



I Want To Know!

Questions and Answers about Strontium Supplements

Since we introduced you to the health benefits of stable **Strontium** in *Advances* 2(3), we've been inundated with questions about this radical new bone health mineral. We're taking the opportunity to lay out the facts as we know them here.

Q The **Strontium** supplements I have found are either **Strontium citrate** or **Strontium carbonate**. But I keep hearing about **Strontium ranelate** in the news. Am I getting the wrong kind of **Strontium**?

A The reason for all the press stories on **Strontium ranelate** is because a major international drug company is now moving this salt of **Strontium** through the clinical trial process in hopes of marketing it as a drug. So it should come as no surprise if the most recent, most lavishly-funded, and most well-publicized studies in recent years have been the ones performed using this form of **Strontium**. However, there is nothing "magical" about this particular **Strontium** form. Independent studies have used many different forms of **Strontium**, including **Strontium lactate**,¹⁻³ gluconate,^{4,5} carbonate,^{5,6} chloride,⁷ acetate,⁸ and still other forms of the mineral. Guess what? They all work.

So why is the drug company using the ranelic acid salt?

Some of the reasons are revealed in a review of the science on **Strontium** written by Dr. Jean-Yves Reginster, an investigator with the World Health Organization (WHO) Collaborating Center for Public Health Aspects of Rheumatic Diseases, and with the Bone and Cartilage Metabolism Unit of the University of Liège.⁹ Dr. Reginster is the author of fourteen peer-reviewed scientific journal articles on the role of **Strontium** in bone health, and was a principal investigator on three of the largest and best-designed trials.^{10,11}

On the other hand, you can get an even *higher* elemental yield from some other forms of **Strontium**. **Strontium carbonate**, for instance, has 593 mg of **Strontium** per gram of the compound. But many of these forms of **Strontium** have poor "gastric tolerance" – in other words, they're more likely to cause upset stomach or diarrhea. The ranelic acid salt has good gastric tolerance.⁹

Dr. Reginster also notes that **Strontium ranelic acid salt** has good bioavailability – about 27%.⁹ However, this really doesn't make much of a difference in the case of **Strontium**: *all* forms of **Strontium** have bioavailabilities in the 25-30% range.⁷

But there is likely another reason why the pharmaceutical company that is now pushing the ranelic acid salt of **Strontium** through the "drug" development pipeline: patent control. **Strontium lactate**, citrate, gluconate, and carbonate are all *natural, unpatentable* forms of **Strontium** – whereas ranelic acid is a purely *synthetic* molecule that does not occur in nature. By using the ranelic acid salt, Big Pharma may be hoping to shore up its market protection and regulatory exclusivity on the "drug" market for what is, fundamentally, a *dietary supplement*: **Strontium**, a naturally-occurring trace mineral in the diet.

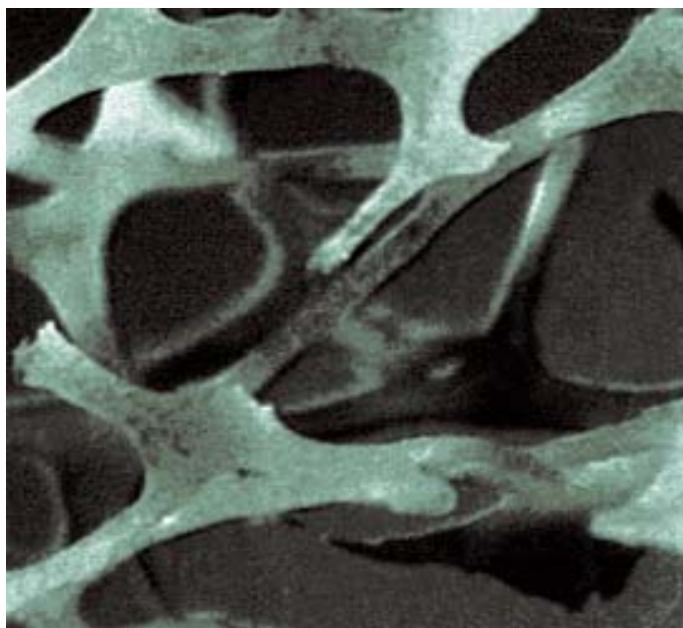
Independent studies
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of **Strontium**.
They all work.

