

REVIEW ARTICLES

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The role of boron in the functioning of the osteoarticular system

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Abstract

Background: Boron was classified by the World Health Organization as 'possible essential elements for human health'. It can be found in different forms in the environment, has beneficial effects on bones and its deprivation can impair calcium and magnesium metabolism and bone development, their health and maintenance. Dietary boron supplementation can help prevent and manage degenerative and inflammatory bones and articular diseases, such as arthritis, osteoarthritis, rheumatoid arthritis and osteoporosis. Relevant articles were identified in PubMed, Google Scholar, ProQuest, and Scopus databases published until June 2021, describing the role of boron in the functioning of the osteoarticular system.

Conclusions: From organic and inorganic boron forms that can enter the human body, organic plant based boron compounds are highly bioavailable. In the functioning of the osteoarticular system boron acts by regulation of calcium and magnesium metabolism, enhancing the vitamin D activation process and influencing serum steroid hormone levels. A boron intake equal to or higher than 3 mg per day can help prevent/or correct arthritis, osteoporosis and osteoarthritis. Calcium fructoborate can reduce pain, joint discomfort and increase endogenous vitamin D level in patients with osteoarthritis. Boron may play a role in pathophysiology of rheumatoid arthritis and its severity and a supplementation with boron element may be useful.

Key words: boron, boron containing compounds, osteoarticular system, osteoarthritis, rheumatoid arthritis.

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Introduction

It is supposed that trace element boron (B) is essential for human health. There is, however, clear evidence that dietary intakes of this element are beneficial to humans. In humans, boron deprivation impairs calcium metabolism and bone health as well as brain function and energy metabolism [1].

B, which was described as a trace element until 1980, was included in the class of 'possible essential elements for human health' by the World Health Organization (WHO). There is also evidence that boron plays a role in the maintenance of healthy bones and joints. It has beneficial effects on bones, especially trabecular and alveolar ones, in ways they are independent of any other nutritional stressor [2].

Following the existing findings, boron is beneficial, if not essential, for trabecular microarchitecture that promotes bone strength through affecting osteoblast and/or osteoclast presence or activity. Boron deprivation decreased bone volume fraction, trabecular thickness and impaired alveolar bone repair [3].

Also, B plays an important role in osteogenesis, and its deficiency has been shown to adversely impact bone development and regeneration. Diet supplementation with B has repeatedly been shown to markedly reduce urinary excretion of both calcium and magnesium and to increase serum levels of estradiol and calcium absorption in peri- and postmenopausal women. This trace element also beneficially impacts vitamin-D utilization [4].

B is widely distributed in the environment combined with oxygen to form compounds called borates. They are found in soils and rocks and also, in different kinds of water. Because they are essential for plants, borates occur naturally in fruits and vegetables and elsewhere in the food chain [5]. Following a database created to assess boron concentration in different foods and beverages from the American diet, the top 2 contributors were coffee and milk, but fruits, vegetables and nuts are also rich in this trace element [6]. Thus, the main sources of boron in the diet are drinking water and food products rich in boron.

Considering the growing interest in boron as a possible essential element for human health, its daily intake and

possible nutritional sources, B influence on osteoarticular system and a lack of research about boron in Moldova, it was decided to search the information about the role of boron in the functioning of the osteoarticular system in order to do a further research about its consumption impact on the osteoarticular health of the Moldovan population.

It was necessary to find out what the PubMed, Google Scholar, ProQuest, and Scopus databases published until June 2021 using the following key terms: "boron", "boron compounds", "organic boron compounds" combined using the Boolean operator AND "osteoarticular diseases", "rheumatoid arthritis", "osteoarthritis". The reference list from the resulting publications was manually searched for any relevant trials with elimination of results not related to the article topic.

Results and discussion

The purpose of this review is to present the role of boron in the functioning of the osteoarticular system, alongside with its dietary sources and active compounds in the form of which it can be found.

Boron is considered to be a biological trace element but there is substantial and growing support for it to be classified as an essential nutrient for humans, depending on its speciation. Similar to other elements, boron doesn't act on its own but as a part of various molecules [7].

Active boron compounds and dietary sources

This trace element can be found both in an inorganic and organic form. The last one, organic boron containing compounds (BCCs), is essential for human health, being involved in the cellular metabolism. Plant based organic BCCs such as sugars and polyalcohol borate esters are very important in the human nutrition. It can be used in cell metabolism during which they are at least partially transformed into boric acid that will subsequently be eliminated as waste [7].

Boric acid and borates are inorganic BCCs found in soils and employed by plants and bacteria for the manufacture of all known B organic natural compounds. It has been known for a long time that B deficiency in soils, leads to depletion of BCCs in fruits and vegetables in the food supply, was correlated with a high incidence of arthritis [7].

There are three main sources that supply B for humans: drinking water, vegetable foods (mainly fruits and vegetables) and products daily used for personal care (soaps, lipsticks, shampoo, skin cream, gastric antacids, cosmetics, detergents, contraceptives and estrogen supplements). These sources, on average, supply around of 0.6, 1.0, and 0.5 mg B a day per person, respectively [8].

