Why Magnesium Chelates are
Better Absorbed and Tolerated

Understanding Magnesium and Bioavailability Studies

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HUMAN NUTRITION & HEALTH

The Trust Factor **to decode magnesium bioavailability**

Magnesium supplementation has rapidly gained prominence, driven by social media and rising consumer interest. However, as we delve into the complexities of magnesium absorption, it's essential to critically evaluate the methods used to assess its efficacy.

This whitepaper critically examines the inherent challenges of measuring magnesium status and bioavailability across multiple methods. It highlights the limitations of relying solely on simplistic solubility metrics or any single model to draw conclusions about magnesium's performance in real-world scenarios, given the inherent challenges in the field.

The rapid growth of the magnesium supplement market, particularly the rising consumer interest in magnesium bisglycinate, has led to confusion regarding the state of the science as it relates to measuring magnesium bioavailability. In the absence of a single gold standard marker to evaluate magnesium bioavailability, it is important to look at multiple lines of evidence when making statements about the performance of a given product. While certain in vitro models- no matter how sophisticated - may produce compelling results in controlled, artificial settings, they often overlook critical aspects of magnesium absorption that are more accurately captured in different methods. Albion® Minerals has tested our Magnesium Bisglycinate using a variety of different models, ranging from in vitro systems to human clinical trials, with a consistent history of performance.

This paper lays a foundation for a more sophisticated understanding of magnesium bioavailability by addressing the complexities involved in real-life nutrient absorption and advocates for a more nuanced approach – one that accounts for physiological, cellular, and metabolic variables influencing magnesium absorption. With the proliferation of unverified claims and press releases, we encourage stakeholders to prioritize robust, independent methodologies. The industry must avoid oversimplifications, instead valuing sources with a proven track record, grounded in comprehensive trials and peer-reviewed publications, to ensure a true understanding of magnesium's role in human health.

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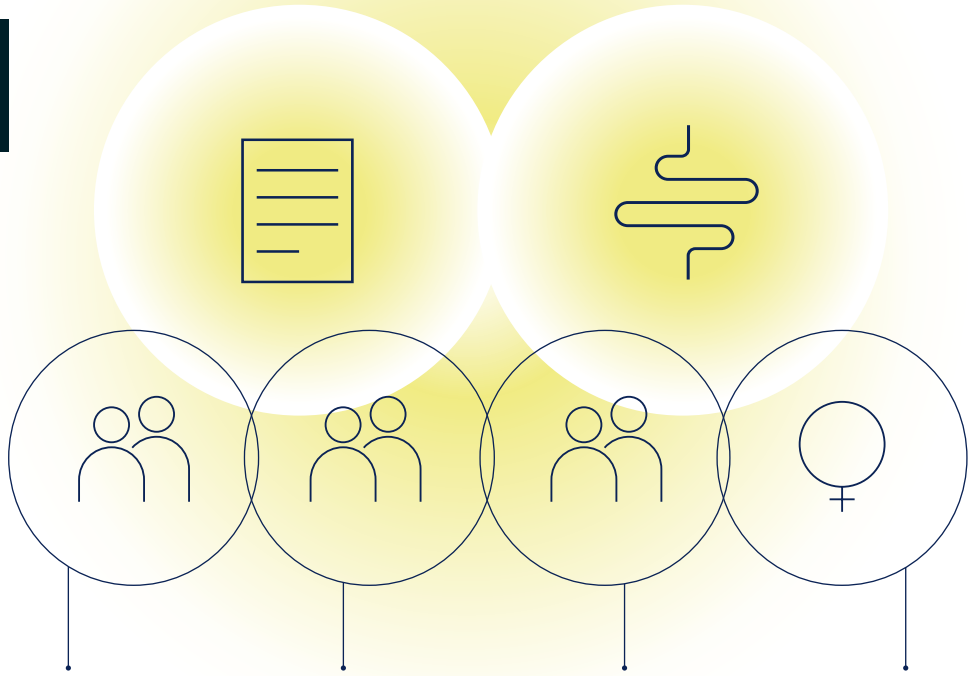
Albion® Minerals – The most Clinically Researched Magnesium Bisglycinate Chelate in the Market

