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Review

Update on human health effects of boron

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ABSTRACT

In vitro, animal, and human experiments have shown that boron is a bioactive element in nutritional amounts that beneficially affects bone growth and central nervous system function, alleviates arthritic symptoms, facilitates hormone action and is associated with a reduced risk for some types of cancer. The diverse effects of boron suggest that it influences the formation and/or activity of substances that are involved in numerous biochemical processes. Several findings suggest that this influence is through the formation of boroesters in biomolecules containing *cis*-hydroxyl groups. These biomolecules include those that contain ribose (e.g., S-adenosylmethionine, diadenosine phosphates, and nicotinamide adenine dinucleotide). In addition, boron may form boroester complexes with phosphoinositides, glycoproteins, and glycolipids that affect cell membrane integrity and function. Both animal and human data indicate that an intake of less than 1.0 mg/day inhibits the health benefits of boron. Dietary surveys indicate such an intake is not rare. Thus, increasing boron intake by consuming a diet rich in fruits, vegetables, nuts and pulses should be recognized as a reasonable dietary recommendation to enhance health and well-being.
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Introduction

Boron has been shown to be essential for the completion of the life cycle (deprivation causes impaired growth, development, or maturation such that procreation is prevented) for organisms in all phylogenetic kingdoms. In the animal kingdom, boron deprivation has been shown to adversely affect reproduction and embryo development in the African clawed frog [1] and zebra fish [2]. Experiments have not been reported showing that boron deprivation interrupts the life cycle in mammals, or finding a specific biochemical function for boron. However, substantial evidence has been reported that indicates boron is a bioactive food component that is beneficial, if not required, for health and well-being. Recent findings continue to show that nutritional amounts of boron fed to animals and humans consuming a diet low in boron induce numerous biochemical and functional responses considered beneficial for bone growth and maintenance, brain function, and perhaps cancer risk reduction.

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Boron and arthritis

Since 1981, occasional reports have appeared suggesting that boron can ameliorate or prevent arthritis. Animal studies have shown that boron can inhibit inflammatory responses to material injected to induce arthritic conditions [3,4]. In 1990, it was reported that 15 individuals with confirmed osteoarthritis completed a double-blind study in which they were given either a supplement of 6 mg boron or placebo daily for eight weeks [5]. Five of the seven subjects consuming the boron supplement reported improved subjective measures such as less pain on movement for their arthritic condition. Only one of eight subjects consuming the placebo reported improved subjective measures.

More recent studies suggesting that boron may ameliorate arthritic conditions includes a report [6] that a 6 mg/d boron supplement in the form of calcium fructoborate, a naturally occurring boron complex found in fruits and vegetables, alleviated subjective measures of mild, moderate, or severe osteoarthritis in 20 subjects. After eight weeks of supplementation, 80% of patients with mild or moderate osteoarthritis reported reduced or eliminated use of painkillers. In addition, joint rigidity essentially disappeared, and mobility was markedly increased. Patients with severe arthritis, who were supplemented daily with 12 mg boron as calcium fructoborate, had a more subdued improvement in mobility and rigidity, but did report a significant reduction in painkillers. The findings in this study, however, are weakened by the non-blinding to treatment and the lack of placebo controls. Subsequently, a double-blind, placebo-controlled pilot study was done to evaluate the effect of calcium fructoborate on systemic inflammation in middle-aged subjects with primary knee osteoarthritis [7]. The study was completed by 60 of 72 subjects in which groups of 15 were supplemented with a placebo or boron at 3, 6, or 12 mg/d as calcium fructoborate for 15 days. When all boron-supplemented subjects were grouped together, inflammatory stress biomarkers serum C-reactive protein, plasma fibrinogen and erythrocyte sedimentation rate were significantly improved compared to the placebo group. Surprisingly, the group given 3 mg boron/d exhibited the greatest improvement in plasma fibrinogen and serum C-reactive protein. These provocative findings need to be supported or confirmed by additional carefully controlled studies, preferably by other research groups. The studies should determine the effect of boron in other forms on objective indicators of arthritic symptoms and inflammatory stress in groups larger than 15 individuals to provide convincing evidence that increased boron intakes or supplementation would be of benefit for some individuals at risk for or who have arthritis.

