

[Miner Electrolyte Metab.](#) 1985;11(1):5-13.

Effect of low doses of stable strontium on bone metabolism in rats.

[Marie PJ](#), [Garba MT](#), [Hott M](#), [Miravet L](#).

The effects of low doses of oral **stable strontium (0.19-0.40% of strontium chloride)** on mineral and bone metabolism were examined in normal rats using biochemical and histomorphometrical methods.

The strontium levels in serum and bone rose according to the intake of the element. Oral strontium supplementation did not produce deleterious effects on body growth or on mineral homeostasis except a transitory slight decrease in serum calcium. At the dosage level of 0.40% however, strontium induced a slight defective bone mineralization. At lower levels, treated rats showed stimulated bone formation evidenced by increased amount of osteoid and increased extent of tetracycline double-labelled surface while the mineralization lag time remained normal.

The osteoclastic surface and the number of acid phosphatase-stained chondroclasts and osteoclasts remained unchanged. Stimulation of bone formation without apparent change in bone resorption resulted in a 10% increase in the trabecular calcified bone volume.

The strontium-induced increased osteogenesis **was not associated** with changes in circulating levels of 1,25(OH)₂ **vitamin D** or in **parathyroid hormone** effects.

The results show that small doses of oral strontium may stimulate bone formation without altering bone resorption in the rat.

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[Metabolism.](#) 1986 Jun; 35(6):547-51.

Short-term effects of fluoride and strontium on bone formation and resorption in the mouse.

[Marie PJ](#), [Hott M](#).

The early effects of sodium fluoride (0.80 mg/kg/d) and **strontium chloride** (0.27%) given alone, or in combination in drinking water, on bone metabolism were examined in the mouse using dynamic histomorphometric methods.

Four weeks of oral strontium supplementation increased the osteoid surface and reduced the number of acid phosphatase-stained osteoclasts. However the trabecular calcified bone volume was not augmented. By contrast, short-term treatment with fluoride produced a rapid stimulatory effect on bone formation at a dose that did not affect the bone mineralization rate. Four weeks of fluoride

supplementation induced a rapid 21.1% increase in the osteoblastic surface and a 26.3% stimulation of the bone matrix apposition rate evaluated by the double tritiated proline labelling method, which resulted in a 29% increase in the amount of osteoid.

This rapid stimulation of the bone formation rate without detectable change in osteoclastic bone resorption led to a 12% increase in the trabecular calcified bone density.

This study **shows that fluoride and strontium produce distinct early effects on bone formation and resorption in the mouse** and that fluoride exerts a rapid stimulatory effect on the bone matrix synthesis rate through an augmentation of the number of bone-forming cells.

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[Bone.](#) **1990**;11(5):313-9.

Effects of low doses of strontium on bone quality and quantity in rats.

[Grynepas MD](#), [Marie PJ](#).

Mount Sinai Research Institute, Toronto, Canada.

Strontium (Sr) has been shown to increase bone mass when given at low doses. In this study, the diets of rats containing 0.50% calcium were supplemented with **Sr (0.19 and 0.40% of SrCl₂ orally) for periods of four and eight weeks.**

Long bones and vertebrae were studied by density fractionation and each fraction was analyzed chemically. X-ray diffraction was used to determine crystal size. Static and dynamic histomorphometric parameters of bone formation were also measured. We found a shift towards lower density in the mineralization profiles of Sr supplemented rats (0.40%), as well as a decrease in bone crystal size at the larger dose of Sr. The CO₃ content and the Ca/Sr ratio of the bone decreased with increasing Sr content.

We found an increase in the vertebral trabecular bone volume together with an increase in osteoid volume in Sr supplemented rats.

This study **shows that Sr at the larger dose induces bone hypomineralization as well as an increase in bone mass in rats** fed a relatively low calcium diet.

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An uncoupling agent containing strontium prevents bone loss by depressing bone resorption and maintaining bone formation in estrogen-deficient rats.

[Marie PJ](#), [Hott M](#), [Modrowski D](#), [De Pollak C](#), [Guillemain J](#), [Deloffre P](#), [Tsouderos Y](#).

INSERM Unité 349, Hôpital Lariboisière, Paris, France.

Trabecular bone loss in estrogen deficiency is associated with enhanced bone resorption with a smaller increase in bone formation. We previously reported that low doses of strontium can increase trabecular bone volume in rodents by affecting bone resorption and formation.

In this study we **determined the effect of a new divalent strontium salt (S12911)** on bone loss induced by E2 deficiency. Sprague-Dawley female rats (230 g, n = 15-25 per group) were sham operated or ovariectomized (OVX) and treated with 17 beta-estradiol (E2, 10 micrograms/kg/day, sc) or S12911 by gavage at the dose of 77, 154, or 308 mg/kg/day or the vehicle.

Treatment for 60 days with S12911 resulted in a dose-dependent increase in plasma, urine, and bone strontium concentrations without any deleterious effect on total or skeletal growth. OVX rats were osteopenic compared to sham rats as shown by decreased femoral dry bone weight and mineral content measured on bone ash and by DXA. Treatment of OVX rats with S12911 prevented bone loss as bone ash and bone mineral content were restored to the values in sham rats. Trabecular bone volume measured by histomorphometry on the tibial metaphysis was decreased by 46% in OVX rats and was corrected by E2.

Treatment of OVX rats with S12911 increased the trabecular bone volume by 30-36%. Histomorphometric indices of bone resorption (osteoclast surface and number) were increased in OVX rats and were reduced by S12911 to the levels in sham rats. (ABSTRACT TRUNCATED AT 250 WORDS)

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Strontium increases vertebral bone volume in rats at a low dose that does not induce detectable mineralization defect.

[Grynpas MD](#), [Hamilton E](#), [Cheung R](#), [Tsouderos Y](#), [Deloffre P](#), [Hott M](#), [Marie PJ](#).

Department of Pathology, University of Toronto, Canada.

Low doses of strontium and fluoride were shown to increase bone formation and trabecular bone density in rodents. To assess whether strontium or fluoride affect the quality of the mineral at doses known to increase bone density, **we have**

determined the effects of low doses of strontium and fluoride on bone formation and bone mineral characteristics in rats.

Adult rats were given **strontium alone (0.20%)**, fluoride alone (1 mg/kg per day), or the combined treatment for 8 weeks. Strontium levels in serum and femur were similar in groups treated with strontium alone or in combination, being about 5% of calcium levels.

Biochemical and neutron activation analyses in femur showed that **calcium and magnesium contents did not differ in the four group of rats**, suggesting that strontium was incorporated in the apatite lattice of the bone minerals in the strontium-treated rats.

The mineralized **bone volume was significantly increased by 17%** in the strontium-treated group, by **20% in the fluoride-treated group**, and by **19% in rats given with the combined treatment**. This was associated with increased osteoid surface, osteoblast surface, and double tetracycline labeled surfaces in the strontium-treated and fluoride-treated groups, showing that the number of bone forming sites was increased.

However, the mineral apposition rate, the osteoid thickness, and the mineralization lag time were similar in controls and treated groups, reflecting the lack of deleterious effects of low doses of strontium and fluoride on bone mineralization.

The density fractionation analysis measured in the femur also **showed that neither strontium, nor fluoride at the low doses used, significantly altered the mineralization profile**.

The results indicate **that treatment with low doses of strontium or fluoride increase the number of bone forming sites and vertebral bone volume in rats**, but does **not have detectable adverse effects** on the mineral profile, bone mineral chemistry or bone matrix mineralization.

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