TRIALS CARRIED OUT WITH Albion® Minerals



Author/ Publication	Schuette SA, et al. JPEN 1994; 18: 430-435.	Crowley D, et al. (internal data)	Ashmead S, et al, 2015. (Abstract)	DiSilvestro RA, et al. Obesity Surg 2019; 29(9):2781-9.
Study Design	Randomized, double blind, crossover trial	Randomized, double blind, crossover trial	Randomized, double blind, intervention trial	Randomized intervention trial
Study Population	N=12 patients with ileal resections	N=15 healthy M&F, age 20-60y	N=66 healthy M&F, age 18-50y	N=26 premenopausal females who recently underwent RNYGP surgery
Duration/ Dosage	**120 Hours** 100 mg labeled Magnesium ^{26}Mg) as: • Mg Oxide • Mg Bisglycinate	**8 Hours** 150 mg Elemental Mg as: • Mg Bisglycinate Chelate • Dimagnesium Malate • Mg Bisglycinate Chelate Buffered • Mg Oxide	**4 Days** 300, 450, and 600 mg/ day of either: • Mg Citrate • Dimagnesium Malate (DMM) • Mg Bisglycinate	**6 Weeks** Meal replacement drinks with either: • Standard mineral salt forms • Meal replacement with mineral chelates (incl. Mg Bisglycinate
Outcome Measures	Mg Absorption (fecal, urinary, & plasma)	Serum Mg Urinary Mg	GI Tolerability	Plasma Mg RBC Mg
Conclusions	• Mg absorption was significantly greater in the Mg Bisglycinate group	• Mg Bisglycinateshowed greater absorption compared to Mg Oxide	• No adverse events were observed with Mg supplementation • Fecal consistency scores were improved with higher doses of DMM and Mg Bisglycinate	• RBC Mg concentrations increased in subgroup analysis in group given meal replacements with mineral chelates

Despite the fact that magnesium has been studied for the past 100 years, it has not occupied a position of prominence in the scientific literature the way other minerals have, like iron and calcium for example.

There are several reasons for this. First, other minerals like iron and calcium are associated with recognizable deficient states like iron deficiency anemia, rickets and osteoporosis and as such, supplementation with iron or calcium makes sense and reverses or at least slows down progression of the respective disease manifestations. It was widely taught in medical schools that magnesium contributes to muscle cramps and tetany in severe deficiency and was used to treat eclampsia of pregnancy. Other than that, it was very much regarded as a background mineral.

The second reason that magnesium has not been as thoroughly treated in the literature, is that as its physiology was elucidated, it became clear that its handling by the body did not seem to obey the same rules to be able to easily measure its status in the body. Furthermore, magnesium deficiency didn't have any easily recognizable clinical hallmarks like small red blood cells (found in iron deficiency anemia) or rickets (calcium deficiency).

In the absence of a pressing need for doctors to measure magnesium status for diagnostic reasons, most physicians' only contact with magnesium was buried in a comprehensive metabolic blood panel and was frequently ignored unless it was very low. It was rarely ordered purposely and when it was (for muscle cramps or restless leg syndrome) levels were typically found to be normal – further contributing to the mineral's enigmatic reputation.

Measuring Magnesium

Only a few laboratories and researchers around the world have been interested in researching the physiology of magnesium and in recognizing the challenges associated with its accurate measurement and only a few have designed tools to some of the issues. Dual isotope techniques have been developed to 'improve' on the precision and reproducibility of the analytic tests,[1] but these require sophisticated, well equipped labs with excellent funding – not easily accessible to the clinical investigator who is constrained by resources. This has led to the inevitable lack of well-designed, controlled human studies that have become the hallmark of Evidence Based Medicine (EBM) which was developed specifically for drugs and NOT nutrients.[2]

This in turn has led to what one mineral expert describes in a recent review **"The state of the research available for magnesium is far from complete and the conclusions that have been drawn are far from clear."**[3] Recognizing this facet of magnesium research, has led several scientists away from human studies to conduct in-vitro or in-vivo in animal models to learn about the differences between different magnesium compounds in a more controlled experimental environment. One such **'Study of magnesium bioavailability from ten organic and inorganic Mg salts in Mg-depleted rats using a stable isotope approach'**[4] is often cited as the most comprehensive bioavailability study of a whole fleet of products – even though it is an animal study.

Human Studies

That notwithstanding, even though the available magnesium literature is imperfect, care must be taken not to discount the valuable conclusions about magnesium that are available in the science. There are signals that can be taken from the hundreds (PubMed search of human magnesium supplement studies revealed 250) of human studies looking into clinical effect, impact or even bioavailability of various magnesium salts. Taken individually, the results of the particular study can be taken as marginally supportive of a particular hypothesis or contradictory. In fact, when a study demonstrates a very clear benefit, it is often regarded as an 'outlier'. Lying out of what? Conventional wisdom has been created over time by an accumulation of 'signals' that support the general knowledge and understanding by the scientific community.

