AOR CODE: AOR04161

Premium

Strontium Support II

Supports Bone Mineral Density

- Stimulates bone growth while slowing bone loss
- Reduces the risk of fractures
- Clinically effective dose & safe for long-term use

Gluten Free  Vegan  Non-GMO

Bone Health

AOR Code       Variant
AOR04161       60 VEGI-CAPS
AOR04204       120 VEGI-CAPS

Details
Strontium is an important mineral for bone health and it is found in most foods where calcium is found.

While supplements like calcium, vitamin D and vitamin K maintain bone health, and conventional bone drugs reduce bone degradation, strontium actually helps rebuild bone. It does this by increasing osteoblast production while decreasing osteoclast production, resulting in increased bone development and decreased bone loss. Since strontium is similar in molecular structure to calcium, it is thought to activate the calcium receptors in the bone, stimulating the building of new bone and telling the body to use calcium effectively in bone tissue, while inhibiting bone breakdown. A recently published study showed that strontium was not only safe to take over the course of 10 years, but also that it continued to reduce the risk of osteoporotic fractures throughout this time period. Strontium Support II is an excellent addition to calcium supplementation for those with osteoporosis or osteopenia, post-menopausal women or those at an increased risk of bone fractures.

In 2002, AOR introduced the world’s first supplemental strontium citrate for those with osteoporosis, osteopenia, post-menopausal women and those at an increased risk of bone fractures. AOR’s Strontium Support II comes in two sizes and provides an effective dose of this bone health powerhouse in a convenient two capsule-a-day formula.
Discussion
Strontium is a trace mineral which concentrates in the skeletal system, where it supports the function of osteoblasts (the cells which form new bone) while reducing the differentiation and activity of osteoclasts (the cells which resorb old bone). Strontium Support II™ helps support bone mineral density.

Product Variation

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<tr>
<th>Product Code</th>
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<tr>
<td>AOR04161</td>
<td>60 VEGI-CAPS</td>
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<tr>
<td>AOR04204</td>
<td>120 VEGI-CAPS</td>
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Supplements Facts

<table>
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<th>Serving Size: 1 Capsule</th>
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<tr>
<td>Strontium (from citrate)</td>
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Non-medical ingredients:


Guarantees

AOR™ guarantees that all ingredients have been declared on the label. Contains no wheat, gluten, corn, nuts, peanuts, sesame seeds, sulphites, mustard, soy, dairy, eggs, fish, shellfish or any animal byproduct.

Adult Dosage

Take 1 or 2 capsules daily on an empty stomach, at least two hours before or after consuming food, calcium or milk since these can significantly reduce strontium absorption if taken together. Ensure an adequate daily intake of calcium and vitamin D.

Cautions

May cause temporary transient increases in levels of creatine kinase that are unassociated with any disorder. Discontinue use and consult a health care practitioner in case of rash or hypersensitivity, as this may be a sign of a serious allergic reaction (DRESS or Stevens-Johnson syndrome). Consult a health care practitioner for use beyond 6 months. Pregnant and breastfeeding women, those who have or are at high risk for blood clots (e.g. if you are temporarily or permanently immobilized, over the age of 80, taking birth control pills, etc.), heart diseases and/or circulatory problems (e.g. Venous Thromboembolism (VTE), heart attack, peripheral arterial disease, stroke, high blood pressure, hyperlipidemia, diabetes, etc.), or have kidney disease must not use this product.

Source

Pharmaceutical synthesis

Main Application

Bone health
Osteoporosis

Osteopenia

Increases bone density

Reduces risk of fractures

**Disclaimer**

The information and product descriptions appearing on this website are for information purposes only, and are not intended to provide or replace medical advice to individuals from a qualified health care professional. Consult with your physician if you have any health concerns, and before initiating any new diet, exercise, supplement, or other lifestyle changes.

**Research**

**Background**

Age-Related Bone Loss

Bone loss accelerates suddenly in menopausal women because the drop in estrogen levels causes an increase in the resorption (teardown) of existing bone. But resorption is only half of the story. Age-related bone loss is also caused by a decrease in the formation of new bone tissue.

Strontium: The First Bone-Building Supplement!

Strontium is a mineral that is able to inhibit bone resorption while simultaneously stimulating bone growth. This effect appears to be due to strontium’s ability to actually increase the production of bone-building cells (osteoblasts) and decrease the production of bone-destroying cells (osteoclasts), shifting the balance toward bone growth. This is a remarkable benefit provided by taking strontium as a supplement, and no other natural substance or drug is known to provide this dual effect. People who are concerned about preserving and regaining healthy bones will certainly be interested in using a high quality strontium supplement. Strontium is a helpful nutrient in bone disorders like osteoporosis in that it builds new bone while maintaining bone quality, unlike current drugs on the market.

Strontium’s History

Strontium is a mineral found in most foods where calcium is found. Like the Strontium carbonate crystals (strontianite) from which it was first isolated, Strontium’s role in bone health was previously hidden in obscurity from the masses. However, research has long suggested that it may be an essential nutrient required for the normal development, structure, function, and health of the skeletal system. Clinical trials going back into the 1940s have supported this conclusion, but recent studies have provided evidence that it can offer unique nutritional support against the loss of bone structure and function.
Research

Strontium Ranelate

Most of the clinical studies that found strontium effective for reducing fractures and increasing bone density were done using strontium ranelate. This form of strontium is a prescription drug used in Europe with excellent results and minimal side effects. However, the “ranelate” portion of this salt form of strontium is inactive; only the strontium produces physiological benefits. The use of strontium ranelate allowed a patent to be developed to protect this amazing discovery.

