Review

# The Role of Magnesium Ions in Bone Formation and Regeneration: A Comprehensive Review

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**Abstract**

Magnesium ions play a pivotal role in bone formation and regeneration, influencing various cellular and molecular mechanisms. This comprehensive review aims to elucidate the multifaceted role of magnesium ions in bone health. The article explores how magnesium is involved in bone formation, its contributions to bone regeneration, its impact on molecular mechanisms, and its applications in orthopaedic implants. An in-depth analysis of existing research provides valuable insights into the potential therapeutic applications of magnesium in bone-related disorders, shedding light on future directions for medical interventions.

**Keywords:** Magnesium, Bone remodeling, Bone regeneration, Osteogenesis, Good health and well-being.

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**How to cite this article:** Janani S P, The Role of Magnesium Ions in Bone Formation and Regeneration: A Commprehensive Review. Int J Clinicopathol Correl. 2023;7:2:34-37.
**Submitted:** 31-Oct-2023 **Revised:** 21-Nov- 2023 **Accepted:** 28-Nov-2023 **Publishesd:**09-Dec-2023

## Introduction:

Magnesium is the fourth most abundant mineral in the human body and is predominantly found in bones, constituting approximately 1% of the bone's weight.(1) This unassuming mineral plays a crucial role in bone metabolism, and its deficiency can lead to a spectrum of skeletal disorders, making it essential to understand how magnesium is involved in bone formation and regeneration. Magnesium ions, while often overshadowed by their more celebrated counterparts like calcium and phosphorus, have recently emerged as key players in the orchestration of bone development and repair. They have been found to affect various cellular functions and signaling pathways related to bone growth and healing.(2) Understanding the mechanisms through which magnesium ions influence osteogenesis is essential for developing innovative approaches to enhance bone regeneration and improve the effectiveness of orthopedic implants.

## The Role of Magnesium in Bone Metabolism:

Magnesium is not merely a passive occupant in the body's skeletal storehouses; it is, in fact, an active participant in the dynamic realm of bone metabolism. The fundamental significance of magnesium in bone health lies in its dual functions as a structural component and a regulatory ion. While calcium predominantly lends its strength to the bone's structural integrity, magnesium plays an integral role in ensuring the proper utilization of calcium in bone tissues. Magnesium ions govern


DOI: 10.56501/intjclinicopatholcorrel.v7i2.926.

several aspects of bone metabolism and can be considered the conductors of a harmonious symphony of cellular processes that culminate in bone formation and regeneration.(3)

One of the primary roles of magnesium is its contribution to osteoblast differentiation and activity. Osteoblasts, the bone-forming cells, play a pivotal role in synthesizing the organic matrix and facilitating the mineralization of bone tissue. Magnesium serves as a cofactor for numerous enzymes involved in osteoblast differentiation, enabling these cells to mature and function effectively. Without sufficient magnesium, osteoblasts may become dysfunctional, jeopardizing the quality and quantity of bone formed. (4)

Furthermore, magnesium's impact extends to the mineralization phase of bone formation. The mineralization of bone involves the deposition of hydroxyapatite crystals, a calcium-phosphate complex, which fortifies the bone's structure. Magnesium exerts its influence over bone health by regulating the secretion and function of parathyroid hormone (PTH). (1) PTH, a hormone secreted by the parathyroid glands, is instrumental in maintaining calcium balance in the body. When calcium levels drop, PTH is released, triggering the release of calcium from bones to restore the body's calcium levels. Magnesium plays a vital role in modulating the secretion and activity of PTH, ensuring that calcium is regulated optimally.(5) Imbalances in magnesium can disrupt PTH function, resulting in increased bone resorption and decreased bone density. This dysregulation is a hallmark of osteoporosis, a condition characterized by weakened bones prone to fractures.

**How Does Magnesium Take Part in Bone Regeneration?**

Bone regeneration is an ongoing process that involves the repair and remodeling of bone tissue, and magnesium is equally critical in this phase. Inflammation and Immune Response: Magnesium helps modulate the immune response and reduce inflammation, crucial for the initial stages of bone repair. This anti-inflammatory effect promotes an optimal environment for bone healing.(6)

Collagen Synthesis: Magnesium is involved in collagen synthesis, a key component of the bone's organic matrix. This strengthens the bone structure during regeneration.

**The Importance of Bone Healing**

Bone fractures are common injuries that often require surgical intervention for proper healing. Traditional orthopedic implants made of permanent metals like titanium and stainless steel have been widely used due to their mechanical strength and biocompatibility. However, these non-biodegradable materials carry the risk of long-term complications and may necessitate additional surgery to remove the implants. (7)This limitation has sparked interest in biodegradable alternatives such as magnesium.

**The Biodegradability of Magnesium**

Magnesium is a biodegradable material that naturally degrades within the human body. This property makes it an attractive option for fabricating orthopedic implants. Several in vivo studies have observed bone healing and new bone formation around implanted magnesium devices, demonstrating their potential in promoting bone regeneration.(8) However, the specific

mechanisms underlying the effects of magnesium ions on osteogenesis remain unclear

## Magnesium Ions and Osteogenic Signalling Pathways

To ensure the safe use of magnesium-based implants and enhance control over the osteogenic outcome, it is crucial to understand the cellular responses and downstream effects induced by corroding magnesium. A doctoral dissertation conducted at the University of Pittsburgh investigated the role of magnesium ions (Mg2+) in bone marrow space and their impact on osteogenic signaling pathways. The study utilized multipotent human bone marrow stromal cells (hBMSCs) to demonstrate the activation of Mg2+-induced osteogenic signaling cascades. Osteogenic gene screenings using qPCR arrays were performed to identify potential signaling pathways regulated by Mg2+. The results revealed significant modulation of canonical Wnt/β-catenin, HIF/COL10, and PKC signaling pathways in response to Mg2+.(9)

## Advancing the Use of Magnesium-Based Implants

This research contributes to the scientific understanding of the mechanisms through which magnesium implants promote bone formation and fracture healing. It provides valuable insights into the cellular responses and downstream effects induced by magnesium ions, paving the way for the development of more effective magnesium-based orthopedic devices.

The findings offer opportunities to advance the use of magnesium-based implants in therapeutic applications and improve patient outcomes. By harnessing the potential of magnesium ions and their influence on osteogenic signaling pathways, researchers and clinicians can explore innovative approaches to enhance bone regeneration and improve the success rates of orthopedic procedures. (6,10)

## Future Directions and Implications

The study discussed the importance of further research to fully elucidate the complex interactions between magnesium ions and bone regeneration. Understanding the specific mechanisms by which magnesium influences osteogenesis will enable the design of tailored implant materials and delivery systems that precisely control the release of magnesium ions. This level of control is crucial for optimizing bone healing processes and achieving superior clinical outcomes.

Additionally, the investigation highlighted the need for continued exploration of related pathways and signaling cascades to expand our knowledge of the broader mechanisms involved in bone formation and regeneration. Understanding the interplay between magnesium ions and other factors, such as growth factors and cytokines, could unveil new avenues for enhancing bone healing and tissue regeneration.

In conclusion, the role of magnesium ions in bone formation and regeneration is a promising area of research with significant implications for orthopedic medicine. The biodegradability of magnesium and its ability to influence osteogenic signaling pathways make it an attractive material for orthopedic implants. By further investigating the mechanisms and cellular responses associated with magnesium-induced osteogenesis, researchers can

unlock new possibilities for improving bone healing and developing innovative solutions for orthopedic treatments.

Conflict of Interest: NIL
Source of Funding: NIL

Acknowledgment: The authors were grateful to thank the institution for their cooperation in completing the Review

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