BONEHELP K2-7

Each tablet contains Calcium Citrate Malate Eq. to Elemental Calcium 250 mg + Vitamin D3 as Cholecalciferol Equivalent to 400 IU + Vitamin K2-7 50 mcg

Dosage Form and Strength

Dosage Form: Tablets.
Dosage Strength: Calcium Citrate Malate Eq. to Elemental Calcium 250 mg + Vitamin D3 as Cholecalciferol Equivalent RTO 400 IU + Vitamin K2-7 50 mcg per tablet.

CLINICAL PARTICULARS

Therapeutic Indication

For the treatment of calcium and vitamin D deficiency states (pregnancy, lactation, growing children).

Posology and Method of Administration

For oral use.

The duration of therapy depends on the response to therapy.

Adults

2 tablets twice daily.

Children

2 tablets per day in one or two divided doses.

The ability of the child to take *BONEHELP K2-7* should be taken into account before prescribing it tochildren, particularly to young children.

PHARMACOLOGICAL PROPERTIES

Mechanism of Action and Pharmacodynamic Properties

Calcium
Calcium is the fifth most abundant element in the body and is a major substrate for mineralization and antiresorptive effect on bone. Calcium is a divalent metal essential for the maintenance of the nervous, muscular, and skeletal systems, as well as for cell membrane and capillary permeability. Its role in bone structure and muscle contraction is well known, but calcium is also important for blood coagulation,

nerve conduction, and electrical conduction in the heart. More than 99% of total body calcium is stored in bones and teeth where it functions to support their structure. Parathyroid hormone (PTH), vitamin D, and, to a lesser extent, calcitonin, glucocorticoids, and magnesium, influence calcium balance. Calcium suppresses PTH secretion, decreasing bone turnover. Increased levels of PTH have been found to be a contributory factor to age related bone loss, especially at cortical sites. Increased bone turnover is an independent risk factor for fractures. When calcium intake is low or calcium absorption is disrupted, bone resorption occurs at a faster rate than bone formation, because the body must use the calcium stored in bones to maintain normal biological processes such as nerve and muscle function. Osteoporosis and osteopenia can result from several factors including chronically low calcium intake, low vitamin D intake, poor calcium absorption, and/or excess calcium excretion.

Vitamin D

Activated vitamin D promotes renal reabsorption of calcium, increases intestinal absorption of calcium and phosphorus, and increases calcium and phosphorus mobilization from bone to plasma. Vitamin D is biologically inert and requires hydroxylation in the body to form the active metabolite. The activated form of vitamin D acts similarly to calcitriol, an active vitamin D analog, in that it appears to promote intestinal absorption of calcium through binding to a specific receptor in the mucosal cytoplasm of the intestine. Subsequently, calcium is absorbed through formation of a calcium-binding protein. Additionally, vitamin D has been studied as an independent factor in promoting skeletal strength by increasing muscle fiber growth and in balance by reducing body sway; a meta-analysis found supplementation with vitamin D reduced the risk of falls in an elderly population by 20 percent. Some evidence suggests that the active moiety of vitamin D acts at the level of the cell nucleus to increase plasma calcium and phosphorus. Once plasma saturation of these electrolytes occurs, bone mineralization takes place. The synthesis of activated vitamin D is enhanced by elevated parathyroid hormone levels and low plasma phosphorus levels. Hypocalcemia causes release of parathyroid hormone, which stimulates the production of activated vitamin D.

Vitamin K2-7

The biologic role of vitamin K is to act as a cofactor for the microsomal gamma - carboxylase that facilities the post - translational conversion of glutamic acid to gamma- carboxyglutamyl residues. Vitamin K2 also activities matrix Gla protein (cMGP) in cartilage and smooth muscle layer of the vessel and MGP prevents calcium from binding to the vessel well (inactive MGP, ucMGP). The reaction is catalyzed by a microsomal enzyme, vitamin K-dependent carboxylase, which in turn is linked to a cyclic salvage pathway known as the vitamin K epoxide cycle.

Pharmacokinetic Properties

Calcium

In general, the absorption of calcium from the intestine is never complete and demands that the calcium be in a soluble, ionized form. Oral bioavailability is influenced by the intestinal pH, the presence of food, the dosage administered, and the presence of calcium deficiency; absorption is increased in patients with calcium deficiency or low-calcium diets. Bioavailability is also influenced by the hormonal influence of PTH and vitamin D. The normal bioavailability of calcium from supplements is usually only 25—35%. The intestinal pH for dissolution and absorption of calcium salts and complexes is typically in the optimal range of 5—7, shortly after a meal in the patient with normal stomach acid status. Thus, it is often recommended that calcium be administered with or up to 1.5 hours after a meal to enhance absorption of the supplement. In patients with achlorhydria or other conditions of low stomach acid, calcium absorption is enhanced by taking the supplement with meals versus after meals so that the small amount of acid produced to aid digestion can also help aid calcium absorption. The anions (i.e., oxalate, phylates, or sulfates) or high fiber percentage present in certain foods may reduce

the bioavailability of calcium.
Calcium is excreted in the urine (roughly 20%); urinary excretion of calcium is often measured as a marker for calcium bioavailability in clinical studies. The amount excreted in the urine varies with the degree of calcium absorption, the rate of bone turnover, and renal conservation status. The fecal excretion of calcium is roughly 80% and represents primarily non absorbed calcium remaining in the gut.

Vitamin D

Oral absorption of vitamin D occurs rapidly and completely in the presence of bile salts. The onset of action following oral administration is 10—24 hours, with maximal effects usually observed in 4 weeks. Vitamin D enters the blood through chylomicrons of lymph. Vitamin D is stored primarily in the liver and fat depots. The parent compound and its metabolites are bound in plasma to alpha-globulins. Vitamin D is converted in the liver by the enzyme vitamin D-25-hydroxylase (cytochrome P450 27) to 25-hydroxyergocalciferol, an active, intermediate. Vitamin D is further converted to its most active form, 1,25-dihydroxyergocalciferol, in the kidneys. The intermediate metabolite of Vitamin D may be distributed into breast milk following high doses. All of the metabolites of vitamin D have not been identified. Elimination of vitamin D and its metabolites occurs principally through the bile, with the remainder excreted renally. The half-life is 19—48 hours.

Vitamin K2-7

Vitamin K2-7 The intestinal absorption of vitamin k follows a well-established pathway that applies to most dietary lipids, which includes bile salt-and pancreatic-dependent solubilisation, uptake of mixed micelles into the enterocytes, the packaging of concentrations of phylloquinone and MK-7 reached a plateau after 3 and 20 d, respectively, with MK-7 attaining serum concentrations that were 7 -to 8- fold higher than those for phylloquinone. These higher concentrations MK-7 were associated with a greater tissue uptake and biological activity in bone as evidenced by an increased proportion of serum gamma-carboxylated osteocalcin that plateaued after 3 d. In the phylloquinone arm but continued to rise for at least 40 d in the MK-7 arm. Humans excrete phylloquinone and MK by a common degradative pathway where by the polyisoprenold side chain is first shortened to major carboxylic acid metabolites with 7- and 5- carbon side chains, respectively, the metabolites are then conjugated, mainly with glucuronic acid, and excreted in to the bile and urine.