Certainly, the ranelic acid part of the **Strontium ranelate** compound contributes nothing to the effects of **Strontium** on your bones. When you swallow **Strontium** bound to ranelic acid, the compound splits apart into two **Strontium** ions and a molecule of ranelic acid. The two are then taken up into the body separately, and while the body absorbs 27% of the **Strontium** in a pill, it absorbs *less than a tenth as much* (2.5%) of the ranelic acid. And of the ranelic acid that is absorbed, 93 to 99% is excreted within 7 days without being metabolized by the body.⁹

Molecular and animal studies have also shown that the effects of the ranelic acid salt of **Strontium** are due to the **Strontium**. In a study on the use of **Strontium ranelate** on bone formation in bone tissue culture, it was seen that **Strontium** bound to ranelic acid enhanced the replication

of pre-osteoblastic cells, but that “neither calcium ranelate nor sodium ranelate, at the same concentration, were able to induce similar effects”.⁹ Again, many other mechanistic studies have used other forms of **Strontium**, such as **Strontium** carbonate and **Strontium** chloride, and shown the same key effects on bone metabolism seen with **Strontium** ranelate.⁷ Indeed, it’s exactly the many animal studies and clinical trials using *other* forms of **Strontium** that got the pharmaceutical companies interested in **Strontium** in the first place.⁹

Strontium citrate enjoys the advantages of a relatively



high elemental yield (about 300 milligrams elemental Sr²⁺ per gram of compound), so you won’t be popping fistfuls of pills to get your daily dose, and of being very soluble, giving it good gastric tolerance and bioavailability compared to many other forms (such as the carbonate). Citric acid is also a *natural* ligand, and is available as a dietary supplement.

Q What do you think about all these new supplements which contain a full day’s dose of **Strontium** along with calcium, magnesium, and other key nutrients all in one convenient bottle?

A They’re a disaster. In his review, Dr. Reginster specifically notes (pg. 1914) that “**The simultaneous intake of [Strontium] and calcium remarkably reduces**

The simultaneous intake of **Strontium** and calcium remarkably reduces the bioavailability of **Strontium**.

the bioavailability of [Strontium]. This is probably due to competition at the sites of active absorption. Simultaneous food intake also has a negative influence on the bioavailability of **[Strontium]**”. Based on this critical factor, Dr. Reginster recommends that high-dose **Strontium** should **not be taken “concomitantly with a meal or a calcium intake.”**⁹

The competition between **Strontium** and calcium for absorption has long been known, and is the basis for the fact that **all of the trials using strontium with major bone-health outcomes have carefully ensured that the supplement is taken on an empty stomach, away from calcium** in food or in supplements.^{2,3,6,10-13} In the largest and best-designed trials,¹⁰⁻¹³ women have taken their **Strontium** first thing in the morning, half an hour to an hour before breakfast, and/or three hours after dinner in the evening; they took their calcium supplements *separately*, with a meal.

This is the protocol supported by pharmacology and by clinical trials, and it is the one that we recommend unless your doctor specifies otherwise. It is obviously impossible to follow this protocol if you’re taking a supplement that combines calcium and **Strontium** *in the same pill or powder!* Such formulations are, therefore, not the “convenient,” “inexpensive” deals they initially seem, but are ill-designed and likely ineffective “kitchen sink” hodgepodes. Persons taking these supplements will not reap the full benefits of **Strontium** documented in the clinical trials. This is a major health issue, especially for people with advanced osteoporosis. If they and their physicians are taking these combination supplements instead of a reliable, separate supplement, or instead of an established drug therapy, the results could be ruinous.

