

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Strontium ranelate is an agonist of the calcium-sensing receptor, which mediates its effects on osteoblasts

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Strontium ranelate is proposed as a preventive and curative treatment of osteoporosis that reduces the risk of both vertebral, nonvertebral, and hip fractures in postmenopausal women. Strontium ranelate has been shown to reduce bone resorption by osteoclasts, and to stimulate bone formation by osteoblasts (OBs), rebalancing bone turnover in favor of bone formation.

This study is aimed at exploring the cellular mode of action of strontium ranelate, especially through the involvement of the extracellular calcium-sensing receptor (CaR), a G protein-coupled receptor first cloned from parathyroid gland also expressed in many other tissues including bone (in OBs and osteoclasts). Strontium ranelate has been shown to reduce osteoclast differentiation and activity, and to stimulate cellular proliferation of pre-OBs, leading to an increased number of OBs, thereby enhancing matrix deposition and bone tissue formation. The CaR has been shown to be expressed in several osteoblastic cell lines and in osteoblasts and their precursors in intact bone. The goal of this study [1] was to evaluate the capacity of strontium ranelate to directly activate the CaR, as assessed by measuring the activation of phospholipase C (PLC), elevation in the cytosolic-free calcium concentration (Ca_i^{2+}), accumulation of inositol phosphates (IPs) and activation of a nonselective cation channel (NCC) in human embryonic kidney (HEK293) cells transfected with the bovine CaR. The results indicate that strontium ranelate is an agonist of the CaR. The role of the CaR in mediating the stimulatory action of strontium on cell proliferation was then examined in rat primary osteoblasts (POBs). The results show that strontium ranelate increases cell proliferation as well as the expression of immediate early genes associated with cell proliferation, and that expression of the functional CaR is required for mediating these effects.

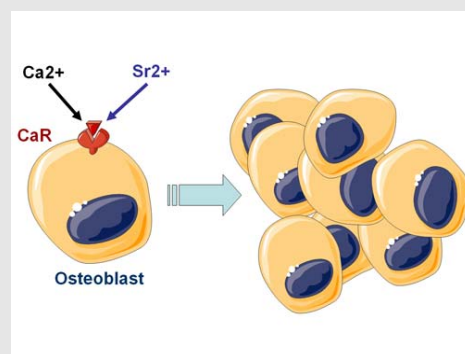
In conclusion, strontium ranelate is an agonist of the CaR in osteoblasts and, therefore, the anabolic effect of strontium ranelate on bone in vivo could be mediated by the CaR.

1. Chattopadhyay N et al. *Biochem Pharmacol.* 2007;74:438-447.

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Osteoblasts and their precursors express at their membrane the calcium-sensing receptor which binds calcium and signals into the cell. Strontium has the ability to bind to the calcium-sensing receptor. Strontium binding results in intracellular signaling and osteoblast proliferation.

In conclusion, strontium ranelate is an agonist of the CaR in osteoblasts and, therefore, the anabolic effect of strontium ranelate on bone in vivo could be mediated, by the CaR.



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