Studies using other forms of strontium are few, but they do exist and also show pronounced effects against bone degeneration, showing that strontium is the important molecule.

In a study using strontium ranelate, BMD showed an increase continuously over 10 years in osteoporotic women. The incidence of vertebral and nonvertebral fracture was lowered between 5 and 10 years than in a matched placebo group over 5 years. Therefore, the results proved that Strontium ranelate’s antifracture efficacy appears to be maintained long term.

Another study investigated bone microstructure changes as a target in osteoporosis treatment to increase bone strength and reduce fracture risk. 83 postmenopausal women with osteoporosis were given a dosage of 2g per day of strontium ranelate for a two year period. The double-double blind exploratory trial observed both bone mineral density and bone turnover markers. Distal tibia bone microstructure was assessed by high-resolution peripheral quantitative computed tomography. Both density and bone thickness were shown to have increased throughout the treatment.

Strontium Citrate

A study that examined the effects of using strontium citrate in combination with other bone building nutrients in 158 adults provides compelling evidence that strontium citrate is effective at mitigating bone loss and stimulating new bone growth. Two groups of study participants agreed to follow an open-label bone-health supplement plan containing 680 mg of strontium citrate for six months after taking a DXA test of bone density, a 43-chemistry blood test panel and a quality of life inventory. Two weeks after the last subject completed, a second group of 58 was enrolled and followed the identical plan, but with a different bone-health supplement which also contained 682mg of strontium citrate.

There were no significant differences between the two groups in baseline bone mineral density (BMD) or in related BMD variables such as (age, sex, weight, percent body fat, fat mass, or fat-free mass). Both groups experienced a significant positive mean annualized percent change (MAPC) in BMD. Both groups also experienced a positive MAPC compared to baseline. The MAPC contrast between compliant and partially compliant subjects was significant for both plans. No clinically significant changes in a 43-panel blood chemistry test were found, nor were there any changes in self-reported quality of life in either group. Increased compliance was associated with greater increases in BMD in both groups. No adverse effects were reported in either group.

Calcium and Strontium: Take Both…

Calcium and Strontium can both play key roles in the health of your bones – if you use them properly. Animal studies suggest that Strontium is not effective if your calcium intake is not adequate and may even be counterproductive. Current “official” recommendations suggest an intake of 1000 milligrams
of calcium for younger adults, and 1200 milligrams for people over the age of 50. Some evidence suggests that a still higher intake (1300-1600 milligrams) of total dietary calcium is more effective for lowering fracture risk in the elderly.

...But Never Together!

At the same time, however, it’s important to take your Strontium supplement separately from your calcium supplements. This is because calcium and Strontium use the same pathways for absorption in the intestinal tract, so swallowing a calcium supplement along with your Strontium can dramatically reduce absorption. So obviously, putting Strontium and calcium in the same pill is a recipe for bone health disaster, in which you don’t get the benefits of either nutrient!

How To Take Your Strontium

The best protocol – and the one used in the most recent clinical trials – is to take your Strontium either three hours after your last meal of the day, or one hour before breakfast in the morning, or both. While before bed might be easiest, studies do suggest that one last dose of calcium just before bedtime can help prevent excessive resorption of bone overnight. It may therefore be best to take all of your Strontium 1-2 hours before breakfast, leaving you free to take a calcium supplement just before you go to bed.

Another option may be to take it at night if you get up to use the washroom. While it is not recommended to do so if you’re not awake already since a good sleep is also essential for bone health and healing, this might be a viable option for those who are already up during the night.

Market Trends

Current Bone Health Options

Existing drugs for treating osteoporosis work by reducing bone resorption. But they do not support the formation of new bone. These drugs reduce the rate of bone breakdown, but they do not help the body to build new bone tissue. In fact, within weeks of starting use of antiresorptive drugs like Fosamax,® the body’s formation of new bone actually decreases. After years of use of bisphosphonate drugs or even before starting, many people turn to natural bone health solutions because of the terrible side effects that bone drugs have a track record of causing.

Even supplements like calcium, vitamin D and vitamin K work by reducing bone resorption and increasing bone mineralization. While these nutrients are extremely important for good bone health, they do not actually rebuild bone; rather, they help maintain bone density.

AOR Advantage
In 2002, AOR was the first company in the world to produce supplemental strontium citrate. AOR’s Strontium Support II comes in two sizes or paired with MBP (see the Related Products section) and provides an effective dose of this bone health powerhouse in a convenient two capsule-a-day formula.

References


Skoryna, SC. Metabolic aspects of the pharmacologic uses of trace elements in human subjects with specific references to stable strontium. Trace Subst. Enviorn Health. 1984;18:3-23
Abstract

Accumulation of bone strontium measured by in vivo XRF in rats supplemented with strontium citrate and strontium ranelate.


Wohl GR, Chettle DR, Pejović-Milić A, Druchok C, Webber CE, Adachi JD, Beattie KA.