Note that these problems do not hold if there is only a small, *nutritional* amount of **Strontium** in a core bone health supplement— doses in the range of 500 micrograms to 5 milligrams, which are typical of human dietary intakes. Such doses are appropriate, as they preserve the ratio of calcium and **Strontium** present naturally in whole-food diets. In fact, all natural calcium sources also have a small amount of **Strontium** in them, because of the similar metabolism of the two nutrients in living beings. The presence of calcium with *no* **Strontium** in calcium supplements might be expected to upset this natural balance, leading to suppression of whatever **Strontium** is in your diet, ultimately perturbing the natural balance of minerals in your bone.

Indeed, some evidence already exists that, over a lifetime, these low, nutritional doses of **Strontium** do have a role to play in your health. For example, it was discovered in the 1960s that areas with more **Strontium** in the water have a

lower incidence of dental caries^{14,15} – a finding which was to be reinforced by the findings of at least eight more studies over the course of the next few decades.¹⁶

Some of these **Strontium**-calcium combination products further shoot their users in the foot by using poor forms of key ingredients. Some, for instance, use poor forms of calcium, such as cheap **calcium carbonate** (which has low gastric tolerance and which reduces your absorption of other nutrients by neutralizing stomach acid) and synthetic **calcium hydroxyapatite** (an extremely poorly-absorbed synthetic calcium phosphate salt, not to be confused with **ossein microcrystalline hydroxyapatite complex (MCHC)**, an extract of bone-health nutrients contained in an intact calcium crystalline matrix). Others use **magnesium carbonate** as a magnesium source; this is another antacid, and like calcium carbonate is poorly absorbed. Likewise, one of these products is even trading off of the research on **Menatetrenone (MK-4)** – the *mammalian* form of vitamin K₂ and the one used in all of the “vitamin K₂” clinical trials – to sell *another* “vitamin K₂” the unproven, bacterial *menaquinones*.

Everyone concerned about their bone health needs a core calcium supplement, along with other key nutrients such as **magnesium, vitamin D₃**, and **Menatetrenone**. In such a supplement, a small, nutritional dose of **Strontium** is a good balancing act, reflecting the trace levels of **Strontium** naturally present in food. But if you need the potent support of a “megadose” **Strontium** supplement, it should absolutely *not* come in a combination with calcium. You need a *separate* **Strontium** supplement, taken at a separate time.

Q The articles in *Advances* say that most trials have used dosages of **Strontium** in the 600-700 milligram range. But I keep hearing stories about trials using one or two *grams* of **Strontium**!

A This comes down to the question of *elemental yield*: the amount of **Strontium** *itself* that is present in a given amount of an **Strontium** *compound*. **Strontium**, like other minerals, does not come “naked,” but as part of a

compound – a salt or chelate *form* of the mineral. And different forms of the mineral are more or less mineral-dense. For instance, one gram (1 000 mg) of

Calcium hydroxyapatite is an extremely poorly-absorbed synthetic calcium phosphate salt, not to be confused with ossein microcrystalline hydroxyapatite complex (MCHC).

calcium carbonate contains 400 mg of *elemental calcium*, while the same amount of *calcium citrate* contains just 210 mg of elemental calcium. Similarly, to get 420 mg of *elemental magnesium* takes 5 600 mg of true, fully-reacted magnesium aspartate, because

this superior form of the mineral is only 7.5% elemental magnesium by weight. By contrast, to get the same amount of elemental magnesium from cheap, dense, low-bioavailability magnesium oxide requires just 696 mg of the compound, because magnesium oxide is over 60% elemental magnesium by weight.

To understand the difference on a supplement label, understand that “Calcium citrate ... 1 000 mg” means



1000 mg of calcium citrate *compound* (yielding 210 mg of *elemental calcium*). By contrast, “Calcium (from calcium citrate) 1 000 mg” or “Calcium (citrate) 1 000 mg” both mean 1 000 mg of *elemental calcium* is present in the number of capsules or tablets listed, in the form of calcium citrate.

