



OSTEOBEN®

NUTRITIONAL SUPPORT FOR BONE HEALTH
120 VEGETARIAN CAPSULES | NPN80051043 | OTB120-CN

Osteoben® is a vitamin and mineral blend formulated to support bone strength and health. It provides nutrients and other compounds necessary for the physical structure and proper maintenance of bone tissue.

The nutrients delivered in Osteoben® are available naturally in food (or can be synthesized with exposure to sunlight, as with vitamin D), but many people do not consume adequate amounts of these nutrients and may need supplementation to reach optimal levels, particularly if they are already experiencing a decline in bone health. Additionally, various pharmaceutical drugs and medical conditions may increase the need for these nutrients above that which would typically be obtained from diet alone. Studies evaluating calcium or vitamin D as single interventions for improvement of bone density are often disappointing. Bone is complex tissue that requires multi-faceted support; synergy between the ingredients in Osteoben® may produce better results than nutrients taken in isolation.¹⁻²

HIGHLIGHTS

Calcium, Magnesium and Zinc: The primacy of calcium for bone health is undeniable. Approximately 99% of the body's calcium is found in the skeleton and a large body of evidence indicates greater calcium intakes are associated with greater bone mass, reduced bone loss and reduced risk for fractures.⁵⁻⁷ Among postmenopausal women not on estrogen therapy, greater total calcium intake (from foods and supplements) is associated with higher whole body bone mineral density (BMD).⁸ However, bones are comprised of far more than just calcium. They are also abundant in magnesium, housing approximately 60% of the body's magnesium. Magnesium is needed for formation of the cell-signaling molecule cAMP, which plays a role in secretion of parathyroid hormone (PTH).⁹ As the magnesium content of bone tissue decreases, the hydroxyapatite crystals may become larger and more brittle; research indicates that compared to those of non-osteoporotic women, bones of women with the condition have lower magnesium content and larger hydroxyapatite crystals.⁹ A small study of women with osteoporosis found that just 30 days of magnesium supplementation resulted in significantly decreased serum PTH level and urinary deoxypyridinoline (DPD, a marker of bone resorption) with a significant increase in serum osteocalcin, suggesting suppressed bone turnover.¹⁰ Other studies confirm that magnesium supplementation increases BMD and reduces risk for fractures.^{11,12}

Studies involving calcium supplementation, including some that also supplemented vitamin D, indicate a modestly increased risk for vascular events in subjects taking calcium. Researchers believe this may be due to suboptimal magnesium status and suggest supplementing magnesium in combination with calcium.¹³ (There may also be a role for vitamin K2, discussed in the next section.) A review looking at the relationship between magnesium and vitamin D status determined that magnesium is required for proper metabolism and activation of vitamin D for regulating calcium and phosphate homeostasis.¹⁴ Multiple enzymes involved in vitamin D metabolism require magnesium, yet between half and two-thirds of people in the US consume less than the Estimated Average Requirement (EAR) for this crucial mineral, which may be why studies employing vitamin D supplementation alone are often disappointing.¹⁵⁻¹⁷ Growing research supports magnesium repletion as an important aspect of vitamin D therapy.^{4,18}

Zinc plays an essential role in the structure of many proteins, including vitamin D receptors inside cells. Zinc is also needed for osteoblastic activity, collagen synthesis, and alkaline phosphatase activity.⁵ Poor zinc status may be an important predictor of bone loss; researchers have written that urinary zinc may be considered a marker of bone resorption and that zinc supplementation may have benefit for reducing fractures in postmenopausal women.¹⁹ Low serum zinc and increased zinc excretion are associated with risk for osteoporosis, possibly owing to zinc deficiency-induced increase in the bone resorbing effect of prostaglandin E2.^{20,21}