Strontium ranelate is an approved pharmacotherapy for osteoporosis in Europe and Australia, but not in Canada or the United States. Strontium citrate, an alternative strontium salt, however, is available for purchase over-the-counter as a nutritional supplement. The effects of strontium citrate on bone are largely unknown. The study’s objectives were 1) to quantify bone strontium accumulation in female Sprague Dawley rats administered strontium citrate (N=7) and compare these levels to rats administered strontium ranelate (N=6) and vehicle (N=6) over 8 weeks, and 2) to verify an in vivo X-ray fluorescence spectroscopy (XRF) system for measurement of bone strontium in the rat. Daily doses of strontium citrate and strontium ranelate were determined with the intention to achieve equivalent amounts of elemental strontium. However, post-hoc analyses of each strontium compound conducted using energy dispersive spectrometry microanalysis revealed a higher elemental strontium concentration in strontium citrate than strontium ranelate. Bone strontium levels were measured at baseline and 8 weeks follow-up using a unique in vivo XRF technique previously used in humans. XRF measurements were validated against ex vivo measurements of bone strontium using inductively coupled plasma mass spectrometry. Weight gain in rats in all three groups was equivalent over the study duration. A two-way ANOVA was conducted to compare bone strontium levels amongst the three groups. Bone strontium levels in rats administered strontium citrate were significantly greater (p<0.05) than rats administered strontium ranelate and vehicle. ANCOVA analyses were performed with Sr dose as a covariate to account for differences in strontium dosing. The ANCOVA revealed differences in bone strontium levels between the strontium groups were not significant, but that bone strontium levels were still very significantly greater than vehicle.

Effects of strontium on the quality of bone apatite crystals: a paired biopsy study in postmenopausal osteoporotic women.


Doublier A, Farlay D, Jaurand X, Vera R, Boivin G.

INTRODUCTION: The potential effect of strontium (Sr) on bone apatite crystals was investigated in
paired biopsies of osteoporotic women treated with either strontium ranelate (SrRan) or a placebo for 36 months.

METHODS: In ten paired biopsies, crystallinity, apparent length and width/thickness of crystals, interplanar distances, and lattice parameters of unit cells were assessed by X-ray diffraction and selected area electron diffraction.

RESULTS: All these parameters, reflecting crystal and unit cell characteristics, were not influenced by the presence of Sr and were similar in SrRan and placebo groups after 36 months of treatment. The mean rate of substitutions of calcium by Sr ions was 4.5 %.

CONCLUSION: Overall, the quality of bone apatite crystals was maintained after 36 months of treatment with SrRan.


BACKGROUND: Strontium ranelate is currently used for osteoporosis. The international, double-blind, randomised, placebo-controlled Strontium ranelate Efficacy in Knee Osteoarthritis triAl evaluated its effect on radiological progression of knee osteoarthritis.

METHODS: Patients with knee osteoarthritis (Kellgren and Lawrence grade 2 or 3, and joint space width (JSW) 2.5-5 mm) were randomly allocated to strontium ranelate 1 g/day (n=558), 2 g/day (n=566) or placebo (n=559). The primary endpoint was radiographical change in JSW (medial tibiofemoral compartment) over 3 years versus placebo. Secondary endpoints included radiological progression, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and knee pain. The trial is registered (ISRCTN41323372).

RESULTS: The intention-to-treat population included 1371 patients. Treatment with strontium ranelate was associated with smaller degradations in JSW than placebo (1 g/day: -0.23 (SD 0.56) mm; 2 g/day: -0.27 (SD 0.63) mm; placebo: -0.37 (SD 0.59) mm); treatment-placebo differences were 0.14 (SE 0.04), 95% CI 0.05 to 0.23, p CONCLUSIONS: Treatment with strontium ranelate 1 and 2 g/day is associated with a significant effect on structure in patients with knee osteoarthritis, and a beneficial effect on symptoms for strontium ranelate 2 g/day.

Efficacy and safety of strontium ranelate in the treatment of osteoporosis in men.


CONTEXT: Strontium ranelate reduces vertebral and nonvertebral fracture risk in postmenopausal osteoporosis.

OBJECTIVE: The objective of this study was to determine the efficacy and safety of strontium ranelate in osteoporosis in men over 2 years (main analysis after 1 year). Design: This was an international, unbalanced (2:1), double-blind, randomized placebo-controlled trial (MALEO [MALE Osteoporosis]).

SETTING: This international study included 54 centers in 14 countries. Participants: Participants were 261 white men with primary osteoporosis. Intervention: Strontium ranelate at 2 g/d (n = 174) or placebo (n = 87) was administered.

MAIN OUTCOME MEASURES: Lumbar spine (L2-L4), femoral neck, and total hip bone mineral density (BMD), biochemical bone markers, and safety were measured.

RESULTS: Baseline characteristics were similar in both groups in the whole population (age, 72.9 ± 6.0 years; lumbar spine BMD T-score, -2.7 ± 1.0; femoral neck BMD T-score, -2.3 ± 0.7). Men who received strontium ranelate over 2 years had greater increases in lumbar spine BMD than those who received placebo (relative change from baseline to end, 9.7% ± 7.5% vs 2.0% ± 5.5%; between-group difference estimate (SE), 7.7% (0.9%); 95% confidence interval, 5.9%-9.5%; P < .001). There were also significant between-group differences in relative changes in femoral neck BMD (P < .001) and total hip BMD (P < .001). At the end of treatment, mean levels of serum cross-linked telopeptides of type I collagen, a marker of bone resorption, were increased in both the strontium ranelate group (10.7% ± 58.0%; P = .022) and the placebo group (34.9% ± 65.8%; P < .001). The corresponding mean changes of bone alkaline phosphatase, a marker of bone formation, were 6.4% ± 28.5% (P = .005) and 1.9% ± 25.4% (P = .505), respectively. After 2 years, the blood strontium level (129 ± 66 ?mol/L) was similar to that in trials of postmenopausal osteoporosis. Strontium ranelate was generally well tolerated.

CONCLUSIONS: The effects of strontium ranelate on BMD in osteoporotic men were similar to those in postmenopausal osteoporotic women, supporting its use in the treatment of osteoporosis in men.

Biocompatibility and biodegradability of Mg-Sr alloys: the formation of Sr-substituted hydroxyapatite.


Bornapour M, Muja N, Shum-Tim D, Cerruti M, Pekguleryuz M.