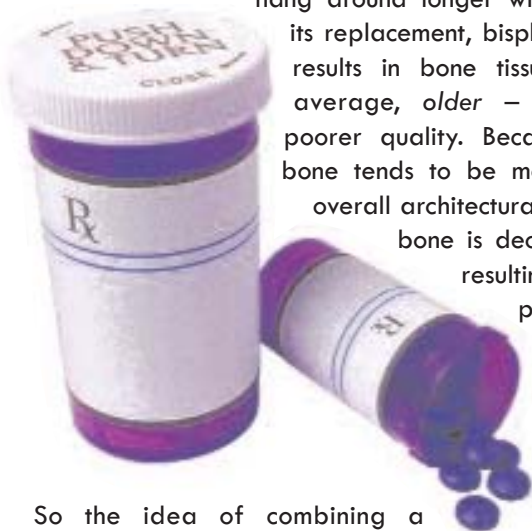
So when you hear that (for instance) some recent trials have used two grams (2 000 mg) of **Strontium ranelate**, they are telling you the amount of the *compound* they used – not the amount of *elemental Strontium*. Two grams of **Strontium ranelate** yield 680 mg of *elemental Strontium*.

Q Can I combine **Strontium** supplements with a bisphosphonate drug, such as alendronate (Fosamax®)?

A That's an important question. **Strontium** is a nutrient, not a drug: you get it in your food, and it may be an essential mineral like calcium, magnesium, or zinc. At high doses, studies show that has the power to help your body to create *new* bone. Bisphosphonates, by contrast, are drugs – purely synthetic molecules, designed explicitly to treat a *disease* (osteoporosis). These drugs don't actually *build* bone – they work by merely *slowing down the rate at which it is torn down (resorbed)*. That's why bisphosphonates are called “**antiresorptive**” drugs.

But that isn't the *only* effect of bisphosphonates on bone. Within weeks after you start taking a bisphosphonate, it also begins to impair your body's formation of *new* bone.¹⁷ Because the rate at which old bone is torn down is reduced by much more than the bone-building activity osteoblasts is hampered when you take a bisphosphonate, the *total mass of bone* slowly increases. But by allowing old bone tissue to

hang around longer without speeding its replacement, bisphosphonate use results in bone tissue that is, on average, *older* – and thus, of poorer quality. Because this older bone tends to be more brittle, the overall architectural quality of the bone is decreased.¹⁸⁻²⁰ The resulting bone is less prone to fracture, but is not the same as youthful, healthy bone.



So the idea of combining a *bone-building* nutrient like **Strontium** with an antiresorptive drug seems to offer a great way to get the best of both worlds. But does it actually work?

The quick answer is: *the trials haven't been done, so we don't know*. However, two recent trials published in the *New England Journal of Medicine*^{21,22} may give us some hint as to the *most likely* impact of a **Strontium**/bisphosphonate combination. These trials did not involve **Strontium**; instead, they were designed to test the effects of

combining a bisphosphonate with **teriparatide (Forteo®)**, a snipped-down version of human **parathyroid hormone (PTH)** that has been modified using biotechnology to include only the biologically active “business end.” But teriparatide, like **Strontium**, works by increasing the formation of new bone. So they *probably* give a good picture of the results that we can expect from taking **Strontium** along with a bisphosphonate drug.

Although the two studies had slightly different methodologies and the results were not *exactly* the same, the overall picture is this. BMD of the *spine* clearly increased *more* in women taking teriparatide only than it did in the combination-therapy group, who in turn seem to have done somewhat better than the women taking Fosamax® alone.^{20,21} Things were a little more complex at the **femoral neck** – the actual site of most so-called “hip fractures,” where the tapered area of bone at the top of the thigh that connects the main length of the thigh bone to the “ball” that fits into the “socket” of the hip.

In the relatively short term (a year²⁰ to a year and a half,²¹ the femoral neck BMD was unchanged in the teriparatide-only groups, or may have been slightly decreased, and any such decrease was prevented by combining teriparatide with the bisphosphonate. But in the *longer* term (30 months), **BMD of the femoral neck was definitely highest in women taking the bone-building agent only, with no bisphosphonate drug.**²¹ Meanwhile, the bone size at the femoral neck was increased by teriparatide – and Fosamax® *impaired the effect.*²⁰

