

Calcium absorption from a new calcium delivery system (CCM)

Absorption of calcium from a highly soluble form of calcium, a mixed calcium citrate-malate, salt (CCM), was tested against calcium carbonate and milk in both rats and humans. The rat method estimated absorption from the 6-day retention of an oral tracer, and the human method employed the standard double-isotope procedure. CCM was given both as a dry powder and in an orange juice beverage. In two experiments in rats calcium from CCM was absorbed at least as well as, if not better than from calcium carbonate or milk. In two separate experiments in humans, calcium from CCM was absorbed significantly better than from calcium carbonate or milk. We conclude that CCM exhibits excellent bioavailability and that this formulation is a useful addition to the forms of calcium now available either for direct supplementation or for food fortification. Smith KT, Heaney RP, Flora L, Hinders SM. *Calcif Tissue Int* 1987 Dec;41(6):351-2.

A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women

Background. The effectiveness of calcium in retarding bone loss in older postmenopausal women is unclear. Earlier work suggested that the women who were most likely to benefit from calcium supplementation were those with low calcium intakes. **Methods.** We undertook a double-blind, placebo-controlled, randomized trial to determine the effect of calcium on bone loss from the spine, femoral neck, and radius in 301 healthy postmenopausal women, half of whom had a calcium intake lower than 400 mg per day and half an intake of 400 to 650 mg per day. The women received placebo or either calcium carbonate or calcium citrate malate (500 mg of calcium per day) for two years. **Results.** In women who had undergone menopause five or fewer years earlier, bone loss from the spine was rapid and was not affected by supplementation with calcium. Among the women who had been postmenopausal for six years or more and who were given placebo, bone loss was less rapid in the group with the higher dietary calcium intake. In those with the lower calcium intake, calcium citrate malate prevented bone loss during the two years of the study; its effect was significantly different from that of placebo (P less than 0.05) at the femoral neck (mean change in bone density [\pm SE], 0.87 \pm 1.01 percent vs. -2.11 \pm 0.93 percent), radius (1.05 \pm 0.75 percent vs. -2.33 \pm 0.72 percent), and spine (-0.38 \pm 0.82 percent vs. -2.85 \pm 0.77 percent). Calcium carbonate maintained bone density at the femoral neck (mean change in bone density, 0.08 \pm 0.98 percent) and radius (0.24 \pm 0.70 percent) but not the spine (-2.54 \pm 0.85 percent). Among the women who had been postmenopausal for six years or more and who had the higher calcium intake, those in all three treatment groups maintained bone density at the hip and radius and lost bone from the spine. **Conclusions.** Healthy older postmenopausal women with a daily calcium intake of less than 400 mg can significantly reduce bone loss by increasing their calcium intake to 800 mg per day. At the dose we tested, supplementation with calcium citrate malate was more effective than supplementation with calcium carbonate. Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. *N Engl J Med* 1990 Sep 27;323(13):878-883.

Spinal bone loss in postmenopausal women supplemented with calcium and trace minerals

The effects of calcium supplementation (as calcium citrate malate, 1000 mg elemental Ca/d) with and without the addition of zinc (15.0 mg/d), manganese (5.0 mg/d) and copper (2.5 mg/d) on spinal bone loss (L2-L4 vertebrae) was evaluated in healthy older postmenopausal women ($n = 59$, mean age 66 y) in a 2-y, double-blind, placebo-controlled trial. Changes (mean \pm SEM) in bone density were -3.53 \pm 1.24% (placebo), -1.89 \pm 1.40% (trace minerals only), -1.25 \pm 1.46% (calcium only) and 1.48 \pm 1.40% (calcium plus trace minerals). Bone loss relative to base-line value was significant ($P = 0.0061$) in the placebo group but not in the groups receiving trace minerals alone, calcium alone, or calcium plus trace minerals. The only significant group difference occurred between the placebo group and the group receiving calcium plus trace minerals ($P = 0.0099$). These data suggest that bone loss in calcium-supplemented, older postmenopausal women can be further arrested by concomitant increases in trace mineral intake. Strause L, Saltman P, Smith KT, Bracker M, Andon MB. *J Nutr* 1994 Jul;124(7):1060-1064.

