Why Magnox is the Most Superior Magnesium Supplement Available

Why do we need a Magnesium supplement?

Magnesium is the fourth most abundant mineral in the body and is essential to good health. Approximately 50% of our total body magnesium is found in our bones. The other half is found predominantly inside the cells of our body tissues and organs. Only 1% of magnesium is found in our blood, but the body works very hard to keep our blood levels of magnesium constant,[1] therefore a blood tests are a good indication of the overallstatus of magnesium in our bodies at any given time (e.g. - whether an individual is suffering from hypo or hypermagnesemia).

Magnesium is needed for more than 300 biochemical reactions in the body. It helps maintain normal muscle and nerve function, keeps heart rhythm steady, supports a healthy immune system, and keeps bones strong. Magnesium also helps regulate blood sugar levels, promotes normal blood pressure, and is known to be involved in energy metabolism and protein synthesis.[2,3] Scientists are currently investigating the role of magnesium in preventing and managing disorders such as hypertension, cardiovascular disease, and diabetes. Dietary magnesium is absorbed by the small intestines. Magnesium is excreted through the kidneys. [1-3,4]

Large epidemiologic surveys show that most people in Western culture do not consume enough dietary magnesium. This magnesium deficiency contributes to an elevated risk for a number of diseases. According to a 1999-2000 NHANES study (National Health and Nutrition Examination Survey)[5], 68% of Americans consumed less than the U.S. recommended daily allowance for magnesium. In addition, the study demonstrated that adults who were deficient in dietary magnesium were about 1.5 times more likely to have elevated inflammation markers than adults who consumed the recommended amount. Adults over were twice as likely to have increased systemic inflammation, which can contribute to chronic diseases such as heart disease, diabetes, and certain cancers. Other epidemiologic trials indicate that a diet high in magnesium can even lower blood pressure[15].

Signs of magnesium deficiency (How do I know if I am magnesium deficient?) [1,3-4].

Early signs of magnesium deficiency include the following:

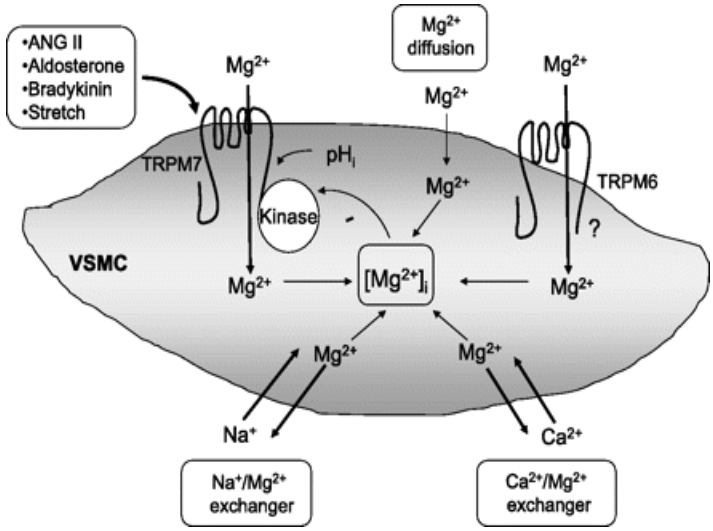
- Fatigue
- Weakness
- Abnormal heart rhythm
- Coronary spasms (which may by asymptomatic or cause chest pain)
- Migraine
- Hot flashes
- Muscle contractions and cramps
- Numbness
- Tingling
- Osteoporosis
- Personality changes - Seizures (sudden changes in behaviors caused by excessive electrical activity in the brain)

- Loss of appetite
- Constipation
- Back pain
- Nausea
- Vomiting

Severe magnesium deficiency can also result in low levels of potassium in the blood (hypokalemia), which can lead to conditions such as muscle weakness, aches and cramps[1,6,7]. In addition, Magnesium deficiency can exacerbate existing medical conditions such as high blood pressure, high bad cholesterol, diabetes and osteoporosis[15].