Magnesium is an attractive material for use in biodegradable implants due to its low density, nontoxicity and mechanical properties similar to those of human tissue such as bone. Its biocompatibility makes it amenable for use in a wide range of applications from bone to cardiovascular implants. Here we investigated the corrosion rate in simulated body fluid (SBF) of a series of Mg-Sr alloys, with Sr in
the range of 0.3-2.5%, and found that the Mg-0.5 Sr alloy showed the slowest corrosion rate. The degradation rate from this alloy indicated that the daily Sr intake from a typical stent would be 0.01-0.02 mg day⁻¹, which is well below the maximum daily Sr intake levels of 4 mg day⁻¹. Indirect cytotoxicity assays using human umbilical vascular endothelial cells indicated that Mg-0.5 Sr extraction medium did not cause any toxicity or detrimental effect on the viability of the cells. Finally, a tubular Mg-0.5 Sr stent sample, along with a WE43 control stent, was implanted into the right and left dog femoral artery. No thrombosis effect was observed in the Mg-0.5 Sr stent after 3 weeks of implantation while the WE43 stent thrombosed. X-ray diffraction demonstrated the formation of hydroxyapatite and Mg(OH)₂ as a result of the degradation of Mg-0.5 Sr alloy after 3 days in SBF. X-ray photoelectron spectroscopy further showed the possibility of the formation of a hydroxyapatite Sr-substituted layer that presents as a thin layer at the interface between the Mg-0.5 Sr alloy and the corrosion products. We believe that this interfacial layer stabilizes the surface of the Mg-0.5 Sr alloy, and slows down its degradation rate over time.

Maintenance of antifracture efficacy over 10 years with strontium ranelate in postmenopausal osteoporosis.


INTRODUCTION: Strontium ranelate has proven efficacy against vertebral and nonvertebral fractures, including hip, over 5 years in postmenopausal osteoporosis. We explored long-term efficacy and safety of strontium ranelate over 10 years.

METHODS: Postmenopausal osteoporotic women participating in the double-blind, placebo-controlled phase 3 studies SOTI and TROPOS to 5 years were invited to enter a 5-year open-label extension, during which they received strontium ranelate 2 g/day (n = 237, 10-year population). Bone mineral density (BMD) and fracture incidence were recorded, and FRAX® scores were calculated. The effect of strontium ranelate on fracture incidence was evaluated by comparison with a FRAX®-matched placebo group identified in the TROPOS placebo arm.

RESULTS: The patients in the 10-year population had baseline characteristics comparable to those of the total SOTI/TROPOS population. Over 10 years, lumbar BMD increased continuously and significantly (P < 0.01 versus previous year) with 34.5 ± 20.2% relative change from baseline to 10 years. The incidence of vertebral and nonvertebral fracture with strontium ranelate in the 10-year population in years 6 to 10 was comparable to the incidence between years 0 and 5, but was significantly lower than the incidence observed in the FRAX®-matched placebo group over 5 years (P<0.05); relative risk reductions for vertebral and nonvertebral fractures were 35% and 38%, respectively. Strontium ranelate was safe and well tolerated over 10 years.

CONCLUSIONS: Long-term treatment with strontium ranelate is associated with sustained increases in BMD over 10 years, with a good safety profile. Our results also support the maintenance of antifracture efficacy over 10 years with strontium ranelate.
The effect of prior bisphosphonate therapy on the subsequent therapeutic effects of strontium ranelate over 2 years.


Middleton ET, Steel SA, Aye M, Doherty SM.

Many osteoporotic women prescribed strontium ranelate have previously received bisphosphonates. Prior bisphosphonate use blunted the spinal bone mineral density (BMD) response for 6 months. Hip BMD was blunted to a degree for 2 years, although there was an overall increase in hip BMD in contrast to the heel where BMD did not increase.

INTRODUCTION: Many osteoporotic women commenced on strontium ranelate have already received treatment with bisphosphonates. This study investigates whether prior bisphosphonate use impairs the subsequent therapeutic response to strontium ranelate.

METHODS: Women were recruited who were either bisphosphonate naïve or currently receiving a bisphosphonate. All women received strontium ranelate and were followed up for 2 years.

RESULTS: One hundred and twenty women were recruited. After 2 years, the bisphosphonate-naïve group had significant BMD increases of 8.9%, 6.0% and 6.4% at the spine, hip and heel, respectively. In the prior bisphosphonate group, BMD increased significantly at the spine (4.0%) and hip (2.5%) but not at the heel. At all time points at all sites, the BMD increase was greater in the bisphosphonate-naïve group. BMD at the spine did not increase during the first 6 months in the prior bisphosphonate group but then increased in parallel with the bisphosphonate-naïve group. In contrast, the difference between the two groups in hip BMD continued to increase throughout the 2 years. P1NP was suppressed in the prior bisphosphonate group for the first 6 months.

CONCLUSIONS: After bisphosphonate exposure, the BMD response to strontium ranelate is blunted for only 6 months at the spine. At the hip, a degree of blunting was observed over 2 years, although there was an overall increase in hip BMD in contrast to the heel where no increase in BMD was observed.

Effects of strontium ranelate and alendronate on bone microstructure in women with osteoporosis. Results of a 2-year study.


Rizzoli R, Chapurlat RD, Laroche JM, Krieg MA, Thomas T, Frieling I, Boutroy S, Laib A, Bock O, Felsenberg D.
Strontium ranelate appears to influence more than alendronate distal tibia bone microstructure as assessed by high-resolution peripheral quantitative computed tomography (HR-pQCT), and biomechanically relevant parameters as assessed by micro-finite element analysis (?FEA), over 2 years, in postmenopausal osteoporotic women.

