**Introduction**

Bone is a dynamic tissue which provides mechanical support for stature and locomotion, protects vital organs, and acts as a mechanical organ which controls mineral homeostasis. In order to carry out these important functions, bone is subjected to modeling and remodeling processes. Bone modeling is responsible for both the growth and the mechanical adaptation of the bone. Conversely, bone remodeling involves the removal of old or damaged bone tissue, a process that is mediated by osteoclasts (bone resorption) and subsequent replacement of new bone formed, which is mediated by osteoblasts (bone formation).

Physiological bone remodeling requires a tight coupling between bone resorption and bone formation to maintain the equilibrium and to guarantee that there is no alteration in bone mass or quality after each remodeling cycle. The remodeling process takes place within functionally and anatomically distinct sites termed basic multicellular units. These basic multicellular units require a strictly coordinated and synchronized action of the main types of bone cells: bone-lining cells, osteocytes, osteoblasts and osteoclasts. Moreover, a balance between bone resorption and bone remodeling is controlled by different molecular mechanisms, such as multiple signaling pathways. Nonetheless, an increase in osteoclast activity may occur under certain bone pathological conditions, so therapies that inhibit osteoclast, such as bisphosphonates, are effective at preventing bone loss. Therefore, these drugs are exploited in the development of new therapies for osteoporosis and other metabolic bone diseases.

The aims of this review are:

- To discuss in depth the cellular and molecular mechanisms of bone remodeling.
- To confirm and understanding of the cellular and biochemical effects that bisphosphonates could have into bone cells.

**Basic Multicellular Units**

**Osteoblast**

- **Role of connexin 43 hemichannels (Cx43) and Wnt/J-catenin signaling pathway in osteocyte function and viability:** Expression of Cx43 in osteocytes is regulated by β-catenin, which has been shown to bind to Cx43 promoter, stimulating Cx43 expression and functional gap junctions between osteocytes. Therefore, the expression of Cx43 and Wnt/J-catenin signaling pathway play a role not only in osteocyte viability in response to shear stress or loading, but also in osteocyte apoptosis, so that their absence leads to cell apoptosis. In this sense, osteocytes apoptosis positively regulate osteoclast function and differentiation, and the same parameters are negatively regulated in osteoblasts by osteocytes.

**Osteocyte**

- **Mechanism of action on osteoclasts:**
  1. Preferential binding into mineral surface of the bone
  2. Concentration in areas of active remodeling
  3. Internalization (endocytosis) into cytoplasm of osteoclasts by bone-resorbing osteoclast by endocytosis
  4. Release into the cytosol of osteoclasts
  5. Biochemical effect: inhibition of prenylated Rab GTTPases
  6. Cellular effect: osteoclast’s inactivation or apoptosis

**References**