Magnesium Absorption Route

Magnesium is absorbed primarily in the distal small intestine, and healthy people absorb approximately 30% to 40% of the magnesium they ingest (Knochel, 1991; White et al., 1992).[8,9] Since magnesium is predominately an intracellular cation (a positive charged ion), thus, the effectiveness of any oral magnesium supplement is assessed by its solubility and rate of uptake from the small intestine into the bloodstream, and by its transformation into a free ion that absorbs into the cells of the tissues through a certain pathways in cell membranes(Sim. 1.). All if this is a complicated way of saying that a magnesium supplement has to be able to be absorbed by the cells of the body in order to be beneficial to the health of the individual taking it. Magnesium levels in the body are regulated by the kidneys. When magnesium levels in the blood are high, the kidneys will rapidly excrete the surplus. When magnesium intake is low, renal excretion drops to prevent the loss of magnesium (White et al., 1992).[9]



Simulation 1: Only free ion (Mg^{++})of magnesium can penetrate cell membrane.

Sim. 1. Putative transport mechanisms regulating intracellular free Mg2+ concentration ([Mg2+]i) in vascular smooth muscle cells (VSMC). Mg2+ influx and efflux are modulated through the Na+/Mg2+ exchanger and via the Ca2+/Mg2+ exchanger.

Body Magnesium Tests

A routine blood panel in a hospital or doctor's office often includes a serum magnesium level. Unfortunately, since the vast majority of magnesium in the body is not in the bloodstream, but in the cells and the fluid surrounding the cells, serum magnesium tests, do not provide an adequate indication of the status of magnesium in the body. Our body has an incredible ability to keep a balanced blood-magnesium level at all times, and our blood is the last storage area of magnesium in the body. Therefore, by the time a hospital test can detect a magnesium deficiency in the blood, it's likely already both severe and dangerous- with up to 99% of the body's magnesium having already been depleted. Hospitals and doctors' offices often check a magnesium level when a patient has certain medical conditions, such as heart or kidney problems. When blood tests come back normal, doctors often assume the patient in question has sufficient magnesium and the inquiry with regards to magnesium ends there. However, blood tests only detect the most severe and dangerous magnesium deficiencies, and are therefore not a reliable indicator of a problem [16].

Intracellular Levels are the only Clinically Significant Measures of Magnesium Levels.

In order to circumvent the short-comings of blood serum level tests with regards to magnesium deficiency diagnosis, a 'Sublingual epithelial cell' magnesium test was developed. This test has been shown to be a valuable tool in the hunt for meaningful magnesium measurements. It is recognized by the medical literature, the FDA and health insurance companies in the US. (Citation) One study compared the intracellular levels of magnesium in cells from the heart wall and cells under the tongue, and found that the levels were equivalent. Even more significantly, this study revealed that low magnesium levels from the sublingual epithelial cell scrapings were an indicator that patients would have abnormal heart arrhythmias after major heart surgery, even when their serum levels were within normal ranges.

Different Intracellular Absorption Rates of Various Magnesium Salts

Magnox was developed in 2010 by Naveh-Pharma and was patented in 2011. It consists of a special granular magnesium oxide combined with a water molecule (H_2O) to create a more bio-available form of magnesium - **Magnesium Oxide Monohydrate**. We employed a revolutionary pharmaceutical technique to create this new compound, which has a high dissolution rate, and a superior mechanism of absorption in the body over magnesium oxide or hydroxide.

Customer feedback has been overwhelmingly positive, demonstrating the immediate beneficial effect of Magnox on muscle cramps (especially those experienced nocturnally), restless legs and vitality. In the personal experience of countless patients, as demonstrated by testimonials, Magnox is more effective than conventionally employed magnesium citrate in treating these conditions.