By way of example, multiple studies have contributed to the acceptance that 'organic' minerals are better absorbed than 'inorganic' minerals.[5] If one or more study shows an inorganic mineral salt to be equally bioavailable to an organic salt, it doesn't collapse the understanding of organic salts being superior, it just forms part of the tapestry of knowledge regarding this mineral or category of minerals – imperfect, but still relevant. In a human study of seven radio labeled calcium compounds, it was determined that fractional absorption of calcium bisglycinate chelate was the most bioavailable calcium from among inorganic and organic calcium products (including calcium citrate and calcium citrate malate) and this was independent of its much higher solubility.[6]

Studies of ferrous bisglycinate also demonstrated improved bioavailability over ferrous salts particularly when studied with food where the chelated iron was able to resist some degree of complexation with interfering substances in a test porridge containing phytates.[7] The advantages of studying a pharmacokinetic profile of iron following single and daily dose iron administration is a reliable way to determine bioavailability, but there are also clinical endpoints to determine the effect of iron supplementation on red blood cell regeneration. Each gram of hemoglobin utilizes 3.44mg of iron and hence bioavailability can be back calculated, as was the case in a study performed by Pineda et al[8] which demonstrated a superior bioavailability of ferrous bisglycinate over ferrous sulfate. The zinc bisglycinate bioavailability was also studied in a human study and when compared against zinc gluconate (an organic salt) was 26% higher.[9]

These are just some of the multiple studies that contribute to the appreciation that chelated minerals have improved bioavailability when compared to certain inorganic and organic salts. It is with this backdrop of confidence in chelated minerals that we look at some studies with magnesium bisglycinate that are in accordance with the positive experience of the category – despite the difficulties that we have now come to understand about studying magnesium in the human population.

Magnesium Deficiency Studies

In designing a study of nutrient compounds, it is imperative to create an environment of deficiency of that nutrient to offer the best opportunity to produce a measurable signal. If the nutritional status is replete, an increase in intake of the index nutrient will produce a null effect. The 10 compound rat bioavailability study[4] cited above, used magnesium deficient rats for this exact reason. In a human clinical study, investigators often look for a disease model or particular patient population with a common and significant nutritional deficiency in order to best test their nutrient intervention.

Ileal Resection

It is for this reason that Schuette and colleagues at the University of Chicago, chose to study subjects who had undergone ileal resection, because of the very high incidence of magnesium deficiency in this cohort.[10] While magnesium can be absorbed through the entire GI tract, the bulk of absorption is in the ileum (distal small intestine) and colon by passive diffusion, hence the severe deficiency state. Second, these patients are often intolerant to oral magnesium, which can manifest with uncontrollable diarrhea after ingesting oral magnesium supplements. The authors conducted the study on 12 subjects to determine whether magnesium bisglycinate was sufficiently bioavailable and tolerable to represent a therapeutic improvement for these patients as compared to magnesium oxide.

They chose the chelate because their review of the literature persuaded them that its attributes of being absorbed higher in the small intestine combined with a lower GI side effect profile, would benefit this cohort.

Both compounds were labeled with ^{26}Mg stable isotope and administered as a single dose with a crossover after a 2-week washout, and blood, urine and feces were collected for 5 days. ^{26}Mg present in stool, urine, plasma or red blood cells in excess of natural isotopic composition is designated as the absorbed magnesium. The study showed that magnesium absorption in ileal resection patients is lower than healthy controls, that both magnesium preparations were similarly absorbed but that **the chelate seemed to offer better bioavailability to those resection patients who had the greatest impairment. The chelate also was absorbed earlier (mean 3.2 hours earlier) supporting a more proximal absorption, and was better tolerated** with 2.4 stools vs 3.7 stools in the 24 hours following chelate and magnesium oxide single doses respectively.[10]

The purpose of discussing this study is because it is a serious piece of research, utilizing multiple state of the art, stable isotope tagged study compounds, multiple body fluids, multiple day collection techniques in a severely magnesium deficient patient cohort with recognized structural barrier to gastrointestinal absorption. In other words, a real life population in need of an oral magnesium supplement that would work with minimal side effects. It is reasonable to describe the magnesium chelate here, which demonstrated superior tolerability, as a **'better bioavailable'** option than the oxide.