Regarding interactions among these nutrients, dietary intake of magnesium, calcium and zinc in postmenopausal women with low bone mineral density is substantially lower than the RDA and studies confirm that low serum levels of magnesium and zinc are associated with osteoporosis and osteopenia in postmenopausal women.²²⁻²⁴ Higher dietary intakes of calcium, magnesium, zinc and protein are associated with greater BMD in postmenopausal Caucasian women.²⁵

Vitamins D & K2: The role of vitamin D in bone tissue health is well understood: when the blood calcium level is low, vitamin D stimulates increased intestinal absorption of calcium from food and directs the kidneys to excrete less calcium to help restore proper levels. It also induces PTH-stimulated osteoclast activity. A systematic review of vitamin D optimization for preventing osteoporosis and osteoporotic fractures determined that a vitamin D intake of 700-800 IU per day along with a calcium supplement reduced risk for osteoporotic fractures, while an intake of 400-700 IU per day is effective in preventing bone loss in late postmenopausal women.²⁶ A study of French

postmenopausal women with osteoporosis, most of whom were meeting or exceeding the guidelines for calcium intake via food and/or supplements, determined that 50 percent of the subjects might benefit from adding a vitamin D supplement, as 78 percent of them were falling far short of the recommended intake and over 50 percent were getting limited sun exposure.²⁷ A study from Spain had similar findings: women with osteoporosis were meeting or exceeding recommendations for calcium intake but falling substantially short for vitamin D.²⁸

Vitamin K2 is often described as a “traffic cop” for calcium; it participates in directing calcium deposition into bones and teeth while preventing deposition in soft tissue such as blood vessels and joints.²⁹ Osteoporosis often goes hand-in-hand with vascular calcification, a phenomenon called the “calcium paradox.”^{30,31} It is not lack of calcium, per se, that leads to osteoporosis, but rather, misdirection of calcium. Vitamin K2 is needed for carboxylation of osteocalcin, the principal non-collagenous protein of bone. Vitamin K deficiency increases under-carboxylated osteocalcin, a less functional form.⁵ Under-carboxylated osteocalcin (ucOC) has been identified as a marker for vitamin K deficiency and risk for fragility fractures.³²⁻³⁵

Vitamin K2 reduces incidence of vertebral fractures in postmenopausal women with osteoporosis, with modest effects on BMD; animal research indicates K2 improves bone architecture and strength even without increasing bone mass.^{36,37} A review of the role of vitamin K in bone metabolism stated, “Vitamin K exerts its anabolic effect on the bone turnover in different ways such as promoting osteoblast differentiation, upregulating transcription of specific genes in osteoblasts, and activating the bone-associated vitamin K dependent proteins which play critical roles in extracellular bone matrix mineralization.”³⁸ A meta-analysis of RCTs determined that vitamin K2 supplementation is, in fact, beneficial for increasing BMD in postmenopausal women with osteoporosis and that it decreases ucOC.³⁹ Postmenopausal women supplemented with either K2 or K1 along with calcium and vitamin D-fortified dairy products showed greater improvement in BMD and reduction in ucOC compared to women receiving the fortified dairy alone.⁴⁰ Even in the absence of other interventions, K2 monotherapy has been shown to reduce fracture incidence in postmenopausal women with osteoporosis.⁴¹

Human osteoblasts cultured in an oxidative environment with added vitamin D3 and K2 showed enhanced proliferation and differentiation with reduced oxidative damage and lipid peroxidation compared to cells not exposed to the vitamins.⁴² (The MK-7 form of K2, as found in Osteoben®, was more effective than MK-4 or K1.) A different study of cultured human osteoblasts in a cytotoxic environment showed that K2 inhibited osteoblast apoptosis and preserved cell number.⁴³ The combination of K2, calcium and vitamin D for supporting bone health is so powerful that researchers have stated, “Vitamin K2 may be a useful adjunct for the treatment of osteoporosis, along with vitamin D and calcium, rivaling bisphosphonate therapy without toxicity.”⁴⁴