Inorganic Magnesium formulations are more Readily Absorbed than Organic formulations:

Professor Michael Schechter, renowned cardiologist and expert in magnesium research at Sackler Faculty of Medicine, Tel Aviv University, and Director, Clinical Research Unit, Leviev Heart Center, Chaim Sheba Medical Center, Tel Hashomer, Israel., authored a theory to explain the superior

intracellular absorption rate of Magnox. His hypothesis was subsequently reinforced by a cross-over comparison trial conducted by Schechter and Saad[17]. All oral formulations of magnesium supplements are not created equal. Absorption rates and bio-availability of preparations vary, as do concomitant side effects. Magnesium preparations consist of a magnesium atom and a ligand, which is an ion or molecule, that binds to a central magnesium atom. The ligand can be organic or inorganic. Inorganic ligands include Chloride, Sulfate, Oxide, and, in our case, Oxide Monohydrate. Organic ligands are usually natural amino acids (such as taurate, glycinate, aspartate, and orotate) or acid compositions naturally occurring in the body (such as lactate, citrate, gluconate, etc.). It was conventionally (and erroneously) believed that magnesium preparations containing organic ligands, and thus highly water-soluble, were more bio-available, since the body would "recognize" the naturally present ligands.

We at Naveh-Pharma opposed this conventional "wisdom," based on the fact that **most organic ligands tend to form a complex, or "chelate," in which the magnesium is surrounded by the ligand's molecules. These chelates are very stable, and the body has trouble dismantling them. Therefore, the body is inefficient at releasing magnesium ions from organic suspensions in order to form free magnesium ions, which are absorable intracellularly. Organic complexes cannot be absorbed by the magnesium channel into cell membranes, and therefore remain in the bloodstream and are eventually excreted.**

The rate of complexation of every magnesium salts is measured by a STABILITY CONSTANT, defined by IUPAC[13]. The stability constant is inversely proportional to the intracellular absorption rate.

The higher the stability constant, the lower intracellular absorption is. Table 1 provides the various stability constant rates of the different magnesium salts. For example, Magnesium Citrate has a stability constant of 2.8.

Why previous surveys that concluded that organic magnesium salts are more bioavailable than inorganic salts are false?

In a trial that examined the bioavailability of magnesium oxide versus magnesium citrate (Lindberg et. Al.)[11], scientists concluded that Mg.citrate is more bioavailable than Mg.oxide . The conclusion derived from the finding that, a greater amount of magnesium citrate than magnesium oxide was found to be present in the urine. Although magnesium oxide is insoluble in water, it is highly soluble in stomach acid, where it turns to magnesium chloride, ionic form of magnesium that is readily absorbed by the cells. Therefore, in the Lindberg trial, because the oxide was well absorbed and present more abundantly inside the cells, only a small amount was excreted through the kidneys. In contrast, the magnesium citrate was found in larger quantities in the urine because as a complex it could not cross the magnesium channels and reach the kidneys, which have no ability to dismantle it either and therefore send the complex to the bladder and out of the body.

This means that the Conclusion of the Lindberg Clinical Trial (and Many Other Similar Trials Measuring Serum or Urine Magnesium) should be reversed!

A close-reading of Lindberg's abstract reveals the scientific fallacy (marked):

J Am Coll Nutr. 1990 Feb;9(1):48-55.
Magnesium bioavailability from magnesium citrate and magnesium oxide.
Lindberg JS, Zobitz MM, Poindexter JR, Pak CY.

Abstract

This study compared magnesium oxide and magnesium citrate with respect to in vitro solubility and in vivo gastrointestinal absorbability. The solubility of 25 mmol magnesium citrate and magnesium oxide was examined in vitro in solutions containing varying amounts of hydrochloric acid (0-24.2 mEq) in 300 ml distilled water intended to mimic achlorhydric to peak acid secretory states. Magnesium oxide was virtually insoluble in water and only 43% soluble in simulated peak acid secretion (24.2 mEq hydrochloric acid/300 ml). Magnesium citrate had high solubility even in water (55%) and was substantially more soluble than magnesium oxide in all states of acid secretion. Re-precipitation of magnesium citrate and magnesium oxide did not occur when the filtrates from the solubility studies were titrated to pH 6 and 7 to stimulate pancreatic bicarbonate secretion. Approximately 65% of magnesium citrate was complexed as soluble magnesium citrate, whereas magnesium complexation was not present in the magnesium oxide system. Magnesium absorption from the two magnesium salts was measured in vivo in normal volunteers by assessing the rise in urinary magnesium following oral magnesium load. The increment in urinary magnesium following magnesium citrate load (25 mmol) was significantly higher than that obtained from magnesium oxide load (during 4 hours post-load, 0.22 vs 0.006 mg/mg creatinine, p less than 0.05; during second 2 hours post-load, 0.035 vs 0.008 mg/mg creatinine, p less than 0.05). Thus, magnesium citrate was more soluble and bioavailable than magnesium oxide.