Leg Cramps in Pregnancy

If ever a practitioner thinks of a common clinical manifestation of magnesium deficiency, it would be leg cramps. 30 – 35% of women in the second half of pregnancy suffer from leg cramps. Because pregnancy is regarded as a physiologic state of magnesium deficiency, 86 women were randomized to receiving 100mg of magnesium chelate vs placebo for 4 weeks to see if this intervention would improve leg cramps in this population.[11] There was a 50% reduction in frequency and severity of cramps in the chelate group ($p<0.007$) and there was no increase in diarrhea or other side effect compared to placebo. This study was chosen to represent a unique population with a common intracellular magnesium deficiency associated manifestation (leg cramps) that **demonstrated a statistically significant improvement with magnesium chelate supplementation for 1 month with no increased GI side effects.** Magnesium chelate is bioavailable and capable of augmenting intracellular magnesium (i.e. being released upon absorption and accessible to the cells) sufficiently to reduce leg cramps, whereas the results have been mixed with magnesium lactate/ magnesium citrate in this pregnant population with leg cramps.[12]

Instead of cherry-picking studies that support a particular opinion and ignoring those that don't, an effort has been made to demonstrate that even studies that have methodological shortcomings can teach the scientific community something. If a farmer's fence has one or two breaches, it doesn't mean that it doesn't form an effective barrier most of the time. But nor should anyone claim that the fence is 100% secure. So too with the majority (if not all) the studies on magnesium. None are totally perfect, some less perfect than others, but this does not invalidate everything about the study, we should just learn to differentiate what the publication can teach us… and what it can't. Furthermore, it is quite acceptable and even desirable when operating in an environment characterized by **'biologic variability', 'indirect measurement', 'suboptimal analytic tools' and 'paucity of disease endpoints'** to combine teachings and draw general conclusions as has been done within this field.

It is in this spirit that doctors may inform patients about certain treatment options, risks and benefits. It is in this spirit that pharmaceutical companies market their products to the doctors and more frequently directly to the consumer and of course, physicians and patients should, by now be able to recognize marketing hyperbole for what it is, as long as the statements are not blatant untruths or misrepresentations and by finding one imperfect study to disprove a claim over another imperfect study that supports it, does not prove that the claim is an untruth.

Ion Forms

In a recently published review of the variety of magnesium compounds available in the US, Dr. Robert DiSilvestro points out that it is critical to understand what form of magnesium is being taken or used in clinical studies.[3] The 'ileal resection' researchers did this when they chose magnesium chelate to compare to conventional magnesium oxide supplementation because they hypothesized that the chelate's properties would be advantageous for this particular study population. But what exactly is a chelate and why is it that doctors in particular have difficulty with the idea that a chelate could be a superior mineral form? The answer to this question lies in the common usage or adaption of the term chelate – which has come to mean a substance or means of 'grabbing' a mineral and not letting it go in order to prevent some negative or noxious effect of that mineral on biological tissues. This will be explained in greater detail later, but first an understanding of what chelation means in chemical terms and how this confers the attributes associated with mineral chelates.

Magnesium Salts

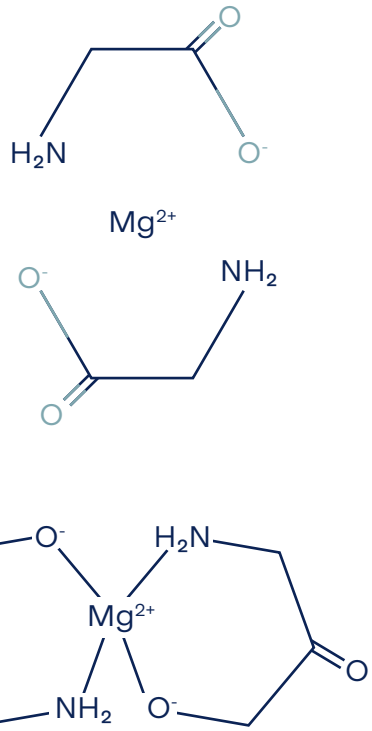
It stands to reason that the physical properties of various Mg^{2+} forms will affect the behavior of that salt in the GI tract and influence a key metric of any compound for oral ingestion – bioavailability. Furthermore, it is generally believed that solubility correlates with bioavailability and hence Mg^{2+} salts that have greater solubility within the physiological pH range of the GI tract are assumed to be more bioavailable. This however, has not been demonstrated convincingly and despite the fact that organic magnesium salts have vastly superior solubility (200 g/L for Mg Citrate vs 0.006g/L of Mg Oxide)[4] Mg Citrate has not been shown to be 30,000 times more bioavailable, 3,000 times, 300 or even 3 times more bioavailable. While there seems to be general agreement that organic salts are better absorbed (slightly to significantly)[13] no studies report the sort of correlation one would expect based on the solubility characteristics of the various compounds tested. This is supported by the Coudray rat study[4] which demonstrated across all Mg salts (organic and inorganic) a consistent decline in solubility from proximal small intestine to colon, matched by a steady rise in pH, but did not demonstrate anything close to the order of magnitude increase in bioavailability expected for the much more soluble organic acids. To be sure, the paper could only describe a 'tendency' toward better bioavailabilty of the organics, but does speak about previous research that demonstrated the effect of fermentable fibres in reducing the pH of the cecum and considerably increasing Mg absorption in animals and humans.[5] This raises the specter of an effect of pH independent of its ability to contribute to Mg salt solubility.[5]

