ALBION®
HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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MAGNESIUM

Clinical And Health Benefits Still Without Limits

A cursory review of published clinical research, as well as the textbooks devoted to nutritional biochemistry that examine or elaborate the roles of magnesium in the maintenance of the human body should convince even the most avid skeptic of the importance of magnesium to health. Data from two national surveys, NHANES III 1988-91[1] and CSF II 1994[2], has indicated that 70% of the US populace receives less than the RDA of this mineral. Recently, magnesium deficiency has been implicated in a host of clinical disorders[3]. Of note, a growing body of studies suggests that intracellular magnesium may play a key role in regulating insulin-mediated glucose uptake and vascular tone. There is some research that suggests that reduced intracellular magnesium might be the missing link in the epidemiological association between non-insulin dependent diabetes mellitus and hypertension[3].

Magnesium is the fourth most abundant cation in the body and is involved in more than 300 enzymatic systems, including ATP metabolism, creatine kinase activation, adenylate cyclase, and sodium-potassium-ATPase. Magnesium has an effect on a variety of cell membranes through a process involving calcium channels and ion transport mechanisms. Magnesium is responsible for the maintenance of the transmembrane gradients of sodium and potassium. Patients with refractory hypokalemia often do not respond to potassium supplements until magnesium deficiency is corrected[4]. Magnesium deficiency should be considered whenever severe potassium deficiency is seen. The basic magnesium body stores are in Figure 1.

Fox C, et al. have chronicled the proven and potential clinical significance for magnesium (Fox C, Ramsoomair D, and Carter C; South Med J: 94(12):1195-1201, 2001). In the course of this article (covering 67 published studies), attention is given to magnesium metabolism, physiology, deficiency diagnosis, biological mechanisms, incidence of deficiency, signs and symptoms of deficiency, and therapeutic usage. In this review, it was pointed out that magnesium deficiency has been implicated in diabetes mellitus, hypertension, cardiac arrythmias, acute myocardial infarction and atherosclerosis. The biological mechanisms that could explain the physiologic effects of magnesium in these disorders include:

- Magnesium deficiency causes dysregulation of the Na-Mg exchanger, resulting in higher intracellular sodium and higher blood pressure.
- A relatively low magnesium level creates an intracellular imbalance between calcium and magnesium, which leads to increased vascular tone in arterial smooth muscle and increased blood pressure.
- Magnesium deficiency causes insulin resistance, which causes hyperinsulinemia, leading to hypertension, diabetes and hyperlipidemia.

Figure 1

MAGNESIUM STORES	
Total body content (70 kilogram – adult)	21-28 grams
Normal serum concentration range	1.7 – 2.5 mg/dl
Mineral phase of skeleton distribution	65%
Intracellular space distribution	34%
Extracellular fluid distribution	< 1%

This article goes on to state that the incidence of hypermagnesemia varies widely, as seen below:

General Populace	6.9%
Hospitalized Patients (Medical/Surgical)	11%
Intensive Care Unit	20%
Post Operative Intensive Care	60%
Diabetics	25%
Hypertensives	24%

NOTE: The incidence of hypomagnesemia is probably higher than listed above. This is due to the difficulty that magnesium presents to clinical laboratory medicine. Serum magnesium correlates poorly to total body stores. Due to this, several intracellular assays for magnesium have been developed from muscle biopsy, lymphocytes and red blood cells. These assays include NMR spectroscopy and ion specific electrode measures. These tests are expensive and feature other requirements which make them impractical for the clinical setting. So, despite its limitation, serum magnesium is what is typically used to assess the magnesium status of patients. It is known that when serum magnesium levels are low, intracellular magnesium is also low. However, many patients with low intracellular magnesium have normal serum magnesium.

The Need for Magnesium – A Growing Body of Evidence

The research based benefits for magnesium supplementation is continuing to grow. A recent study in Brazil, which will be reported at a pulmonary health symposium this fall in Austria, shows that magnesium (as amino acid chelate from Albion Advanced Nutrition) has definite benefits to children and adolescents suffering from asthma. A complete accounting of this study will be presented in a future Albion Research Notes, once the research team has presented its findings. Below are a few more recent works on magnesium and its health benefits.