Our thesis is simple :

- Most magnesium salt supplements sold worldwide are composed of organic salts.
- Only an intracellular magnesium test, provides an accurate indication of body magnesium levels.
- To date, most conventional clinical trials measuring magnesium absorption and efficacy have been based on serum or urine magnesium tests.
- Organic magnesium salts, tend to form complexes that cannot enter the cells and cannot be absorbed in the body, therefore are excreted and useless to the body.
- Considering that only 30-40% of magnesium supplements are absorbed into the serum and most of it are un-absorbable complexes, the intracellular absorption and the efficacy of organic magnesium salts is low.

Conclusion:

- **Organic magnesium supplements are ineffective to replenish magnesium in the body.**

Schechter and His Team proved this Theory Correct with their Cross-Over Comparison Trial

The following excerpt from Schechter's study[17] demonstrates why Magnox is more readily absorbed by the body than organic magnesium supplements:

Magnox Vs. Magnesium Citrate . Schechter et. Al. *Magnesium Research* 2012; March: 1-12

We investigated the impact of supplemental oral magnesium citrate versus magnesium oxide on intracellular magnesium levels ([Mg2+]i) and platelet function in healthy subjects with no apparent heart disease. In a randomized, prospective, double-blind, crossover study, 41 (20 women) healthy volunteers [mean age 53±8 (range 31-75) years] received either magnesium oxide monohydrate tablets (520 mg/day of elemental magnesium) or magnesium citrate tablets (295.8 mg/day of elemental magnesium) for one month (phase 1), followed by a four-week wash-out period, and then crossover treatment for one month (phase 2). [Mg2+]i was assessed from sublingual cells through x-ray dispersion (normal values 37.9±4.0 mEq/L), serum magnesium levels, platelet aggregation, and quality-of-life questionnaires were assessed before and after each phase. Oral magnesium oxide, rather than magnesium citrate, significantly increased [Mg2+]i (34.4±3 versus 36.3±2 mEq/L, $p<0.001$ and 34.7±2 versus 35.4±2 mEq/L, $p=0.097$; respectively), reduced total cholesterol (201±37 versus 186±27 mg/dL, $p=0.016$ and 187±28 versus 187±25 mg/dL, $p=0.978$; respectively) and low-density lipoprotein (LDL) cholesterol (128±22 versus 120±25 mg/dL, $p=0.042$ and 120±23 versus 121±22 mg/dL, $p=0.622$; respectively). Noteworthy is that both treatments significantly reduced epinephrine-induced platelet aggregation (78.9±16% versus 71.7±23%, $p=0.013$ and 81.3±15% versus 73.3±23%, $p=0.036$; respectively). Thus, oral magnesium oxide treatment significantly improved [Mg2+]i, total and LDL cholesterol compared with magnesium citrate, while both treatments similarly inhibited platelet aggregation in healthy subjects with no apparent heart disease.

Teachings of the Schechter et al. Trial:

- To the best of our knowledge, that is the *only* clinical trial to date that tested intracellular absorption of magnesium, rather than blood or urine rates.
- It was a **cross over*** trial (in which every patient was administered both Magnox and magnesium citrate).
- Statistical processing by **Power Calculation**** reinforces the findings[14].
- Magnox was found to be 2.7 times more readily absorbed into the cells than magnesium citrate.
- Magnox reduced LDL (bad) Cholesterol and HsCRP (marker for inflammation in the body that is linked to atherosclerosis and heart disease), while Citrate was not effective at reducing either.
- Both treatments inhibited platelet aggregation (since both supplements are absorbed into the bloodstream).