Taken together, the trials give the pretty clear picture that antiresorptive drugs, in the long term, wind up *reducing* the effectiveness of teriparatide.^{20,21} The most likely reason for this is that, as we've noted, bisphosphonates don't *just* slow down the resorption of bone, but also reduce the overall “turnover” of bone by impairing the *bone-forming* activity of osteoblasts. But it's just these bone-building cells that teriparatide depends work, by helping them mature more quickly, boosting their activity, and allowing them to live a little longer on average. So ultimately, teriparatide's full bone-building potential is straightjacketed by bisphosphonate use. There is some direct molecular evidence that this is the case: one of the two studies²¹ measured markers of the rate at which *new* bone was being laid down, and found that **only people taking teriparatide without Fosamax® showed evidence of increased bone formation.**

BMD was definitely highest in women taking the bone-building agent only, with no bisphosphonate drug.

While we can't say for sure, it seems very likely that the same thing would apply with **Strontium**. Overall, then, the results seem to suggest that **Strontium** supplementation will be



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B ₆ (Pyridoxine)	25 mg
B ₁₂ (Cyanocobalamin)	24 mcg
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Biotin	300 mcg
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alpha-tocotrienol	3 mg
beta-tocotrienol	0.1 mg
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Calcium (Citrate-Malate, D-Gluconate)	300 mg
Chromium (Picolinate)	100 mcg
Copper (Citrate)	1.5 mg
Iodine (Potassium Iodide)	150 mcg
Lithium (Orotate)†	1000 mcg
Magnesium (Citrate, Aspartate, Oxide, Ascorbate)	210 mg
Manganese (Glycinate)	2.3 mg
Molybdenum (Na Molybdate)	45 mcg
Selenium (Se-Methylselenocysteine)	200 mcg
Silicon (Na Metasilicate)	50 mg
Strontium	1.5 mg
Vanadium (Citrate)	18mcg
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much less effective if it is combined with bisphosphonate use.



While you'll have to consult with your doctor to decide what these data means for you as an individual (and certainly, you should *not* discontinue taking a bisphosphonate drug without your physician's full understanding and consent), these studies do not necessarily mean that a person using **Strontium** should never use a bisphosphonate – or vice-versa. For one thing, it bears repeating that these studies were not performed with **Strontium**, and it is possible that future studies will show that bisphosphonates do not have the same restraining effect on **Strontium** that they do on teriparatide. Alternatively, you may decide in consultation with your doctor do adapt a protocol in which you take either **Strontium** or a bisphosphonate drug for a period of two to three years, and then to switch over to the other. In fact, there are already some preliminary data for just such a protocol, in osteoporotic women taking teriparatide for two years and then switching over to alendronate.²³

While you weigh the implications of these findings, remember that your physician must be an actively-involved, fully-informed player in any decision about your bone health – but especially where prescription drugs are involved.

References

- 1 Alwens. Ueber die beziehungen der unterernährung zur osteoporose und osteomalazie. *Munchn Med Wochenschr.* 1919 Sep 19;66(38):1071-5.
- 2 Shorr E, Carter AC. The usefulness of strontium as an adjuvant to calcium in the remineralization of the skeleton in man. *Bull Hosp Joint Dis.* 1952 Apr;13(1):59-65.

