Boron

Introduction

Boron is essential to the life cycles of some animal species, but in regard to humans is considered only *probably* essential. There is, however, clear evidence that dietary intakes of this element are beneficial to humans (Nielsen 2000). In humans, boron deprivation impairs calcium metabolism and bone health as well as brain function and energy metabolism.

Studies of dietary deprivation on boron in animals have reported adverse effects (e.g., on growth, serum steroid hormone concentrations, and bone calcification) that can be corrected by increasing boron intake. The effects of low boron intakes are more marked when accompanied by low status for other nutrients (e.g., vitamin D and magnesium) (European Food Safety Authority [EFSA] 2006).

Boron occurs in foods as borate and boric acid.

Safety Considerations

Boron has a low potential for causing obvious adverse effects in adult humans, as indicated by the widespread use of boric acid between 1870 and 1920 as a food preservative. This use of boric acid led to boron intakes of up to 500 mg per day without adverse effects other than nausea and loss of appetite (Nielsen 1996). Intakes of 500 mg boric acid (72 mg boron) per day for 50 days by adults have disturbed appetite and digestion (Nielsen 1996).

In short- and long-term animal studies, oral exposure to boron at levels greater than 13 mg per kg per day have resulted in various adverse effects. Reproductive and developmental toxicity were the most critical adverse effects reported in these studies. In pregnant rats, dietary boric acid (13 mg boron per kg and higher) can cause fetal development defects and growth deficits (Price et al. 1996). In studies with dogs, high intakes of boric acid (29 mg boron per kg per day) have caused testicular atrophy and moderately decreased sperm production (Weir and Fisher 1972). No

evidence of carcinogenicity has been reported in long-term animal studies, and the available data indicate that boric acid is not genotoxic.

To calculate a safe intake (i.e., a reference dose, or RfD), the U.S. Environmental Protection Agency (EPA) relied on the dog study reported in Weir and Fisher (1972). In this study, adverse effects were found with an intake of 29 mg per kg per day over 38 weeks of treatment, and this level became the LOAEL. The next lower dose, of 8.8 mg per kg per day, produced no adverse effects; this intake level became the NOAEL. The EPA applied a hundredfold margin of safety to the NOAEL in dogs to calculate an RfD of 0.09 mg per kg per day, or 6.3 mg per day in a 70-kg human (EPA 2004).

For humans, the data are too scant and the effects too vague to identify a specific LOAEL value. Although more information is needed, the gastrointestinal effects associated with intake of 500 mg of boric acid (72 mg boron) may be considered undesirable rather than harmful. Moreover, they should be self-limiting due to consumer awareness. Thus, EPA could not propose a LOAEL value for boron intake by humans (EPA 2004).

Clinical trials with an upper intake of 3 mg per day produced no adverse effects (Meacham et al. 1994; Nielsen 2000). However, because so few other intake levels have been subjected to clinical study, 3 mg may be lower than appropriate to identify as a NOAEL for humans. The EPA value of 0.09 mg per kg per day, or 6.3 mg per day in a 70-kg man, may be considered a safe level of human intake. This intake level cannot be identified as a NOAEL, however, because it is based on calculation rather than observation.

Official Reviews

Institute of Medicine (IOM 2001). The IOM found that most data on the adverse effects of boron in humans were associated with an accidental single episode or short-term ingestion of boric acid. In the absence of human dose-response data judged useful, the IOM extrapolated from animal data to set a human UL. From the data of Price and coworkers (Price et al. 1996), the IOM identified a NOAEL of 9.6 mg per kg per day for developmental toxicity in mice, and it

selected a composite UF of 30 (3 for interspecies variability and 10 for extrapolation from mice to humans) to derive an UL of 0.3 mg per kg per day. Correction to a reference adult weight of 61 kg gave the IOM an adult UL of 20 mg boron per day.

Expert Group on Vitamins and Minerals (EVM 2003). The UK's EVM found the long-term clinical study of Meacham and colleagues (Meacham et al. 1994) to be an insufficient basis for an SUL or guidance level. Instead, using the same data on developmental toxicity in mice (Price et al. 1996) that the IOM studied, the EVM identified the NOAEL as 9.6 mg per kg per day and applied a composite UF of 60 (10 for interspecies variability and 6 for interindividual variability). This resulted in a SUL of 9.6 mg per day for a 60-kg person.

EFSA (2004). EFSA reviewed the safety of boron and established an UL of 10 mg per person per day for adults. This value is based on the NOAEL of 9.6 mg per kg per day for decreased fetal body weight in rats following in utero exposure (Price et al. 1996) and extrapolated to humans by applying a UF of 60.

CRN Recommendations

A clinical trial (Meacham et al. 1994) with an intake of 3 mg per day produced no adverse effects. Other studies confirmed this observation (Nielsen 2000), and that intake may be considered the highest observed intake (HOI) for supplementation. Intakes from conventional foods are almost always less than 3 mg per day (EVM 2003).

For boron intakes by adults, the EPA value of 6.3 mg per day may used as a well-substantiated human NOAEL; that is, it does not require application of any additional safety factor (in other words, a safety factor of 1.0 is sufficient) to calculate a safe human intake.

In the face of these quantitative uncertainties, CRN recommends a supplemental UL of 6 mg per day, based on the EVM UL of 9.6 mg and the fact that food intakes rarely exceed 3 mg.

Quantitative Summary for Boron

CRN UL, supplemental intake	6 mg/day
IOM UL, total intake	20 mg/day
EFSA UL, total intake	10 mg/day
EC supplement maximum	Not determined
EVM SUL, total intake	9.6 mg/day

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