

Magnesium

Function

Magnesium plays a vital role in a wide range of biochemical and physiological processes, particularly those involving energy metabolism and utilization (Shils 1999). Clinical consequences of magnesium deficiency include a variety of neurological and neuromuscular signs such as tremors, spasms, and altered reflexes. In addition, magnesium deficiency may cause or exacerbate myocardial infarction, arrhythmia, and associated mortality; it is often brought on not only by dietary inadequacy but also by malabsorption, kidney dysfunction, endocrine disorders, genetic and congenital disorders, and alcoholism (Shils 1996). Magnesium is efficiently absorbed in the intestine, and body concentrations are controlled primarily through the regulation of urinary excretion rates. It is stored and reserved in the skeleton (Shils 1996, 1999).

Safety Evidence

Healthy human kidneys are capable of rapidly excreting large amounts of absorbed or injected magnesium. Even after large intakes, serum levels usually stay within the usual range (Shils 1999). Subjects with normal kidneys can excrete 40 to 60 g of magnesium per day without side effects when the mineral is administered via persistent infusion. Elevated serum levels may occur when drugs that contain magnesium, usually antacids and cathartics, are taken in excess of 15 g per day on a chronic basis (Smilkstein et al. 1988). Moderate increases in plasma magnesium levels may induce symptoms such as nausea, vomiting, and hypotension (Shils 1996, 1999). Due to the major involvement of magnesium in neurological functions, the elevated plasma levels that occur as a result of large intravenous infusions can cause adverse effects to become more severe and sometimes life-threatening.

Adverse effects of magnesium are primarily related to three conditions: neonatal neural depression after intravenous maternal treatment for eclampsia, accidental or deliberate poisoning with very large single doses, and increased sensitivity to magnesium-containing drugs in persons with renal failure (Flink 1976). Aside from osmotic diarrhea related to unabsorbed magnesium, there is no evidence that large quantities of oral magnesium are harmful to persons with normal kidney function (Food and Nutrition Board 1997).

Total dietary intakes by U.S. adults range between 300 and 400 mg per day (Food and Nutrition Board 1997). Supplemental intakes of 375 mg have no known adverse effects (Stendig-Lindberg et al. 1993), and it is not until supplements reach levels greater than 10 mg per kg per day (700 mg in a 70 kg person) that

plasma magnesium concentrations become elevated (Durlach et al. 1994). Possible negative consequences of calcium's interaction with magnesium have not been reported.

Published Official Reviews of Magnesium Safety

The FNB review concluded that the magnesium found in foods has not been found to produce adverse effects, and that “the primary initial manifestation of excessive magnesium intake from nonfood sources is diarrhea” (Food and Nutrition Board 1997). The physiological effects of longer-term, high intake of oral magnesium have been observed only in persons with abnormal kidney function. Thus, the critical adverse effect identified as the appropriate basis for a magnesium UL is diarrhea. In its dose-response evaluation, FNB identified a few studies that found some increase in the incidence of diarrhea with supplemental intakes of magnesium chloride or other soluble salts in the range of 360 to 460 mg of magnesium per day (Bashir et al. 1993; Marken et al. 1989; Ricci et al. 1991), but noted that foods enriched with 452 mg of magnesium as magnesium oxide did not cause diarrhea (Altura et al. 1994). Another study (Stendig-Lindberg et al. 1993) found no diarrhea in postmenopausal women who were given up to 678 mg magnesium as magnesium hydroxide. Similarly, diabetic subjects supplemented with 400 mg magnesium as an oxide or chloride experienced no diarrhea (Nadler et al. 1992). Elderly subjects given 372 mg of magnesium did not have any increase in diarrhea or gastrointestinal complaints (Paolisso et al. 1992). On the basis of these studies as well as that done by Bashir and coworkers in particular, FNB identified a LOAEL of 360 mg for nonfood magnesium. To derive the UL, FNB selected a UF of 1.0, even though it was being applied to a LOAEL. The FNB stated that this decision was justified because of “the very mild, reversible nature of osmotic diarrhea caused by ingestion of magnesium salts.”

The EC SCF agreed that osmotic diarrhea is the critical effect for identification of a UL for magnesium (Scientific Committee on Food 2001). It identified a LOAEL of 360 mg and a NOAEL of 250 mg per day for nonfood magnesium. Selecting a UF of 1.0 for application to the 250 mg NOAEL, EC SCF derived a UL of 250 mg per day.

The UK EVM concluded that osmotic diarrhea is the adverse effect of concern, but also that the data are insufficient to establish an SUL value (Expert Group on Vitamins and Minerals 2003). Instead, UK EVM established a GL of 400 mg per day for nonfood magnesium per day because “it would not be expected to result in any significant adverse effects.”

All three official reviews found no evidence that food magnesium causes osmotic diarrhea, but instead determined that nonfood sources such as supplements, laxatives, and antacids have the potential to produce these mild, reversible

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adverse effects. Thus, the UL or GL values identified were applied to nonfood sources only.

CRN ULS for Magnesium

The only severe adverse effects reliably attributed to oral consumption of magnesium relate to prolonged use in multiple-gram quantities as an antacid or cathartic. Mild to moderate but easily reversible diarrhea can result from nonfood magnesium intakes at levels above 400 mg per day. This mild, infrequent, reversible diarrhea found at lower levels does not merit a LOAEL, but does justify selection of a UF of 1.0 for use in deriving a ULS. Thus, the CRN ULS for supplemental magnesium is 400 mg per day for healthy adults. Owing to intestinal transit time considerations, a large supplement of magnesium consumed in a single dose is more likely to bring about diarrhea than multiple doses separated by several hours. Persons consuming supplements should be aware that some antacids and laxatives also contain magnesium.

Comparison of Safety Values for Magnesium

CRN ULS	400 mg
US FNB UL, nonfood sources	350 mg
EC SCF UL, nonfood sources	250 mg
EC supplement maximum	Not established (as of May 2004)
UK EVM GL, supplement	400 mg

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