The effect of calcium supplementation and Tanner stage on bone density, content and area in teenage women

One hundred and twelve Caucasian girls, 11.9 +/- 0.5 years of age at entry, were randomized into a 24-month, double-masked, placebo-controlled trial to determine the effect of calcium supplementation on bone mineral content, bone area and bone density. Supplementation was 500 mg calcium as calcium citrate malate (CCM) per day. Controls received placebo pills, and compliance of both groups averaged 72%. Bone mineral content, bone mineral area and bone mineral density of the lumbar spine and total body were measured by dual energy X-ray absorptiometry (DXA). Calcium intake group. The supplemented group received, on average, an additional 360 mg calcium/day from CCM. At baseline and after 24 months, the two groups did not differ with respect to anthropometric measurements, urinary reproductive hormone levels or any measurement of pubertal progression. The supplemented group had greater increases of total body bone measures: content 39.9% versus 35.7% ($p = 0.01$), area 24.2% versus 22.5% ($p = 0.15$) and density 12.2% versus 10.1% ($p = 0.005$). Region-of-interest analyses showed that the supplemented group had greater gains compared with the control group for bone mineral density, content and area. In particular, in the lumbar spine and pelvis, the gains made by the supplemented group were 12%-24% greater than the increases made by the control group. Bone acquisition rates in the two study groups were further compared by subdividing the groups into those with below- or above-median values for Tanner score and dietary calcium intake. In subjects with below-median Tanner scores, bone acquisition was not affected by calcium supplementation or dietary calcium level. However, the calcium supplemented subjects with above-median Tanner had higher bone acquisition rates than the placebo group with above-median Tanner scores. Relative to the placebo group, the supplemented group had increased yearly gains of bone content, area and density which represented about 1.5% of adult female values. Such increases, if held to adult skeletal maturity, could provide protection against future risk of osteoporotic fractures. Lloyd T, et al. *Osteoporos Int* 1996;6(4):276-83.

Calcium, phosphorus and magnesium intakes correlate with bone mineral content in postmenopausal women

Qualitative and quantitative differences in the dietary habits of postmenopausal women were studied to assess their influence on bone health and osteoporosis. A total of 194 postmenopausal women were studied with forearm DEXA densitometry. 70 were osteoporotic and 124 served as controls. Women had been menopausal for 5-7 years, and had never been treated with hormone replacement or drug therapy. A 3-day dietary recall was completed on Sunday, Monday and Tuesday after the examination: the results were processed by computer and daily calcium, phosphorus and magnesium intakes were related to bone mineral content (BMC). Data were compared with Student's t-test and significance was assessed at $p < 0.05$. Regression analysis was performed to correlate BMC and intake levels. The dietary intake of calcium, phosphorus and magnesium was significantly reduced in osteoporotic women and correlated with BMC. Calcium and magnesium intakes were lower than the recommended daily allowance even in normal women. The results suggest that nutritional factors are relevant to bone health in postmenopausal women, and dietary supplementation may be indicated for the prophylaxis of osteoporosis. Adequate nutritional recommendations and supplements should be given before the menopause, and dietary evaluation should be mandatory in treating postmenopausal osteoporosis. Tranquilli AL et al. *Gynecol Endocrinol* 1994 Mar;8(1):55-8.

Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women

A study was done to examine the effects of aluminum, magnesium, and boron on major mineral metabolism in postmenopausal women. This communication describes some of the effects of dietary boron on 12 women between the ages of 48 and 82 housed in a metabolic unit. A boron supplement of 3 mg/day markedly affected several indices of mineral metabolism of seven women consuming a low-magnesium diet and five women consuming a diet adequate in magnesium; the women had consumed a conventional diet supplying about 0.25 mg boron/day for 119 days. Boron supplementation markedly reduced the urinary excretion of calcium and magnesium; the depression seemed more marked when dietary magnesium was low. Boron supplementation depressed the urinary excretion of phosphorus by the low-magnesium, but not by the adequate-magnesium, women. Boron supplementation markedly elevated the serum concentrations of 17 beta-estradiol and testosterone; the elevation seemed more marked when dietary magnesium was low. Neither high dietary aluminum (1000 mg/day) nor an interaction between boron and aluminum affected the variables presented. The findings suggest that supplementation of a low-boron diet with an amount of boron commonly found in diets high in fruits and vegetables induces changes in postmenopausal women consistent with the prevention of calcium loss and bone demineralization. Nielsen FH, Hunt CD, Mullen LM, Hunt JR. *FASEB J* 1987 Nov;1(5):394-397.