Magnesium Oxide

Mg Oxide is known in the pharmaceutical industry as a powerful alkalizing agent and is used to improve bioavailability of a basic drug when luminal pH is required to be high. The addition of Mg Oxide to a hydrochlorthiazide (HCTZ) formulation was able to increase the pH in the rat intestine in the vicinity of the dosing site for up 90 min and increase absorption of HCTZ up to 3-fold when compared to HCTZ without Mg Oxide[14].

So while there is no denying that poor solubility of Mg Oxide plays a role in its poorer absorption when compared to other organic salts, the major alkalinizing effect it has on the duodenal, jejunal and ileal lumen, particularly in a large doses is likely contributing just as much (if not more) to its reputation as being poorly absorbed. These three characteristics (solubility, alkalinity and quantity) are all modifiable and the substantial advantage that 50% elemental Mg that Mg Oxide offers formulators has made Mg Oxide a favorite salt despite these unfavorable determinants of bioavailability.

Chelates



There are four inviolate chemical requirements for a chelate:

1) The ligand must possess two functional groups, each capable of donating electrons to the metal cation to grab the metal like a lobster claw (chele, Greek). The carboxyl group of the amino acid glycine has an electron for a covalent bond with the metal and the amino group has a pair of electrons to form a coordinate bond with the metal.

2) The functional groups have to be positioned to form a ring structure with the metal being the closing member. If two glycine molecules are used, a two-ring structure can be formed with a single metal cation.

3) The reaction has to be sterically possible. One ligand should not interfere spacially with the other ligand.

4) The reaction has to be energetically possible and the charges on the chelated complex have to be stochiometrically correct and balanced to achieve optimal chelation.[15]

The binding of the metal has to be complete (i.e. occupy all of its electrochemical coordination sites) or enough of them to reduce the reactivity of the metal with other substances. That is why a chelate can offer some protection from an otherwise irritant and biologically reactive metal. It can protect the metal from been bound by substances like phytates found in cereals that prevent absorption. This is why the degree of chelation is so important, because a partially chelated metal will still react and be sequestered by phytates and other substances.[7]

The ligands are also chosen depending on the purpose of the chelate. Besides being able to fulfill the chemical conditions described above, the degree to which the ligand binds with the metal under various physiologic conditions will determine what that chelate can be used for. Some chelates bind their metals very strongly and are used clinically by doctors to scavenge the blood for that metal, bind it up tightly and not let it go. Desferroxamine, a good example of this, was introduced in the 1960s and is administered intravenously to bind and therefore treat conditions of iron overload. EDTA (ethylene-diamine-tetra-acetic acid) is also an effective chelating agent.