INTRODUCTION: Bone microstructure changes are a target in osteoporosis treatment to increase bone strength and reduce fracture risk.

METHODS: Using HR-pQCT, we investigated the effects on distal tibia and radius microstructure of strontium ranelate (SrRan; 2 g/day) or alendronate (70 mg/week) for 2 years in postmenopausal osteoporotic women. This exploratory randomized, double-blind trial evaluated HR-pQCT and FEA parameters, areal bone mineral density (BMD), and bone turnover markers.

RESULTS: In the intention-to-treat population (n = 83, age: 64 ± 8 years; lumbar T-score: -2.8 ± 0.8 [DXA]), distal tibia Cortical Thickness (CTh) and Density (DCort), and cancellous BV/TV increased by 6.3%, 1.4%, and 2.5%, respectively (all P < 0.005), with SrRan, but not with alendronate (0.9%, 0.4%, and 0.8%, NS) (P < 0.05 for all above between-group differences). Difference for CTh evaluated with a distance transformation method was close to significance (P = 0.06). The estimated failure load increased with SrRan ( 2.1%, P < 0.005), not with alendronate (-0.6%, NS) (between-group difference, P<0.01). Cortical stress was lower with SrRan (P < 0.05); both treatments decreased trabecular stress. At distal radius, there was no between-group difference other than DCort (P < 0.05). Bone turnover markers decreased with alendronate; bALP increased (21%) and serum-CTX-I decreased (-1%) after 2 years of SrRan (between-group difference at each time point for both markers, P < 0.0001). Both treatments were well tolerated.

CONCLUSIONS: Within the constraints of HR-pQCT method, and while a possible artefactual contribution of strontium cannot be quantified, SrRan appeared to influence distal tibia bone microstructure and FEA-determined biomechanical parameters more than alendronate. However, the magnitude of the differences is unclear and requires confirmation with another method.

Changes in total body bone mineral density following a common bone health plan with two versions of a unique bone health supplement: a comparative effectiveness research study.

Nutrition Journal 2011, 10:32

Michalek et al.

Background: The US Surgeon General’s Report on Bone Health suggests America’s bone-health is in jeopardy and issued a “call to action” to develop bone-health plans that: (1) improve nutrition, (2) increase health literacy and, (3) increase physical activity. This study is a response to this call to action.

Methods: After signing an informed consent, 158 adults agreed to follow an open-label bone-health plan for six months after taking a DXA test of bone density, a 43-chemistry blood test panel and a quality of life inventory (AlgaeCal 1). Two weeks after the last subject completed, a second group of 58 was enrolled and followed the identical plan, but with a different bone-health supplement
Results: There were no significant differences between the two groups in baseline bone mineral density (BMD) or in variables related to BMD (age, sex, weight, percent body fat, fat mass, or fat-free mass). In both groups, no significant differences in BMD or related variables were found between volunteers and non-volunteers or between those who completed per protocol and those who were lost to attrition. Both groups experienced a significant positive mean annualized percent change (MAPC) in BMD compared to expectation [AlgaeCal 1: 1.15%, p = 0.001; AlgaeCal 2: 2.79%, p = 0.001]. Both groups experienced a positive MAPC compared to baseline, but only AlgaeCal 2 experienced a significant change [AlgaeCal 1: 0.48%, p = 0.14; AlgaeCal 2: 2.18%, p < 0.001]. The MAPC in AlgaeCal 2 was significantly greater than that in AlgaeCal 1 (p = 0.005). The MAPC contrast between compliant and partially compliant subjects was significant for both plans (p = 0.001 and p = 0.003 respectively). No clinically significant changes in a 43-panel blood chemistry test were found nor were there any changes in self-reported quality of life in either group.

Conclusions: Following The Plan for six months with either version of the bone health supplement was associated with significant increases in BMD as compared to expected and, in AlgaeCal 2, the increase from baseline was significantly greater than the increase from baseline in AlgaeCal 1. Increased compliance was associated with greater increases in BMD in both groups. No adverse effects were reported in either group.

**Distribution of strontium and mineralization in iliac bone biopsies from osteoporotic women treated long-term with strontium ranelate.**

_Eur J Endocrinol._ 2011 Sep;165(3):469-76.

Doublier A, Farlay D, Khebbab MT, Jaurand X, Meunier PJ, Boivin G.

OBJECTIVE: To investigate interactions between strontium (Sr) and bone mineral and its effects on mineralization in osteoporotic women treated long-term with Sr ranelate (SrRan).

DESIGN: In this study, 34 iliac bone biopsies were analyzed after 2, 12, 24, 36, 48, and 60 months of treatment with SrRan.

METHODS: Sr global distribution was analyzed by X-ray cartography and the percentage of bone area containing Sr was calculated in the bone samples. The focal distribution of Sr in all bone samples was investigated by X-ray microanalysis. The degree of mineralization was assessed by quantitative microradiography.

RESULTS: Absent from old bone formed before the beginning of treatment, Sr was exclusively present in bone formed during this treatment with a much higher focal Sr content in new bone structural units than in old ones. A progressive increase in the extent of areas containing Sr was observed during treatment. The focal bone Sr content in recently formed bone was constant over treatment. Secondary mineralization was maintained at a normal level during treatment.
CONCLUSION: Thus, the quality of bone mineralization (density and heterogeneity at tissue level) was preserved after a long-term treatment with SrRan.

A comparative effectiveness study of bone density changes in women over 40 following three bone health plans containing variations of the same novel plant-sourced calcium.