Boron and bone

Early findings indicating that boron deprivation was detrimental to bone growth independent of another stressor affecting bone health included decreased maturation of the bone growth plate in chicks [8] and induced limb teratogenesis in the African clawed frog [1]. Since those findings, considerable evidence has appeared to support the contention that boron has a beneficial effect on trabecular and alveolar bone growth and maintenance. Most of this evidence has come from animals and cell culture experiments.

When rats fed diets containing 0.1 mg boron/kg were compared to those fed 3.0 mg boron/kg diet, microcomputed tomography of the fourth lumbar vertebra revealed decreased bone volume fraction and trabecular thickness, and increased trabecular separation and structural model index (low values indicating a preferable more plate-like structure) [9]. Boron deprivation (0.07 vs. 3 mg/kg diet) in rats also has been shown to decrease alveolar bone (primary support structure for teeth) repair that is initiated immediately after tooth extraction [10]. Boron deprivation decreased osteoblast surface and increased quiescent bone-forming surface in the alveolus. In addition, boron deprivation for nine weeks impaired alveolar bone formation without tooth extraction in mice [11]. Boron deprivation decreased osteoblast surface and increased bone-forming surface in both the lingual and buccal side of periodontal alveolar bone. Boron supplementation (3 mg/d for 10 or 20 days) also has been found to stimulate dental bone formation and increase bone mineral density in rabbits undergoing orthopedically expanded suture [12]. In contrast to alveolar bone, enamel mineralization was not affected by 14 days of boron deprivation (0.07 vs. 3 mg/kg diet) in rats aged 21 days, although enamel thickness was reduced (hypoplasia) [13].

Recent studies with bioactive glasses, which are used for bone tissue engineering and in situ bone tissue regeneration, provide supporting evidence that boron is beneficial for bone formation. Bone formation is enhanced when bioactive glasses are modified to contain boron [14–16]. Some of this enhancement might be caused by an effect on angiogenesis, which is critical for wound repair and tissue engineering. Borosilicate bioactive glass ionic dissolution products increased angiogenesis in quail embryos [17].

Cell culture studies also support the concept that boron is beneficial for bone formation and maintenance. Boron supplementation at 1 or 10 ng/mL compared to supplementation at 0 and 0.1 ng/mL increased mineralized nodule formation and mineralized tissue-associated mRNA expressions of type 1 collagen, osteopontin, bone sialoprotein, osteocalcin, and RunX by cultured osteoblasts (MC3T3-E1) [18]. In addition, the boron supplementation increased bone morphogenetic proteins 4, 6, and 7 levels.

The changes in bone structure and formation induced by boron deprivation might be a risk factor for osteoporosis. Six months of supplementation with calcium fructoborate (226 mg/d) incorporated into margarine was found to improve bone density in 66 of 100 patients with osteoporosis [19]. This finding resulted in the suggestion that calcium fructoborate may be a good adjuvant in the treatment of osteoporosis.

Although there is convincing evidence from animal and cell culture studies that boron is beneficial to bone growth and maintenance, the limited findings with humans will be an impediment to acceptance of this being a bioactive effect that would stimulate consideration for providing dietary guidance for boron. More studies determining the relationship between boron and bone health in humans are definitely needed.

Boron and the central nervous system

Findings showing that nutritional intakes of boron have beneficial effects on the central nervous system are among the most supportive of the suggestion that boron is a beneficial trace element for humans. Under well-controlled dietary conditions, boron supplementation (3 mg/d) to older men and women after consuming diets providing about 0.25 mg boron/2000 kcal for about 63 days altered electroencephalograms (EEG) such that there was a shift toward less activity in the low frequencies and more activity in the high, dominant frequencies of the EEG spectrum [20,21]. A similar effect was found in rats [22]. Increased low-frequency activity is typical of states of reduced behavioral activation and has been associated with reduced performance in psychomotor tasks. Decreased high-frequency activity has been associated with impaired memory performance. Subjects supplemented with boron after deprivation exhibited improved psychomotor skills of motor speed and dexterity, and cognitive processes of attention and short term memory [20,21]. Since 1990s when these findings were found, there apparently have been no further studies involving the effect