Also, since 1990, two more important sources of boron, such as supplements and nutraceuticals have appeared. They can supply between 3 and 10 mg of B per day. The essentiality of B in humans is not yet widely accepted, but the scientific information indicates that to ensure an adequate nutrition, humans require between 2 and 6 mg B per day for one person [8].

According to recently published research, people older than 40 can prevent/or correct arthritis, osteoporosis and osteoarthritis by taking B equal to or higher than 3 mg per day. In the countries following the famous healthy Mediterranean diet that includes staple foods rich in B such as grape, broccoli, garlic, tomato, pomegranate and olives combined with the consumption of drinking water with high levels of B, daily intake of this trace mineral frequently results higher than 13 mg per day [8].

On average, dried fruits, nuts and avocados contain between 1 and 4.5 mg of boron/100 g. Fresh fruits, vegetables, and honey, contains between 0.1 to 0.5 mg boron/100 g, whereas animal foods provide only 0.01 to 0.06 mg of boron/100 g. Another important source of boron is water, and the content varies according to geographic location [9].

Osteoarticular diseases in which boron may be involved

Epidemiologic evidence suggests that in the areas of the world where boron intakes usually were 1 mg or less / day, the estimated incidence of arthritis ranged from 20 to 70%. On the other hand, in areas of the world where boron intakes were usually 3 to 10 mg, the estimated incidence of arthritis ranged from 0 to 10% [10].

In the diet, many people do not consume more than one milligram of B a day, which may be a clinical concern. Soils are depleted, and certain fertilizers inhibit boron absorption into plants. Low boron levels were correlated with higher serum levels of rheumatoid factor (RF), the antibody that causes destruction of the joints in rheumatoid arthritis, and in osteoarthritis, which were correlated with disease duration and severity [11].

In the 1980s, boron was discovered to play a role in regulating mineral metabolism (such as calcium and magnesium) and enhancing the vitamin D activation process in humans. These discoveries led to the hypothesis of using boron both in the prevention of osteoporosis and in the treatment of osteoarthritis. Although, studies assessing these purposes are at preliminary stages, reports are promising [12].

It was found that boron is located almost entirely and exclusively within the mineral portion of bone. Boron is suggested to affect bone mineral by influencing serum steroid hormone levels (estrogen and testosterone) and the metabolism and utilization of calcium and other mineral elements of bone. Some studies suggest that calcium fructoborate, when administered orally, is effective in reducing discomfort and stiffness associated with osteoarthritis disorders, and bone loss [13].

Calcium fructoborate is sugar-borate ester which is a complex of calcium, fructose, and boron found naturally in fresh and dried fruits, vegetables and herbs, and wine [14].

A growing number of researches indicate that the calcium fructoborate significantly reduces serum levels of the C-reactive protein in humans, suggesting that it may contribute to bone health by controlling the inflammation associated with loss of bone mineral density [14].

In one study which was performed on 53 postmenopaus-

al women aged 55–60 living in Turkey, where the subjects are naturally exposed to high (≥ 1 mg/L) or low (< 1 mg/L) boron concentration in drinking water, it was detected that serum concentration of osteocalcin, a sensitive and specific indicator of osteoblast function, together with dietary boron may play a role in bone metabolism. According to this study, daily boron intake of 1 mg/L and more through drinking water may affect bone metabolism in postmenopausal women positively [15].

Chronic and granulomatous inflammation (including that associated with osteoarticular diseases) was decreased in a rat model through the combination of boron with dexamethasone [16].

Inadequate boron intake is involved in inflammatory processes, including joint swelling, restricted movement, as well as body temperature, antibody production, blood hemostasis, serine protease (which is linked to platelet aggregation), activity of lipoxygenase (an enzyme that helps control inflammation), and metabolism of leukotrienes, chemical mediators of inflammation [17].

Below will be described the boron role in preventing osteoarticular diseases, such as osteoarthritis and rheumatoid arthritis. Its implication in osteoporosis will be avoided because this disease is multifactorial, and the role of boron is difficult to follow.

Boron and osteoarthritis

Osteoarthritis is a chronic disease that involves progressive destruction of articular cartilage which results in impaired joint motion, severe pain, and, ultimately, disability. This disease affects mostly elderly people [18].

Alongside with nonpharmacological interventions (weight loss, education programs, exercise, and so on) and pharmacological treatments (paracetamol, nonsteroidal anti-inflammatory drugs [NSAIDs], nutraceuticals and functional foods could provide an advantageous alternative. These nutraceuticals and functional foods that contain boron may have a beneficial effect in osteoarthritis too [18].

Joint discomfort is a common complaint in osteoarthritis which is associated with limited joint function, decreased feelings of energy and decreased quality of life. Pietrkowski Z. et al. reported, after conducting placebo-controlled clinical study on 60 participants with self-reported knee discomfort, that supplementation with 110 mg calcium fructoborate twice per day was associated with improving knee discomfort during the 2 weeks of intake [19].

