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Effects of thirty elements on bone metabolism

Michael Dermience[a,*], Georges Lognay[a], Françoise Mathieu[b], Philippe Goyens[b,c]

[a] University of Liège – Gembloux Agro Bio Tech, Unit Analyzes, Quality, Risks, Laboratory of Analytical Chemistry, Passage des Déportés, 2, B-5030 Gembloux, Belgium
[b] Kashin–Beck Disease Fund asbl-vzw, Rue de l'Aunee, 6, B-6953 Forrieres, Belgium
[c] Department and Laboratory of Pediatric, Free Universities of Brussels, Brussels, Belgium

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ABSTRACT

The human skeleton, made of 206 bones, plays vital roles including supporting the body, protecting organs, enabling movement, and storing minerals. Bones are made of organic structures, intimately connected with an inorganic matrix produced by bone cells. Many elements are ubiquitous in our environment, and many impact bone metabolism. Most elements have antagonistic actions depending on concentration. Indeed, some elements are essential, others are deleterious, and many can be both. Several pathways mediate effects of element deficiencies or excesses on bone metabolism. This paper aims to identify all elements that impact bone health and explore the mechanisms by which they act. To date, this is the first time that the effects of thirty minerals on bone metabolism have been summarized.

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* Corresponding author.
E-mail addresses: m.dermience@ulg.ac.be (M. Dermience), georges.lognay@ulg.ac.b (G. Lognay), francoise.mathieu@kbdfund.org (F. Mathieu), pgoyens@ulb.ac.be (P. Goyens).

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1. Introduction

The human skeleton is made of 206 bones. It plays several essential roles in the human body, including providing support, protecting vital organs, allowing movement, and storing minerals. Bones contain both organic and inorganic components. Organic components comprise osteoblasts, osteoclasts, osteocytes, the organic matrix (fibrous proteins), globular proteins (osteonectin and osteocalcin), and ground substances (proteoglycans and glycoproteins). The organic matrix confers flexibility and strength to bones. The inorganic fraction, 65% of total bone weight, is comprised of hydroxyl apatite, which confers hardness and rigidity. Bones also contain small amounts of minerals and trace elements, which can be essential or toxic, depending on concentrations [1].

The main objective of this review is to provide an overview of the effects of elements on bone metabolism and bone health. Thirty elements, known to impact bone metabolism, bone health, osteogenesis, and homeostasis and those used as anti-osteoporosis drugs, were reviewed. Because beneficial and adverse effects can depend on very narrow concentration ranges, elements are listed in alphabetical order and not grouped by mechanism of action. Majors elements (C, H, O, N), as well as sulfur as not been discussed in this review. It also does not include quantitative information, including it would require consideration of aspects as divergent as dietary intake, supplements, toxicological threshold, and pharmacological doses. Readers interested in quantitative values related to dietary intakes or supplements are referred to World Health Organization (WHO) (http://www.who.int/nutrition/publications/all_documents/en/). The national recommendations from the Workshop Summary of the National Research Council on dietary reference intakes [2] provide exhaustive recommendations for many elements, depending on age and gender. For a reference on bone mineral trace element content, the reader is referred to [3], which lists bone composition of 59 elements, according to age and gender.

2. Impacts of thirty minerals on bone metabolism

2.1. Aluminium

Aluminium, an element widely distributed on earth, has a negative impact on bone health. Aluminium negatively affects collagen synthesis, inhibits bone formation, and impairs bone remodeling, which can lead to adynamic bone disease, a variety of renal osteodystrophy, and osteomalacia [4–7]. The deleterious impacts of aluminium are exacerbated when calcium and magnesium are deficient [8,9]. Despite low bioavailability, 60% of aluminium stored in the body is in bones, which increases its half-life and makes toxicity cumulative [6,8]. Despite strong affinity for bone, aluminium has not been correlated with occurrence or extent of osteoporosis and does not seem to play a role in etiology [10,11].

Adverse effects of aluminium are exerted through multiple pathways, affecting bone mineralization, cell number, and cell activities. At the intestinal level, [12] reported that chronic exposure to aluminium reduced absorption of inorganic phosphorus and promoted bone accretion. In contrast, Zafar et al. [9] reported decreased calbindin (CaBP)-D9k expression, a gene coding for a protein that mediates transport of calcium through the enterocyte barrier, and lower calcium deposition in bone. How aluminium reduces synthesis of calcium-binding proteins is not known, but it may be involved in renal production of calcitriol (1α,25-Dihydroxycholecalciferol) [9,12]. However, there is no doubt that the deposition of aluminium on the mineralization front induces physiochemical changes that disturb calcium accretion and enhance calcium release (Table 1).

Several studies revealed that toxicity of aluminium in osteoblasts and osteoclasts is caused by inhibition of proliferation and cellular activities [6,9,13]. The mechanisms are not clear, although they seem to be closely related to parathyroid function. An experimental study suggested a direct toxic action of aluminium on osteoblasts [14]. In addition to this direct action, aluminium is known to decrease parathyroid function by accumulating in the gland and elevating serum calcium levels [15]. Rats fed high levels of aluminium also presented with decreased calcitonin, osteocalcin, procollagen carboxy-terminal propeptide, and bone alkaline phosphatase levels [5].

At this stage of our knowledge, no doubt that aluminium negatively impacts bone metabolism. Human observations, animal testing, and in vitro experimentations, all conclude in deleterious effects of aluminium. However, the different pathways by which it acts are still to be cleared.

2.2. Arsenic

Arsenic is both essential and toxic. Essential roles are associated with methionine metabolism, and phosphorylation. However, deprivation of arsenic in rat and hamster models showed no pathological effects on bone metabolism [16–18] except depressed growth [19]. However, other work in rats watered with a solution of arsenic (0.21 mg/kgb.w./day for 45 days) showed inhibition of endochondral ossification [20], suggesting possible adverse effects on bone metabolism. Despite conflicting results, recommended intakes extrapolated from animal experiments are very low, ranging from 12 to 25 μg/day, and no human deficiency has ever been reported [21].

To investigate the effects of arsenic trioxide, which is used in tumor treatment, Hu et al. [22] conducted an in vivo study on bone remodeling and osteoblast metabolism. Rats received intraperi-