- 3 McCaslin FE Jr, Janes JM. The effect of strontium lactate in the treatment of osteoporosis. *Proc Staff Meetings Mayo Clin.* 1959; 34(13): 329-34.
- 4 Skoryna SC. Effects of oral supplementation with stable strontium. *Can Med Assoc J.* 1981 Oct 1;125(7):703-12.
- 5 Skoryna SC. Metabolic aspects of the pharmacologic use of trace elements in human subjects with specific reference to stable strontium. *Trace Subst Environ Health.* 1984; 18:3-23.
- 6 Marie PJ, Skoryna SC, Pivon RJ, Chabot G, Glorieux FH, Stara JF. Histomorphometry of Bone Changes in Stable Strontium Therapy. *Trace Subst Environ Health.* 1985;19:134-48.
- 7 Marie PJ, Ammann P, Boivin G, Rey C. Mechanisms of action and therapeutic potential of strontium in bone. *Calif Tissue Int.* 2001 Sep;69(3):121-9.
- 8 Pi M, Quarles LD. A novel cation-sensing mechanism in osteoblasts is a molecular target for strontium. *J Bone Miner Res.* 2004 May;19(5):862-9.
- 9 Reginster JY. Strontium ranelate in osteoporosis. *Curr Pharm Des.* 2002;8(21):1907-16.
- 10 Reginster J-Y, Sawicki A, Devogelaer JP, Padrin JM, Kaufma5 JM, Doyle DV, Fardellone7 P, Graham J, Felsenberg D, Tulassay Z, Soren-Sen OH, Luisett G, Rizzoli R, Blotman F, Pheneko C, Meunier PJ. Strontium ranelate reduces the risk of hip fractures in women with postmenopausal osteoporosis. *Osteoporos Int.* 2002 Nov;13 (Suppl 3): S14(AbsO14).
- 11 Meunier PJ, Slosman DO, Delmas PD, Sebert JL, Brandi ML, Albanese C, Lorenz R, Pors-Nielsen S, De Vernejoul MC, Rocas A, Reginster JY. Strontium ranelate: dose-dependent effects in established postmenopausal vertebral osteoporosis – a 2-year randomized placebo controlled trial. *J Clin Endocrinol Metab.* 2002 May;87(5):2060-6.
- 12 Reginster JY, Deroisy R, Dougados M, Jupsin I, Colette J, Roux C. Prevention of early postmenopausal bone loss by strontium ranelate: the randomized, two-year, double-masked, dose-ranging, placebo-controlled PREVOS trial. *Osteoporos Int.* 2002 Dec;13(12):925-31.
- 13 Meunier PJ, Roux C, Seeman E, Ortolani S, Badurski JE, Spector TD, Cannata J, Balogh A, Lemmel EM, Pors-Nielsen S, Rizzoli R, Genant HK, Reginster JY. The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis. *N Engl J Med.* 2004 Jan 29;350(5):459-68.
- 14 Losee FL, Adkins BL. A study of the mineral environment of caries-resistant Navy recruits. *Caries Res.* 1969;3:223-31. Cited by (10).
- 15 Schroeder HA, Tipton IH, Nason AP. Trace metals in man: strontium and barium. *J Chronic Dis.* 1972 Sep;25(9):491-517.
- 16 No author listed. Strontium and dental caries. *Nutr Rev.* 1983 Nov;41(11):342-4.
- 17 Eastell R. Treatment of postmenopausal osteoporosis. *N Engl J Med.* 1998 Mar 12;338(11):736-46.
- 18 Turner CH. Biomechanics of bone: determinants of skeletal fragility and bone quality. *Osteoporos Int.* 2002;13(2):97-104.
- 19 Meunier PJ, Boivin G. Bone mineral density reflects bone mass but also the degree of mineralization of bone: therapeutic implications. *Bone.* 1997 Nov;21(5):373-7.
- 20 Mashiba T, Hirano T, Turner CH, Forwood MR, Johnston CC, Burr DB. Suppressed bone turnover by bisphosphonates increases microdamage accumulation and reduces some biomechanical properties in dog rib. *J Bone Miner Res.* 2000 Apr;15(4):613-20.
- 21 Black DM, Greenspan SL, Ensrud KE, Palermo L, McGowan JA, Lang TF, Garnero P, Bouxsein ML, Bilezikian JP, Rosen CJ, PaTH Study Investigators. The effects of parathyroid hormone and alendronate alone or in combination in postmenopausal osteoporosis. *N Engl J Med.* 2003 Sep 25;349(13):1207-15.
- 22 Finkelstein JS, Hayes A, Hunzelman JL, Wyland JJ, Lee H, Neer RM. The effects of parathyroid hormone, alendronate, or both in men with osteoporosis. *N Engl J Med.* 2003 Sep 25;349(13):1216-26.
- 23 Rittmaster RS, Bolognese M, Ettinger MP, Hanley DA, Hodsman AB, Kendler DL, Rosen CJ. Enhancement of bone mass in osteoporotic women with parathyroid hormone followed by alendronate. *J Clin Endocrinol Metab.* 2000 Jun;85(6):2129-34.