StimuCal™
WITH BONE STIMULATING PROTEIN

Independent Research Summary

StimuCal™ Human Clinical Trial

StimuCal™ produces lower peak blood calcium levels than either calcium carbonate or calcium citrate while maintaining an identical effect on markers of bone turnover.

StimuCal™ was rigorously tested in an independently designed, randomised, placebo controlled trial of 100 postmenopausal women, conducted by the Department of Medicine at the University of Auckland, New Zealand.[1] The women were randomised to receive 1000 mg per day of calcium as either StimuCal™, Calcium Carbonate, Calcium Citrate, or placebo.

Acute changes in blood calcium levels were monitored over an 8 hour period (Figure 1) and key biochemical markers of bone turnover were measured at baseline and at three months as a measure of efficacy.

Results

Peak blood calcium levels after ingestion of StimuCal™ were 45% - 49% lower than peak blood calcium levels after ingestion of the same amount of calcium from either calcium carbonate or calcium citrate.

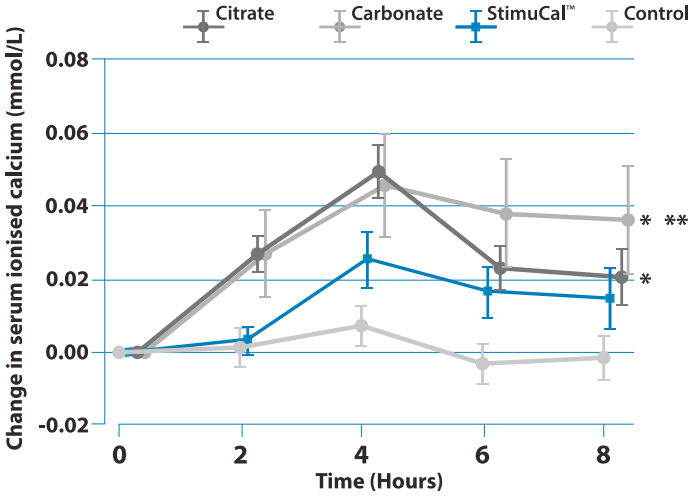

Figure 1: Change in serum ionized calcium over 8 hours.

* Average change over 8-hours significantly different from control, $p < 0.05$;

** Average change over 8-hours significantly different from StimuCal™, $p < 0.05$; Values are means ± SEM.

Furthermore, after ingestion of StimuCal™ average increases in blood calcium over an 8 hour period did not reach statistical significance. By contrast, after the ingestion of the same amount of calcium as either calcium carbonate or calcium citrate, average increase in blood calcium levels were statistically significantly different to control.

After three months continuous supplementation, the ability of StimuCal™ to supress key markers of bone turnover was identical to that of calcium carbonate and calcium citrate

Conclusion

The authors conclude "preparations of StimuCal™ resulted in smaller increases in ionised calcium than conventional calcium supplements, yet had a comparable effect on bone turnover. Preparations of StimuCal™ may therefore represent a safer form of calcium supplementation.

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StimuCal™
WITH BONE STIMULATING PROTEIN

StimuCal™ Cultured Osteoblast Study

StimuCal™ has demonstrated ability to promote bone matrix deposition and mineralisation (bone formation).

As StimuCal™ contains protein from bone it is, unlike regular calcium supplements, a source of naturally occurring growth factors and cytokines.

The effect of the protein fraction of StimuCal™ on bone metabolism was examined recently in an in vivo study by the Bone and Joint Research Group at the University of Auckland.[2]

Mineralisation of osteoblasts in 3D cultures, with or without the addition of StimuCal™ protein particulates, was assessed through calcein staining (Figure 2). Calcein is a fluorescent dye that binds to calcium and calcium phosphates to produce a green hue in cultures.

Results

The addition of StimuCal™ protein extract to cultures of rat osteoblasts resulted in a significant increase in bone metabolism, an effect that was dose dependent (i.e. higher doses of StimuCal™ resulted in greater increases in the area of mineralised bone).

This appeared to be through an effect of StimuCal™ on osteoblast differentiation, as bone mineralisation is a function of mature osteoblasts.

3D gel cultures with the addition of either of two separate batches of StimuCal™ particulates, showed higher levels of calcein staining at both 14 and 21 days, compared to the control gels without particulates.

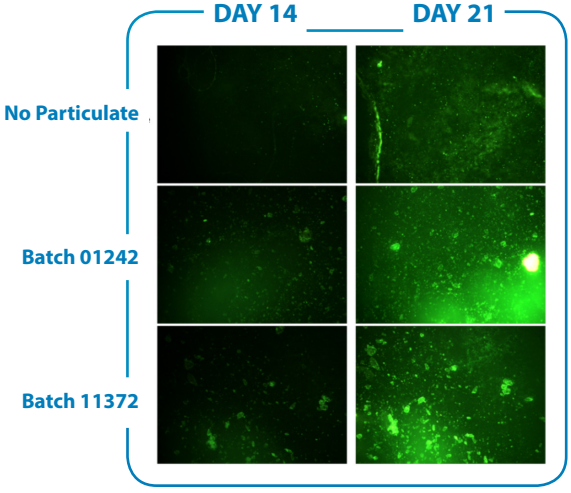

Figure 2: Calcein staining of 3D osteoblast cultures with or without StimuCal™ particulates incorporated.

StimuCal™ also appeared to reduce osteoblast proliferation, which would allow greater differentiation to take place.

Conclusion

This apparent mechanism of action suggests that StimuCal™ acts in a similar manner to parathyroid hormone, the most potent anabolic therapy for bone, and which also decreases the proliferation of osteoblasts while increasing their differentiation and bone formation.

1. Reid, I.R., Bristow, S., Effects of StimuCal, calcium citrate and calcium carbonate on serum calcium markers of bone turnover in postmenopausal women. A randomised controlled trial. Bone and Joint Research Group, Department of Medicine, Faculty of Medical and Health Sciences. The University of Auckland, New Zealand, 2012.
2. Musson, D.S., et al., Preliminary study on the role of StimuCal on the growth and differentiation of primary rat osteoblasts cultured in 3D. Bone and Joint Group University of Auckland, New Zealand, 2012.

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