Low Magnesium and arthrosclerosis: an evidence-based link.
Maier JA
Mol Aspects Med
2003 Feb 6;24(103):137-46.

Accumulated data indicate that magnesium deficiency due to poor diet and/or errors in its metabolism could be the link between diverse cardiovascular risk factors and atherosclerosis. This review points out that low plasma levels of magnesium accelerate atherogenesis by increasing LDL concentrations and their oxidative modifications, and the promotion of inflammation. In vitro studies have shown that low magnesium results in endothelial dysfunction, the first event in the formation of plaque. In addition, oral magnesium therapy has been demonstrated to improve endothelial function in patients with coronary artery disease. This review states that magnesium is an inexpensive, natural and safe element that could be useful in preventing atherosclerosis and could also be an adjuvant treatment for patients with clinical manifestations of the disease.

Alteration of Myocardial Mechanics in Marginal Magnesium Deficiency.
Nair RR and Nair P.
Magnesium Res
2002 Dec;15(3-4):287-306.

In this review article on magnesium research and cardiology, the effects of hypomagnesemia are critically reviewed. Magnesium is an element with diverse roles in the regulation of cardiac contractility. Experimental and clinical research studies indicate that marginal decrease in myocardial magnesium can have real cardiovascular impact. Reduction in extracellular magnesium affects myocardial excitability and contractility by modulation of the levels of other ions that have an influence on cardiac mechanics. In vitro experiments on isolated ventricular tissue of myocytes show an inverse relationship between magnesium concentration and the strength of myocardial contraction. Animal studies have demonstrated that low magnesium diets lead to a decrease in myocardial contractility and other whole animal or organ research has shown that magnesium deficiency causes coronary vasospasm, defective energy metabolism, and excessive free radical generation – all possibly impacting myocardial function. Magnesium deficiency enhances electrical excitability, and arrhythmic changes are typically presumed to be due to a disturbance in potassium balance. The heretofore poor ability to detect clinical magnesium deficiency has lead to its neglect by medical practitioners. Magnesium deficiency with stress may be of clinical significance, leading to arrhythmic, hemodynamic, and ischemic changes in the heart. Chronic magnesium deficiency is accompanied by increased free radical generation, which can impact myocardial excitability and contractility. Stress of all kinds will promote free radical generation, and the additive effect

of the free radical generation from a magnesium deficiency and stress could potentially be the reason for enhanced sensitivity to stress in the presence of magnesium deficiency. The total cardiac consequence of magnesium deficiency needs much greater clinical attention.

Research Findings on Albion's Magnesium

Albion's patented Magnesium Chelazome® has been the subject of a variety of clinical trials. Researchers have evaluated this magnesium to determine its impact on physical performance, clinical symptoms, absorption, safety, and tolerability. In one such study[5], Magnesium Chelazome was administered to a group of women suffering from dysmenorrhea. At a dose of 400 mg of magnesium per day (4 divided doses), Magnesium Chelazome significantly reduced or eliminated the abdominal pain associated with the onset of menstruation in these women. The most studied of Albion's Magnesium Chelazomes is Magnesium Bisglycinate Chelate (CAS Number 14783-68-7). This magnesium is pharmaceutically pure and anion free.

Bioavailability studies conducted by Abrams, et al.[6], Schuette, et al.[7], and Roussouw and Brummelen[8] have all shown that Magnesium Bisglycinate Chelate is a highly bioavailable form of magnesium. In the double blind study by Roussouw and Brummelen, the bioavailability of Magnesium Bisglycinate Chelate was compared to magnesium chloride. For the study, the volunteers (healthy athletic women) were divided into two groups, with one group being administered Magnesium Bisglycinate Chelate and the other magnesium chloride. Blood samples for serum magnesium were drawn at 0, 1, 2, 3, 4, 8, 12, and 24 hours after administration, while urinary magnesium was measured at 0-4, 4-8, 8-12, and 12-24 hours post administration. The differences in the serum magnesium for the two groups over 24 hours can be seen in Figure 2, while Figure 3 demonstrates the differences in 24 hour magnesium excretion for the two groups.