Kaats GR, Preuss HG, Croft HA, Keith SC, Keith PL.

BACKGROUND: The US Surgeon General’s Report on Bone Health suggests America’s bone-health is in jeopardy and issued a “call to action” to develop bone-health plans incorporating components of (1) improved nutrition, (2) increased health literacy, and (3) increased physical activity.

OBJECTIVE: To conduct a Comparative Effectiveness Research (CER) study comparing changes in bone mineral density in healthy women over-40 with above-average compliance when following one of three bone health Plans incorporating the SG’s three components.

METHODS: Using an open-label sequential design, 414 females over 40 years of age were tested, 176 of whom agreed to participate and follow one of three different bone-health programs. One Plan contained a bone-health supplement with 1,000 IUs of vitamin D(3) and 750 mg of a plant-sourced form of calcium for one year. The other two Plans contained the same plant form of calcium, but with differing amounts of vitamin D(3) and other added bone health ingredients along with components designed to increase physical activity and health literacy. Each group completed the same baseline and ending DXA bone density scans, 43-chemistry blood test panels, and 84-item Quality of Life Inventory (QOL). Changes for all subjects were annualized as percent change in BMD from baseline. Using self-reports of adherence, subjects were rank-ordered and dichotomized as “compliant” or “partially compliant” based on the median rating. Comparisons were also made between the treatment groups and two theoretical age-adjusted expected groups: a non-intervention group and a group derived from a review of previously published studies on non-plant sources of calcium.

RESULTS: There were no significant differences in baseline BMD between those who volunteered versus those who did not and between those who completed per protocol (PP) and those who were lost to attrition. Among subjects completing per protocol, there were no significant differences between the three groups on baseline measurements of BMD, weight, age, body fat and fat-free mass suggesting that the treatment groups were statistically similar at baseline. In all three treatment groups subjects with above average compliance had significantly greater increases in BMD as compared to the two expected-change reference groups. The group following the most nutritionally comprehensive Plan outperformed the other two groups. For all three groups, there were no statistically significant differences between baseline and ending blood chemistry tests or the QOL self-reports.

CONCLUSIONS: The increases in BMD found in all three treatment groups in this CER stand in marked contrast to previous studies reporting that interventions with calcium and vitamin D(3) reduce age-related losses of BMD, but do not increase BMD. Increased compliance resulted in increased BMD levels. No adverse effects were found in the blood chemistry tests, self-reported quality of life
and daily tracking reports. The Plans tested suggest a significant improvement over the traditional calcium and vitamin D(3) standard of care.

**Effects of strontium ranelate administration on bisphosphonate-altered hydroxyapatite: Matrix incorporation of strontium is accompanied by changes in mineralization and microstructure.**


Strontium ranelate (SR) is one therapeutic option for reducing risk of fracture in osteoporosis. The effects of SR treatment on hydroxyapatite (HA) previously altered by bisphosphonate (BP) administration remain to be established. Patients who have received long-term BP treatment and present with persistent high fracture risk are of particular interest. Paired iliac crest biopsies from 15 patients post-BP therapy were subjected to a baseline biopsy and a follow-up biopsy after treatment with 2g SR day?¹ after either 6 months (n=5) or 12 months (n=10). Dual energy X-ray absorptiometry scans, serum parameters and biochemical markers were obtained. Quantitative backscattered electron imaging and energy-dispersive X-ray analyses combined with micro-X-ray fluorescence determinations were performed to observe any mineralization changes. Static 2-D histomorphometry was carried out to evaluate cellular and structural indices. After 6 months of SR treatment, increases in osteoid surface and strontium content were observed, but no other indices showed significant change. After 12 months of SR treatment, there was a significant increase in bone volume and trabecular thickness, and further increases in strontium content and backscattered signal intensity. These structural changes were accompanied by increased numbers of osteoblasts and increased osteoid surface and volume. Additionally, low bone resorption, as measured by beta-cross-laps, and a low number of osteoclasts were observed. SR treatment led to increased strontium content within the BP-HA nanocomposites and to increased osteoid indices and bone volume, which is indicative of newly formed bone, while osteoclasts were still suppressed. These data points suggest that SR might be considered as a therapeutic option for patients following long-term BP treatment.

In osteoporotic women treated with strontium ranelate, strontium is located in bone formed during treatment with a maintained degree of mineralization.

*Osteoporos Int.* 2010 Apr;21(4):667-77.

Boivin G, Farlay D, Khebbab MT, Jaurand X, Delmas PD, Meunier PJ.

In postmenopausal osteoporotic women and up to 3 years of treatment with strontium ranelate, strontium was present only in recently deposited bone tissue resulting from formation activity during the period of treatment. Strontium was shown to be dose-dependently deposited into this newly formed bone with preservation of the mineralization.

**INTRODUCTION:** Interactions between strontium (Sr) and bone mineral and its effects on mineralization were investigated in women treated with strontium ranelate.
METHODS: Bone biopsies from osteoporotic women were obtained over 5-year strontium ranelate treatment from phases II and III studies. Bone samples obtained over 3-year treatment were investigated by X-ray microanalysis for bone Sr uptake and focal distribution, and by quantitative microradiography for degree of mineralization. On some samples, Sr distribution (X-ray cartography) was analyzed on whole sample surfaces and the percentage of bone surface containing Sr was calculated. Bone Sr content was chemically measured on whole samples.

RESULTS: In treated women, Sr was exclusively present in bone formed during treatment; Sr deposition depended on the dose with higher focal content in new bone structural units than in old ones constantly devoid of Sr, even after 3-year treatment. A plateau in global bone Sr content was reached after 3 years of treatment. Cartography illustrated the extent of surfaces containing Sr, and formation activity during strontium ranelate treatment was higher in cancellous than in cortical bone. Mineralization was maintained during treatment.