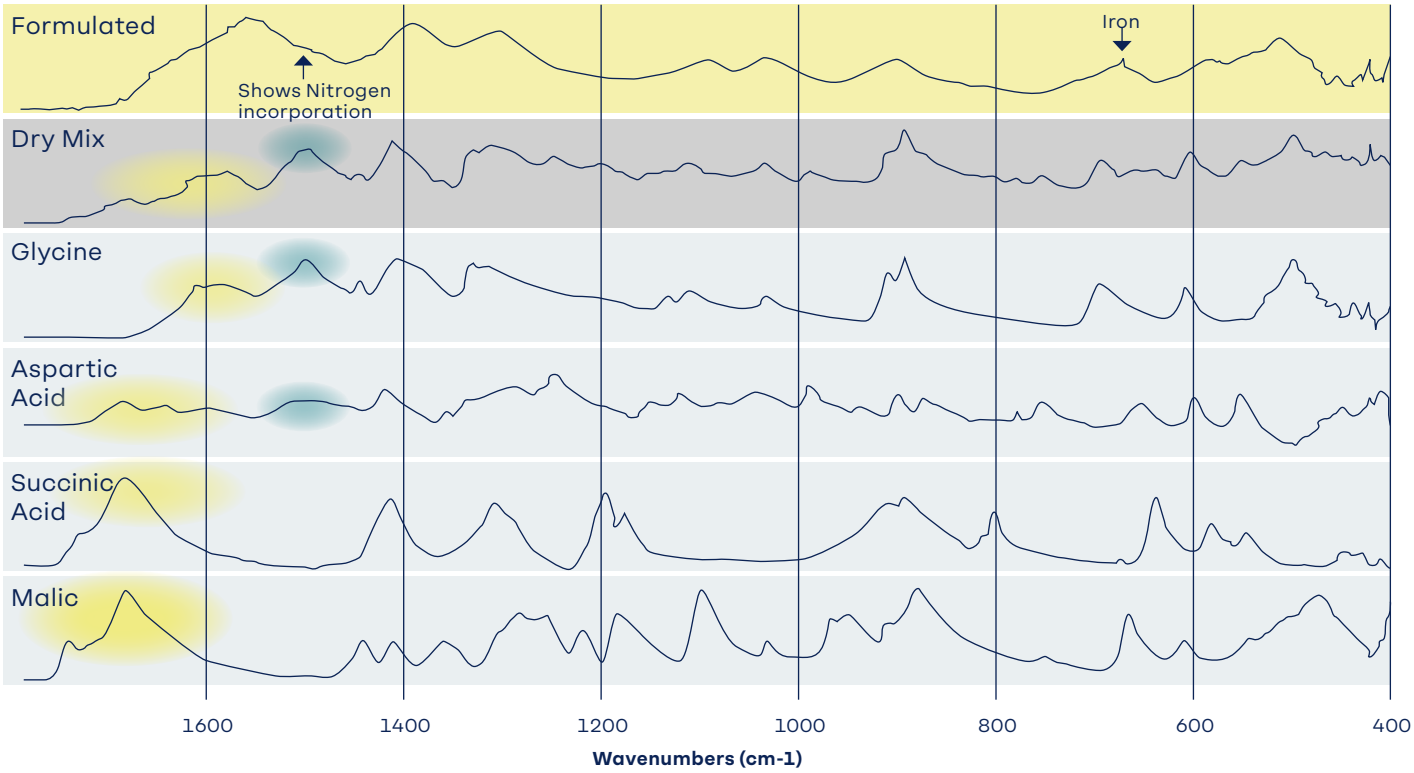
Note that when the medical literature refers to a chelating agent, which is the way that most doctors understand the term, it is referring to a compound that will bind to an unwanted mineral and prevent it from being biologically active. Hence the common misconception about mineral chelates being used for mineral replacement. The key point here is that the affinity that the metal has for the ligand, determines whether the complex will be a scavenger to remove the metal from biological tissue (a chelator) or whether it will bind with sufficient strength to reduce interfering substances from binding and preventing that mineral's absorption. The strength of the chelate bond is called the stability constant and describes the extent to which the ligand and metal dissociate in a solution according to various physiologic standards like pH, temperature and concentration. A very low stability constant (< 1) indicates that the chelate is very soluble in water and readily dissociates into the ligand and the ionic form of the metal at a pH range of 2 – 7.4. The higher the stability constant, the less likely the metal will dissociate. So for example a stability constant above 6 will result in little dissociation across this pH range.

