sure of what you're getting. Then, be prepared for the small added cost of genuine **Magnesium Orotate**, and the need to fit an extra capsule or two into your pill box. These minor inconveniences will pay major dividends in the health of your heart.

Authentic **Magnesium Orotate** is a supplement with solid, proven benefits in supporting the health of the heart and in restoring performance and quality of life in people whose hearts have been challenged. If you - or someone you love - have a history of, or are at risk for, a stay in a real "Heartbreak Hotel," you owe it to yourself to look seriously into this powerful nutritional combination.

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