CONCLUSION: The quality of bone mineral was preserved after treatment with strontium ranelate, supporting the safety of this agent at the bone tissue level.

Five years treatment with strontium ranelate reduces vertebral and nonvertebral fractures and increases the number and quality of remaining life-years in women over 80 years of age.

Bone. 2010 Apr;46(4):1038-42.


INTRODUCTION: Longevity has resulted in a greater proportion of the population entering a time of life when increasing bone fragility and falls predispose to fractures, particularly nonvertebral fractures. Women over 80 years of age constitute 10% of the population but contribute 30% of all fractures and 60% of all nonvertebral fractures. Despite this, few studies have examined antifracture efficacy of treatments in this high-risk group and none has provided evidence for benefits beyond 3 years.

MATERIALS AND METHODS: To determine whether strontium ranelate reduces the risk of vertebral and nonvertebral fractures during 5 years, we analyzed a subgroup of 1489 female patients over 80 years of age (mean 83.5 /-3.0 years) with osteoporosis from the SOTI (spinal osteoporosis therapeutic intervention) and TROPOS (treatment of peripheral osteoporosis) studies randomized to strontium ranelate 2 g/d or placebo. All received a supplement of calcium plus vitamin D.

RESULTS: By intention to treat, vertebral fracture risk was reduced by 31% (relative risk, RR=0.69; 95% confidence interval, CI 0.52-0.92), nonvertebral fracture risk by 27% (RR=0.73; 95% CI 0.57-0.95), major nonvertebral fracture risk by 33% (RR=0.67; 95% CI 0.50-0.89) and hip fracture risk by 24% (RR=0.76; 95% CI 0.50-1.15, not significant). Treatment was cost-saving as it decreased cost and increased QALYs and life-years.
DISCUSSION: Strontium ranelate safely produced a significant reduction in vertebral and nonvertebral fracture risk during 5 years in postmenopausal women over 80 years of age and was cost saving.

**Effect of long-term treatment with strontium ranelate on bone strontium content.**

*Bone. 2009 Aug;45(2):200-6.*

*Bärenholdt O, Kolthoff N, Nielsen SP.*

AIM: To investigate the kinetics and magnitude of human bone strontium uptake and retention during and after long-time treatment with strontium ranelate (SrR).

METHODS: Bone strontium was measured by a novel DPA method developed by us. 32 osteoporotic female patients volunteered to participate in a 3 years open study of the effect on bone Sr. The group was treated with 2 g SrR/day, 17 of the group had received active treatment for 4-5 years before the study. DXA BMD measurements and DPA measurements of the relative bone strontium hydroxyapatite termed %Sr (SrHA/(CaHA SrHA)) were done simultaneously ultra-distally (UD) on the non-dominant radius every six months during the study and three and six months after treatment stop.

RESULTS: The highest relative Sr content was found in patients who had been treated for 7-8 years. The variability was pronounced; a mean of 1.1 % Sr was measured at the end of treatment. No effect was demonstrated on distal radius relative bone Ca hydroxy apatite. Bone strontium uptake and retention data were compatible with a power function model. Withdrawal of SrR resulted in a decline in bone Sr, but 73 %Sr and 67 %Sr, respectively remained in UD-radius three and six months after drug withdrawal.

CONCLUSION: The rise in bone Sr content measured by DPA as well as BMD measured by DXA was most marked initially. After the treatment was stopped bone Sr decreased rapidly only during the first months. In UD-radius the apparent BMD corrected for the influence of %Sr measured by DPA showed a slight decline like in an untreated population. Strontium containing drugs may influence DXA bone mineral measurements several years after treatment withdrawal. According to the power function model the skeletal retention three and six months after stopping the treatment would average 66% and 58%, respectively after three years of treatment, and 76% and 70%, respectively after eight years of treatment. However, individual predictions are uncertain due to large inter-individual variations, and the values cannot be extrapolated to other bone sites.

**Combination of Micronutrients for Bone (COMB) Study: Bone Density after Micronutrient Intervention.**

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*Genuis, SJ & Bouchard, TP.*

Along with other investigations, patients presenting to an environmental health clinic with various
chronic conditions were assessed for bone health status. Individuals with compromised bone strength were educated about skeletal health issues and provided with therapeutic options for potential amelioration of their bone health. Patients who declined pharmacotherapy or who previously experienced failure of drug treatment were offered other options including supplemental micronutrients identified in the medical literature as sometimes having a positive impact on bone mineral density (BMD). After 12 months of consecutive supplemental micronutrient therapy with a combination that included vitamin D3, vitamin K2, strontium, magnesium and docosahexaenoic acid (DHA), repeat bone densitometry was performed. The results were analyzed in a group of compliant patients and demonstrate improved BMD in patients classified with normal, osteopenic and osteoporotic bone density. According to the results, this combined micronutrient supplementation regimen appears to be at least as effective as bisphosphonates or strontium ranelate in raising BMD levels in hip, spine, and femoral neck sites. No fractures occurred in the group taking the micronutrient protocol. This micronutrient regimen also appears to show efficacy in individuals where bisphosphonate therapy was previously unsuccessful in maintaining or raising BMD. Prospective clinical trials are required to confirm efficacy.

Strontium ranelate improves bone microarchitecture in osteoporosis.


Hamdy NA.