* **CROSS OVER** In a crossover trial, participants are randomly assigned to a sequence of treatments. In the simplest design there are two treatments. For example, a trial was conducted in patients with asthma to compare laser acupuncture with a sham ('placebo') procedure. Patients were randomized either to receive acupuncture for five weeks (first period) and then a placebo for five weeks (second period), or a placebo for the first period and then acupuncture for the second. Symptoms were assessed for each patient during each period, allowing for assessment of the effect of treatment and control *within* each patient. In a cross over design we do not have to allow for variation that occurs *between* patients, which is present in a parallel group trial, making the cross over data more significant.

** **POWER CALCULATION** Performing power calculation for sample size estimation is an important aspect of experimental design, because without such calculation, sample size may be too high or too low. If sample size is too low, the experiment will lack the precision to provide reliable answers to the questions it is investigating. If sample size is too large, time and resources will be wasted, often for minimal gain [14].

The Schechter Trial Revolutionizes Scientific Thinking about Magnesium Absorption

In sum, the Schechter trial published March 2012,is about to change the perception of magnesium absorption and its effect on the human body. Conventional wisdom about organic versus inorganic magnesium supplements is incorrect. Yes, it has been clinically proven that organic compounds are soluble and very well absorbed into the bloodstream as a complex, but they are excreted without any beneficial effect on the health. These organic magnesium complexes have minimal intracellular absorption and thus minimal efficacy!

In conclusion – taking organic magnesium salts such as magnesium citrate, magnesium aspartate, magnesium taurate, magnesium orotate, magnesium glycinate or magnesium lactate, is worthless! Magnox is a more effective method of promoting healthy magnesium levels in the body.

STABILITY CONSTANTS OF VARIOUS MAGNESIUM COMPLEXES

from Chapter 6 - Sequestrants in Foods, by Thomas E. Furia, in CRC Handbook of Food Additives, 2nd ed. 1972 latest revision October 26, 2006

Complex	LIGAND	Stability constant
Magnesium oxide monohydrate	Oxide and water	0
Magnesium citrate	Citric acid	2.80
Magnesium glutamate	Glutamic acid	1.9
Magnesium glycinate	Glycine	3.45
Magnesium lactate	Lactic acid	0.93
Magnesium maleate	Malic acid	2.24
Magnesium orotate	Orotic acid	5.34
Magnesium aspartate	Aspartic acid	2.43

Table-1

Better compliance - One More Benefit of Magnox – meets 100% of magnesium RDA .

One capsule of Magnox, provides all of the RDA (recommended daily allowance) of magnesium. The weight of the magnesium in Magnesium Oxide Monohydrate is 42% (see Figure- 1), whereas in organic magnesium formulations it is 16% (for citrate) or less for other compounds. Therefore, one capsule of Magnox provides all the magnesium you need, as opposed to 2-10 capsules of organic compounds. Simplify your life and your routine by taking Magnox!

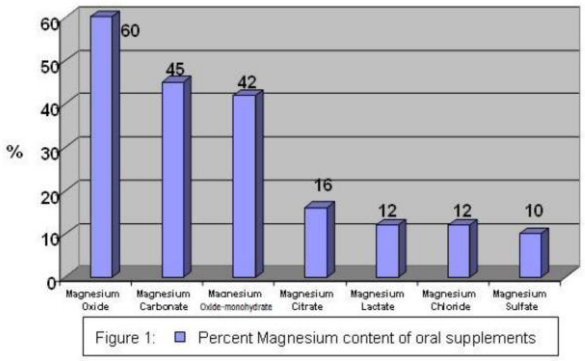


Figure 1: Percent Magnesium content of oral supplements

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