Ligand Stability Constant

The stability constant for magnesium glycinate is 3.45, for EDTA-Mg it is 8.69 and for desferroxamine-Fe is an enormous 32.5.[16] Hence the magnesium glycinate is eminently capable of releasing its metal load under physiologic conditions, whereas desferroxamine will not – ever. How do we know that chelated minerals maintain their binding integrity to ward off unwanted interference from phytates? When Bovell-Benjamin's group gave radiolabeled ferrous bisglycinate chelate and radiolabeled ferrous sulfate to 10 iron deficient men in a high phytate corn porridge, the bioavailability of ferrous bisglycinate chelate was 4-5 fold higher than the ferrous sulfate salt, thereby demonstrating that the ferrous sulfate was mainly complexed with phytates and prevented from being absorbed whereas the ferrous chelate was able to resist being sequestered by the phytates to some degree and hence demonstrated better bioavailability.[7]

Measuring Chelation

How do we know that the amino acid ligand has reacted functionally with the metal – thereby occupying its reactive coordination sites? The Fourier Transform Infrared Spectroscopy (FTIR) is an analytical technique used to identify organic (and in some cases inorganic) materials. This technique measures the absorption of various infrared light wavelengths by the material of interest. These infrared absorption bands identify
specific molecular components and structures like the sites of the amino acid that would form the coordinate and covalent bonds with the metal.



48% Glycine, 15% Aspartic Acid, 8% Malic Acid, 7% Succinic Acid, 21% Iron

Carboxylic Acid Peaks Nitrogen Peaks

The FTIR panel above is for illustrative purposes only in demonstrating the spectroscopic pattern of a variety of component molecules of an iron chelate called ferrous asparto-glycinate, in which two different amino acids are used to form two rings with Fe^{++} being the closing member.[17] Two organic acids are also used to drive the chelation reaction (malic and succinic acid). The light blue panels show the patterns of each individual component and highlighting the carboxyl groups (common to all) and the nitrogen groups in the two amino acids. The second to top panel (grey) demonstrates the spectroscopic pattern of a dry blend of all these components. A quantitative assay will report all the correct amounts of the complex and will not be able to distinguish the dry (unreacted blend) from the reacted chelate. The top panel (yellow) is of the fully reacted aspartic acid – glycine chelate. The single peak on the extreme left shows the disappearance of the carboxylic acid peaks (on the left hand side of the peak) of the glycine, aspartic acid and succinic and malic acids, and the disappearance of the nitrogen (from the amino acid) peaks of the glycine and aspartic acid on the right hand side of that peak. Their disappearance shows that these two binding sites on the amino acid are fully reacted with the metal and are now incorporated into the chelate complex. In contradistinction, all the carboxylic acid and nitrogen peaks can be seen in the dry blend – proving that none are reacted.

This very sensitive signature can determine the degree of chelation that has taken place and if a significant percentage of the compound is not chelated (i.e. 30 – 40% not chelated) then the carboxyl and nitrogen peaks of these unreacted ligands would show up in a similar way to the unblended panel (grey).

Magnesium Chelates - Mechanisms of Bioavailability Advantage

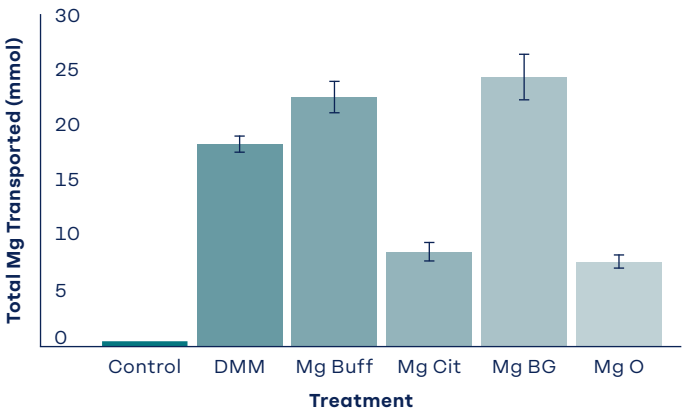
1. The chelation of the Mg^{2+} ion by two glycine molecules (bis-glycinate) and glycine and lysine molecules (MLG) occupies the reactive sites of the mineral which then reduces the ability of the ion to get complexed with phytates or polyphenols which will then prevent the inhibitory effects of these substances on absorption.
2. The occupation of these sites may reduce hydration of the molecule, which could reduce the frequently encountered problem of laxation (as typical magnesium salts are known for).
3. The chelation with glycine and lysine will make the whole compound more soluble.
4. There is evidence to suggest that a portion of the chelated minerals may be absorbed via the amino acid active transport pathway.
5. The buffering impact of amino acids on the chelated Mg will enhance its absorption through the saturable active transcellular transport pathway by making the compound more soluble.
6. By contributing to a lower luminal pH (5.5-6.5) that is vital to maintaining claudin transporters functional at the paracellular tight junctions.
7. The glycine and lysine combination (MLG) further extends the range of buffering capacity and to enhance Mg^{2+} absorption via the passive non-saturable pathway.