In osteoporosis, disruption of bone remodelling leads to bone loss, microarchitectural damage and increased fracture risk, and the goal of any treatment for osteoporosis is to decrease this fracture risk. Available anti-resorptive and anabolic agents effectively achieve this goal by either suppressing or stimulating the activation frequency of bone remodelling units, and by improving the biomechanical properties of bone by a number of different mechanisms. Strontium ranelate represents a novel approach in the management of osteoporosis with proven anti-fracture efficacy. Two putative mechanisms have been proposed for the unique dual mode of action of strontium ranelate, rebalancing bone turnover in favour of bone formation: activation of the calcium- or other cation-sensing receptor, and increase in the expression of osteoprotegerin (OPG), coupled with a decrease in RANK ligand expression by the osteoblasts. In addition to these cellular changes, micro-CT analysis of bone biopsies from strontium ranelate-treated patients demonstrate improvement in intrinsic bone tissue quality as evidenced by increased trabecular number, decreased trabecular separation, lower structure model index and increased cortical thickness, associated with a shift in trabecular structure from rod-to plate-like configuration compared with controls. This review examines the evidence for the ability of strontium ranelate to improve bone microarchitecture in osteoporosis and explores the cellular and microstructural changes by which its anti-fracture efficacy may be achieved. No attempt is made at comparing the effects of strontium ranelate on bone microarchitecture with that of other anti-resorptive or anabolic osteoporosis agents.

Histomorphometric and microCT analysis of bone biopsies from postmenopausal osteoporotic women treated with strontium ranelate.
Strontium ranelate is a new anti-osteoporotic treatment. On bone biopsies collected from humans receiving long-term treatment over 5 yr, it has been shown that strontium ranelate has good bone safety and better results than placebo on 3D microarchitecture. Hence, these effects may explain the decreased fracture rate.

INTRODUCTION: Strontium ranelate’s mode of action involving dissociation of bone formation and resorption was shown in preclinical studies and could explain its antifracture efficacy in humans.

MATERIALS AND METHODS: One hundred forty-one transiliac bone biopsies were obtained from 133 postmenopausal osteoporotic women: 49 biopsies after 1-5 yr of 2 g/d strontium ranelate and 92 biopsies at baseline or after 1-5 yr of placebo.

RESULTS AND CONCLUSIONS: Histomorphometry provided a 2D demonstration of the bone safety of strontium ranelate, with significantly higher mineral apposition rate (MAR) in cancellous bone (9% versus control, \( p = 0.019 \)) and borderline higher in cortical bone (10%, \( p = 0.056 \)). Osteoblast surfaces were significantly higher (38% versus control, \( p = 0.047 \)). 3D analysis of 3-yr biopsies with treatment (20 biopsies) and placebo (21 biopsies) using microCT showed significant changes in microarchitecture with, in the strontium ranelate group, higher cortical thickness (18%, \( p = 0.008 \)) and trabecular number (14%, \( p = 0.05 \)), and lower structure model index (-22%, \( p = 0.01 \)) and trabecular separation (-16%, \( p = 0.04 \)), with no change in cortical porosity. The changes in 3D microarchitecture may enhance bone biomechanical competence and explain the decreased fracture rate with strontium ranelate.

Several medications have proved effective in reducing the fracture risk in postmenopausal women with osteoporosis. The optimal duration of use of these medications remains to be established, however. Gains in bone mineral density (BMD) persisted throughout 10 years of treatment with alendronate or 7 years with risedronate. However, proof of long-term protection against fractures was obtained only for shorter treatment periods, 4 years with alendronate and 5 years with risedronate. The persistence of treatment effects after drug discontinuation varies across medications, and further studies are needed before this point can be incorporated into treatment decisions. With raloxifene, the BMD effect observed after 3 and 4 years persisted when the drug was given for 8 years, and the fracture risk reduction was similar after 4 years and after 3 years. The long-term safety profile also was similar, with a significant decrease in the incidence of invasive estrogen-receptor-positive breast cancer and a persistent increase in the risk of deep vein thrombosis. However, a sharp drop in BMD occurred upon raloxifene discontinuation. Thus, 4 years may be appropriate for anti-resorptive drug.
therapy. However, the optimal treatment duration should be determined on a case-by-case basis according to the results of regular fracture-risk evaluations.

Effects of oral supplementation with stable strontium.


Skoryna SC.

The biologic effects of stable strontium, a naturally occurring trace element in the diet and the body, have been little investigated. This paper discusses the effects of oral supplementation with stable strontium in laboratory studies and clinical investigations. The extent of intestinal absorption of various doses of orally administered strontium was estimated by determining serum and tissue levels with atomic absorption spectrophotometry. The central observation is that increased oral intake produces a direct increase in serum levels and intracellular uptake of strontium. The results of these studies, as well as those of other investigators, demonstrate that a moderate dosage of stable strontium does not adversely affect the level of calcium either in the serum or in soft tissues. In studies of patients receiving 1 to 1.5 g/d of strontium gluconate, a sustained increase in the serum level of strontium produced a 100-fold increase in the strontium:calcium ratio. In rats, studies indicate that an increase in intracellular strontium content following supplementation may exert a protective effect on mitochondrial structure, probably by means of a stabilizing effect of strontium on membranes. The strontium:calcium ratio in animals receiving a standard diet is higher in the cell than in the extracellular fluid; this may be of physiologic significance. An increase in density that corresponded to the deposition of stable strontium was observed in areas of bone lesions due to metastatic cancer in patients receiving stable strontium supplementation. This suggests the possibility of using strontium to mineralize osteophenic areas and to relieve bone pain. Also, because of reports of an inverse relation between the incidence of dental caries and a high strontium content in drinking water, the use of natural water containing relatively high levels of stable strontium should be considered. In each of these instances it is important to maintain a normal dietary intake of calcium.