By taking a look at the area under the curve for the serum levels for the two groups, it was shown that the magnesium from Magnesium Bisglycinate Chelate was absorbed at a rate that was 228% higher than that of the magnesium from

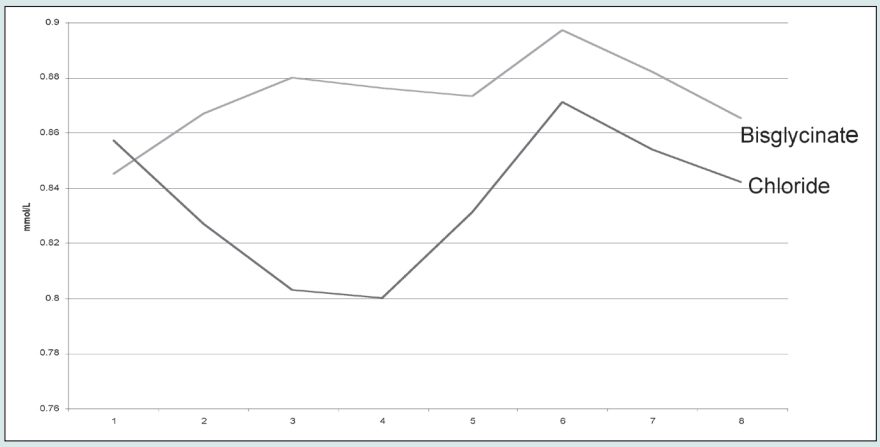

Figure 2. Changes in serum magnesium for women taking magnesium bisglycinate or magnesium chloride over 24 hour period. The total difference is significant (p<0.05).

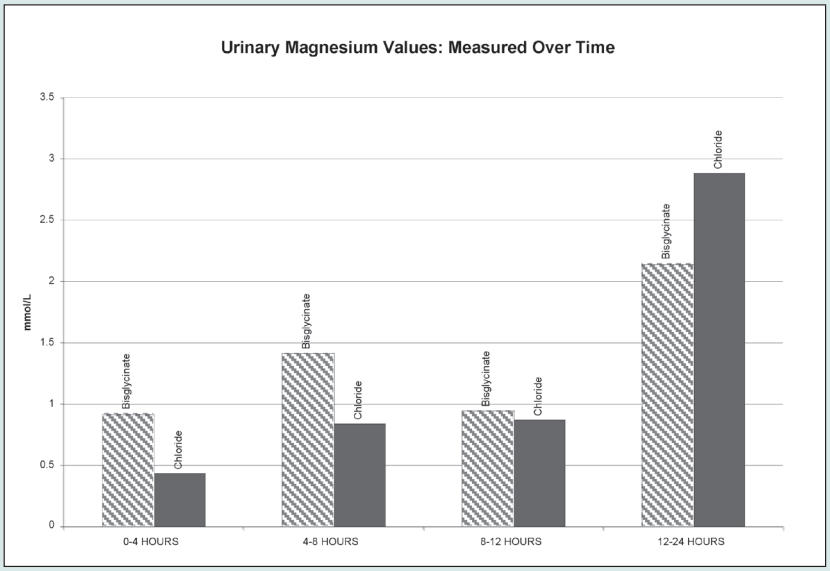

Figure 3. Urinary magnesium values measured over time follow a single dose of Magnesium Bisglycinate or magnesium chloride. Total values are about the same for both groups.

magnesium chloride. It is of further note that the overall urinary excretion of magnesium from the magnesium chloride group was higher, indicating that there was greater utilization of the magnesium from Magnesium Bisglycinate Chelate to go along with it higher absorption.

Albion's Magnesium Bisglycinate Chelate has been shown to be a better tolerated form of magnesium7, as well, causing less laxation potential than other forms of magnesium, such as oxide.

Magnesium Bisglycinate Chelate is a fully reacted, pharmaceutically pure, anion free chelate. It is CAS registered, Kosher-Parvé, clinically tested, and laboratory validated.

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