Caco2 Cell Studies

An immortalized line of colon adenocarcinoma cell culture that has been recognized as possessing all the proteins, enzymes and transport apparatus of a small intestine cell (enterocyte) has become a standard and well-accepted tool to explore absorption of small molecules, nutrients and minerals across a monolayer of these cultured cells.

Two experiments were conducted to determine the bioavailability of various magnesium forms. It must be stated that even though this is an in-vitro test, there can be differences noted between results obtained from separate experiments conducted on different days (inter-experiment variation), but the intra-experiment variability is minimal. In the first experiment 50mM of

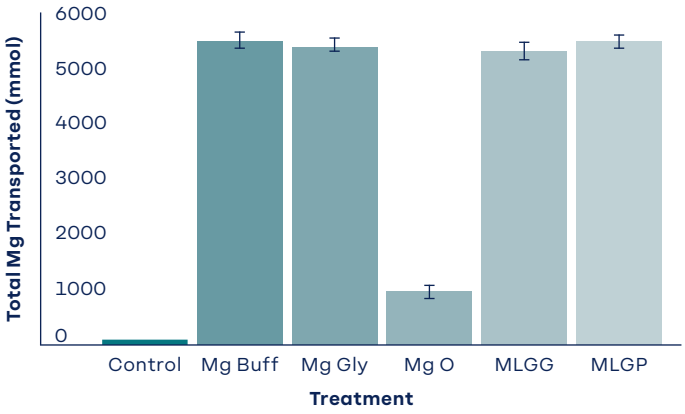
Magnesium Transport



	Apical Conc. mMol	**Basolateral Conc.** mMol	**Bioavail-ability**
Control		0.32	
Mg bisGlycinate	50	24.5	48%
Mg Glycinate – Buffered	50	22.55	44%
DMM	50	18.24	36%
Mg Citrate	50	8.43	16%
Mg Oxide	50	7.61	15%

5 magnesium forms and 1 negative control were studied. The active forms were Mg Bisglycinate, Mg Bisglycinate Buffered, DiMagnesium Malate, Mg Oxide and Mg Citrate. The results are shown below and has been published as an abstract at Experimental Biology in 2016.[18]
Another Caco2 cell study tested Magnesium Lysinate Glycinate Granular, Magnesium Lysinate Glycinate Powder, Magnesium Bisglycinate Chelate (Mg Gly), Magnesium Bisglycinate Chelate Buffered (Mg Buff), and Magnesium Oxide. The amount of magnesium transported through the cell model is shown below and which has not been published yet.[19]

Magnesium Absorption



	Apical Conc. mMol	**Basolateral Conc.** mMol	**Bioavail-ability**
Control		2.8	
Mg Glycinate – Buffered	1250	549.4	44%
Mg Oxide	1250	94.3	7%
Mg Lysinate Gly – Granular	1250	530.1	42%
Mg Lysinate Gly – Powder	1250	547.7	44%

The two cell lab experiments corroborate each others, findings and consistently show a bioavailability of the chelated magnesium that is higher than the two salts and are between 2.75 to 6.25 fold more bioavailable than the oxide or even the citrate salts, with a bioavailability of 42-44% vs 7% - 15% for Mg oxide. The key point is that between the two experiments, Mg oxide and Mg Glycinate – Buffered were used in both and thereby provided a bridge connecting the two studies. The Caco2 cell model removes all of the variables imposed by normal physiologic mixing of magnesium pools that make being able to distinguish the administered Mg^{2+} (test material) from the body's mobilization, excretion and secretion of magnesium. This makes the need for stable isotope labeling of Mg unnecessary and doesn't require 24-hour urine and stool specimen collection or muscle or bone or other tissue harvesting for testing (which usually can only be approved in animal experiments).

Conclusion

The goal of this white paper is several-fold. Firstly, that while magnesium is critical to so many metabolic processes, it doesn't have the easily identifiable clinical manifestations of other nutritional deficiencies and is further complicated by the dearth of actionable analytic testing methods that can be used by caregivers and consumers. There is always a need (in the supplement industry and beyond) to understand which magnesium forms offer the best efficacy and tolerability. The literature can be confusing and commonly held beliefs can be misleading. There is a large body of accumulated clinical research supporting superior absorption and tolerability of chelated minerals, including magnesium bisglycinate. Furthermore, the bioavailability advantage of chelates over other organic and inorganic magnesium salts is quantified in standardized Caco2 studies.

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