The role of trace minerals in osteoporosis

Osteoporosis is a multifactorial disease with dimensions of genetics, endocrine function, exercise and nutritional considerations. Of particular considerations are calcium (Ca) status, Vitamin D, fluoride, magnesium and other trace elements. Several trace elements, particularly copper (Cu), manganese (Mn) and zinc (Zn), are essential in bone metabolism as cofactors for specific enzymes. Our investigations regarding the role of Cu, Mn and Zn in bone metabolism include data from studies with animals on Cu- and Mn-deficient diets. We have also demonstrated cellular deficiencies using bone powder implants, as well as fundamental changes in organic matrix constituents. In clinical studies we have demonstrated the efficacy of Ca, Cu, Mn and Zn supplementation on spinal bone mineral density in postmenopausal women. Each of these studies demonstrated the necessity of trace elements for optimal bone matrix development and bone density sustenance. Saltman PD, Strause LG. *J Am Coll Nutr* 1993 Aug;12(4):384-389

Efficacy of ipriflavone in established osteoporosis and long-term safety

Ipriflavone (i.p.), an isoflavone derivative, is currently used in several countries for prevention and treatment of osteoporosis. Recently, 149 elderly, osteoporotic women (65-79 years) with prevalent vertebral fractures were enrolled in two Italian, multicenter, double-blind, 2-year studies. Women were randomly allocated to receive either oral i.p. (200 mg T.I.D. at meals) or matching placebo, plus 1 g oral calcium daily. One hundred eleven subjects completed the 2-year treatment period. A significant increase in forearm bone mineral density (BMD), measured by dual photon absorptiometry (DPA), was obtained after i.p. treatment. Women receiving the placebo showed only a limited bone loss during the treatment period, probably due to calcium supplement; however, a significant between-treatment difference was obtained in both studies. Urinary hydroxyproline was significantly decreased in i.p.-treated patients, suggesting a reduction in bone turnover rate. A reduction of incident vertebral fractures was observed in i.p.-treated women compared with control subjects. A significant improvement of bone pain and mobility has also been pointed out in one of the studies. To date, 2769 patients have been treated with i.p., for a total of 3132 patient/years, in 60 clinical studies performed in Italy, Japan, and Hungary and reviewed for long-term safety assessment. The incidence of adverse reactions in ipriflavone-treated patients (14.5%) was similar to that observed in subjects receiving the placebo (16.1%). Side effects were mainly gastrointestinal. Few patients presented reversible modifications of laboratory parameters. The data from the above studies show that long-term treatment with i.p. may be considered safe, and may increase bone density and possibly prevent fractures in elderly patients with established osteoporosis. Agnusdei D, Bufalino L. *Calcif Tissue Int* 1997;61 Suppl 1:S23-7.

Potassium, magnesium, and fruit and vegetable intakes are associated with greater bone mineral density in elderly men and women

BACKGROUND: Osteoporosis and related fractures will be growing public health problems as the population ages. It is therefore of great importance to identify modifiable risk factors. OBJECTIVE: We investigated associations between dietary components contributing to an alkaline environment (dietary potassium, magnesium, and fruit and vegetables) and bone mineral density (BMD) in elderly subjects. DESIGN: Dietary intake measures were associated with both cross-sectional (baseline) and 4-y longitudinal change in BMD among surviving members of the original cohort of the Framingham Heart Study. Dietary and supplement intakes were assessed by food-frequency questionnaire, and BMD was measured at 3 hip sites and 1 forearm site. RESULTS: Greater potassium intake was significantly associated with greater BMD at all 4 sites for men and at 3 sites for women ($P < 0.05$). Magnesium intake was associated with greater BMD at one hip site for both men and women and in the forearm for men. Fruit and vegetable intake was associated with BMD at 3 sites for men and 2 for women. Greater intakes of potassium and magnesium were also each associated with less decline in BMD at 2 hip sites, and greater fruit and vegetable intake was associated with less decline at 1 hip site, in men. There were no significant associations between baseline diet and subsequent bone loss in women. CONCLUSION: These results support the hypothesis that alkaline-producing dietary components, specifically, potassium, magnesium, and fruit and vegetables, contribute to maintenance of BMD. Tucker KL et al. *Am J Clin Nutr* 1999 Apr;69(4):727-36.