Genistein Aglycone: Genistein is a phytoestrogen that acts as a mild selective estrogen receptor modulator, which may positively regulate bone cell metabolism without the adverse side-effects seen in some instances of postmenopausal hormone replacement therapy. The genistein aglycone in Osteoben® is from a non-soy plant source. Research on phytoestrogens indicates that an effective dose for health effects is 40-70 mg/day⁴⁵; Osteoben® provides 54 mg in one 4-capsule serving. Epidemiological evidence suggests high isoflavone intake has bone-sparing effects, and that the beneficial effects of genistein on bone turnover—decreased bone resorption and enhanced formation—is due to estrogenic activity.⁴⁶ Specifically, genistein inhibits osteoclast activity and stimulates osteogenic differentiation and maturation of bone marrow stromal progenitor cells and osteoblasts.^{47,48} A meta-analysis of RCTs assessing the effect of isoflavone extracts on bone mineral density in menopausal women found that 6-12 months of isoflavone supplementation significantly increased spine bone mineral density (but had no significant effect on the femoral neck, hip or trochanter).⁴⁹ A separate review and meta-analysis determined that compared to placebo, isoflavone supplementation significantly decreased urinary DPD but had no effect on osteocalcin or bone alkaline phosphatase (BAP).⁵⁰ Other systematic reviews come to the same conclusion: that isoflavone supplementation decreases DPD and increases bone mineral density even in the absence of significant increases in markers of bone formation, although one review did note an increase in BAP along with increased bone formation and decreased resorption.^{51,52} Compared to vitamin D alone, administration of vitamin D with genistein (plus quercetin and resveratrol) resulted in improved bone mineral density and reduced osteoclast number in aged ovariectomized female rats.⁵³ Human studies show that when added to calcium and vitamin D, genistein leads to a significant decrease in DPD and increase in BAP among postmenopausal women with osteopenia.⁵⁴

Male patients may also benefit from the genistein phytoestrogens. Genistein is protective of prostate health in men in a manner similar to the way it protects breast health in women.^{55,56} Men who are concerned about bone health are likely older and may also have concerns about prostate health. Osteoben® may therefore provide a dual benefit in these patients. Research has shown that genistein does not lower testosterone. A meta-analysis looking at the effect of isoflavones on reproductive hormones in adult men found no significant effect on total or free testosterone, sex hormone binding globulin, or free androgen index.⁵⁷ Phytoestrogens have extremely mild estrogenic effects, in the range of 1,000 to 10,000 times less potent than estradiol. There is no data showing an excess estrogenic effect from genistein in men when taken at dosages similar to that found in Osteoben®.

A Note about Protein

Protein accounts for approximately 50% of the physical structure of bone, with collagen making up nearly 95% of this protein portion.⁵⁸ Higher protein intakes, including from animal sources, has been shown to be beneficial for bone health, particularly among the elderly.⁵⁸⁻⁶² Many older individuals and those following certain restrictive diets may not be consuming adequate protein to support bone health, especially considering amounts above the RDA are recommended for this population. (As much as 40% of adult women and 38% of adult men do not meet even the RDA for protein, which many researchers posit is inadequate to begin with.⁶³⁻⁶⁵) For patients with low bone mineral density, consider augmenting Osteoben® with a supplemental protein source, such as Whole Body Collagen, WheyCool™, PurePaleo™, or PurePea™.

Medicinal Ingredients (per capsule):

Calcium (Dicalcium malate).....	100 mg
Magnesium (Dimagnesium malate)	100 mg
Genistein	13.5 mg
Zinc (Zinc bisglycinate)	2 mg
Vitamin K2 (Menaquinone 7)	12.5 mcg
Vitamin D3 (Cholecalciferol)	6.25 mcg

Non-Medicinal Ingredients: Hypromellose, microcrystalline cellulose, magnesium stearate (vegetable source). **Recommended Dose:** Post-menopausal women: 2 capsules 2 times per day with food, or as directed by a physician. Take a few hours before or after taking other medications. Consult a health care practitioner for use beyond one year.

REFERENCES

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