Boron

Boron is a nonmetallic element that occurs in nature bound to oxygen (1). Boron has been shown to be essential for the completion of the life cycle for organisms in all phylogenetic kingdoms. In plants, boron is required for growth, flowering, pollination, and seed formation (1). Boron forms crosslinks with pectin apiose in rhamnogalacturonan II to provide cell wall rigidity in plants (1). Boron has not been shown to be essential for humans. However, an increasing number of cell culture, animal, and human studies indicate that boron in nutritional amounts has beneficial health effects (2). This apparently occurs because boron as boric acid or as a borate forms ester complexes with several biologically important sugars containing *cis*-hydroxyl groups, especially ribose (3). As a result, the function of biochemical entities containing ribose, such as S-adenosylmethionine, diadenosine phosphate, NAD^+, and the NAD^+ metabolite cyclic ADP ribose (cADPR), may be modified by boron. These entities are involved in bone formation and maintenance, cardiovascular health, cancer risk, and neurological function, with which boron has been beneficially associated.

Deficiencies

Only experiments with frogs and zebrafish have provided evidence for boron essentiality in animals (3). Boron is essential for cleavage of zebrafish zygotes to the 2 and 4 cell preblastula stage and for normal morphogenesis of the frog *Xenopus laevis*. However, animals and humans fed a diet low in boron have been found to beneficially respond to boron supplementation. In animals fed a low-boron diet, boron supplementation improved trabecular and alveolar bone growth and formation. In boron-deprived humans, boron supplementation improved mental alertness, attention, short-term memory, and motor speed and dexterity. Ecological epidemiological studies have found that low boron intakes are associated with an increased risk of prostate cancer in men and lung cancer in women.

Depriving various cells in culture has found that boron can modulate the response to oxidative and inflammatory stress (2–4). For example, in cultured human prostate cells, boric acid acts as a reversible noncompetitive inhibitor of cADPR leading to decreased endoplasmic reticulum Ca^{2+} (4). The decreased Ca^{2+} results in the E74 like ETS transcription factor 2α activating transcription factor 4 (ATF4) and nuclear factor erythroid 2 like 2 (Nrf2), which increases the mRNA levels of antioxidant response element genes. Nrf2 directly regulates the induction of anti-inflammatory genes and indirectly counteracts inflammation by modulating reactive oxygen species and reactive nitrogen species. This has been suggested as a basis for boron preventing oxidative DNA damage and enhancing antioxidant status (4, 5). ATF4 is a transcription factor required for the differentiation of osteoblast cells, osteogenesis, and thus bone remodeling.

Boron supplementation in the form of boric acid, borates, and the boroester fructoborate to humans with conditions that elevate inflammatory stress markers (e.g., C-reactive protein) ameliorated those markers (2). Animal studies have shown that the addition of boron to bioactive glasses, which are used for bone engineering and in situ bone tissue regeneration, enhances bone formation (2).

Diet Recommendations

Neither RDAs nor Adequate Intakes have been established for boron (6). However, humans in depletion–repletion experiments positively responded to boron supplementation after consuming a diet supplying only 0.2–0.4 mg/d for 63 d. Thus, a dietary boron intake >0.4 mg/d may be useful for bone and brain health and in modulating inflammatory and oxidative stress (2, 3). Extrapolation of data from animal experiments suggests that 1.0 mg B/d would achieve the nutritionally beneficial effects of boron. Both animal and human data were used by the WHO to suggest that an acceptable safe range of population mean intake of boron for adults could be 1–13 mg/d (2, 3). The FDA has not established a Daily Value for boron for food and dietary supplement labeling purposes.

Food Sources

Reports showing the boron content of commonly consumed foods indicate that boron is abundant in many foods and drinks obtained from plants, including fruits, leafy vegetables, and nuts (7). Foods especially high in boron include avocado, dried fruits such as raisins, peanuts, pecans, prune juice, grape juice, wine, and chocolate powder. However, the amount of boron in food and beverages varies based on the environment in which they are produced.

Clinical Uses

A 600 mg boric acid vaginal suppository per day for 7–14 d is used for yeast and bacterial infections. Boric acid is used as an antiseptic and buffering agent in eye wash solutions.

Toxicity

The Upper Intake Levels (ULs) set by various organizations (2, 5) indicate that boron is a relatively nontoxic element. The US and Canada ULs (5) are, for children aged 1–3 y, 3 mg/d; and aged 4–8 y, 6 mg/d. The UL for adolescents aged 9–18 y is 17 mg/d, and for adults, 20 mg/d. The WHO has indicated that a safe upper intake would be 0.4 mg/kg body weight or ~28 mg/d for a 70-kg person. The European Food Safety Authority established an Acceptable Daily Intake for boron at

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0.16 mg/kg body weight, or ~11.2 mg/d for a 70-kg person. The lack of finding adverse effects on health and fertility caused by drinking water with high boron concentrations and the past use of boric acid and borates as food preservatives is evidence of the low order of toxicity for boron (3). A dosage of 500 mg boric acid/d (87 mg B) was used to show disturbances in appetite, digestion, and health in human volunteers (3).

Recent Research

Recent research in boron in the form of boric acid, borates, and fructoborate has focused on several different areas (2, 5, 8). These include the evaluation of the ability of boron to prevent oxidative damage caused by different chemical and physical agents; establishing the beneficial effect of boron on the risk and amelioration of pathological conditions characterized by inflammatory and oxidative stress; determining cellular transport mechanisms for boron; and the use of boron for bone engineering and regeneration. Because boron may be bioactive through forming diester complexes with phosphoinositides, glycoproteins, and glycolipids that contain *cis*-hydroxyl groups in membranes, recent research has examined whether these boroesters influence membrane receptors and signal transduction and may thus be the basis for boron enhancement of insulin, vitamin D, and progesterone effects.

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Abbreviations used: ATF4, activating transcription factor 4; cADPR, cyclic ADP ribose; Nrf2, nuclear factor erythroid 2 like 2; UL, Upper Intake Level.

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