Another study has shown that boron levels, along with those of lead and zinc, were reduced in patients with osteoarthritis of the hip when those patients went for hip replacement. Also, the level of demineralization in the osteoarthritis patients is greater than in those who don't suffer from this disease [20]. So, boron key role played in the chemical make-up of bones and joints through its effects on calcium metabolism is very important fact for prevention and treatment of osteoarthritis [21].

Naza M. A. et al. released a clinical evaluation and measurement of serum boron concentration, erythrocyte sedi-

mentation rate and total white blood cell count of 43 patients with knee OA. The results were compared with those of healthy individuals. After these, the authors concluded that serum boron levels were significantly lower in patients with knee OA, and negatively correlated with the duration and severity of the disease [22].

Another study researched the influence of calcium fructoborate (commercially marketed under the trade name FruiteX-B®) on symptoms associated with OA conditions. In this study, calcium fructoborate was tested for fourteen days at a serving of 108 mg twice a day on subjects diagnosed with minor osteoarthritis conditions of the knees by CT scan. Blood level of C-Reactive Protein in 7 out of 10 subjects was found reduced up to 37% compared to day 1 baseline levels. Also, the study showed that blood level of endogenous 1.25(OH) vitamin D was increased more than 19% compared to baseline [23].

In a double-blind study conducted in Australia, 20 patients with confirmed osteoarthritis were given a placebo or a supplement providing 6 mg of boron daily for 8 weeks; 15 patients completed the study. Of the 7 patients consuming the boron supplement, 5 reported improved subjective measures for their arthritic condition (e.g., less pain on movement), whereas only 1 of 8 patients consuming the placebo reported an improvement in their arthritic condition [24].

In two clinical cases which were presented by Hesselink J. M. and Russell A. L. in order to reveal the role of boron salts (fructoborate) in the treatment of symptoms in osteoarthritis was demonstrated the effectiveness of boron in treating the pain of osteoarthritis to a level of good control and that when taken long term it prevents exacerbations of pain [25].

Following the USA nutritional protocol for osteoarthritis, for patients it is recommended a boron supplementation of 6 mg of B a day [26].

Boron and rheumatoid arthritis

Rheumatoid arthritis (RA) is a common, systemic autoimmune disease of unknown cause that primarily affects the peripheral joints in a symmetric pattern. It is characterized by chronic inflammation of the synovial joints which can lead to progressive joint destruction including symmetric joint swelling with stiffness, warmth, tenderness and pain and affects approximately 1-2% of the general population worldwide [27].

Trace elements may play a critical role in the onset, progress and curing of the disease. Some studies have reported reduced serum selenium, magnesium, zinc, elevated serum copper in RA patients. A cross sectional study which enrolled 107 RA patients and 214 controls found a significant low serum boron level in patients with rheumatoid arthritis. Rheumatoid factor titer was significant predictor of low serum boron level. This may suggest that boron element may play a role in pathophysiology of RA and its severity and a supplementation with boron element and diets rich in fruits, vegetables, nuts, and pulses may be useful [27].

Following the results of a double-blind randomized pla-

cebo-controlled clinical trial with 60 days supplementation period with calcium fructoborate and sodium tetraborate for 72 Iraqi patients with active rheumatoid arthritis (RA) maintained on etanercept, boron as an adjuvant has potentiated therapeutic outcomes in RA patients by improvement of the clinical scores and significantly decreases the inflammatory markers in RA patients [28].

The safety of boron supplements when used in pharmacological doses as adjuvant with etanercept in treatment of RA patients was studied and the results showed that boron supplements – calcium fructoborate and sodium tetraborate have no negative impact on erythrocyte sedimentation rate, hemoglobin, white blood cells, platelets count, hepatic and renal functions [29].

Although the role of boron in functioning of osteoarticular system has been investigated in numerous studies, at this moment more research at this subject is needed in order to recommend boron as an essential trace mineral for bones, joints and human body in general.

Following this aim, the next step is to study the link between different boron concentrations in drinking water from the different regions of the Republic of Moldova and osteoarticular morbidity (by osteoarthritis and rheumatoid arthritis) of the population.

Conclusions

1. Boron can enter the human body in an organic and inorganic form. The organic plant based boron compounds are highly bioavailable.

2. In the functioning of the osteoarticular system boron acts by regulation of mineral metabolism (such as calcium and magnesium), enhancing the vitamin D activation process and influencing serum steroid hormone levels.

3. A boron intake equal to or higher than 3 mg per day can help prevent/or correct arthritis, osteoporosis and osteoarthritis.

4. Boron, especially calcium fructoborate, can reduce pain, joint discomfort and increase endogenous vitamin D level in patients with osteoarthritis.

5. Boron may play a role in pathophysiology of rheumatoid arthritis and its severity and a supplementation with boron element may be useful.

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Authors' contribution

MVR designed the trial and drafted the first manuscript; IRS and IP interpreted the data and revised the manuscript critically. The authors revised and approved the final version of the manuscript.

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Ethics approval and consent to participate

No approval was required for this study.

Conflict of Interests

The authors declare no conflict of interests.

