

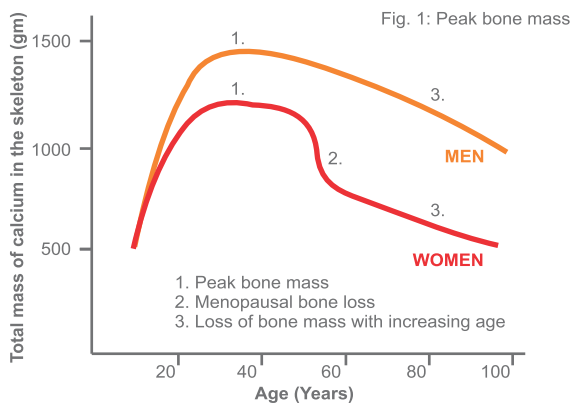
MenaquinGold[®]

Natural Vitamin K2-7

**For effective Calcium Utilization
& Metabolism**

Bone & Heart Health





40 years old



60 years old



70 years old

Fig. 2 : The Osteoporosis process

The Calcium Paradox

Calcium is essential for bone health and for keeping the bone mass in the human skeleton. Sufficient intake of calcium has a significant role in building and maintaining maximum bone mass and consumers should not doubt the effectiveness of calcium.

Both men and women are losing calcium when they become older. From age of 35 we are losing bone mass and height as the illustrations show (fig 1 & 2). Especially when women enter menopause, they simultaneously lose calcium from bone and increase its deposition in arteries- a negative "double whammy" called the "Calcium Paradox," which greatly increases the risk of both osteoporosis and cardiovascular disease.

Calcium has for decades been the most obvious choice of dietary supplement for improving bone health. The large majority of calcium (99%) in our bodies is in our skeleton and some in teeth, only 1% is found in the circulation. We need calcium to keep up with the turnover of the skeleton. However, we also require that the body can optimize the use of calcium. Too much calcium also seems no good.

For many years, the general medical industry has been pushing calcium supplements as your primary form of insurance against osteoporosis, proclaiming that "calcium builds strong bones and teeth". Calcium is added to everything these days, from pasteurized milk to baby formula, orange juice, and breakfast cereals. The belief that calcium builds strong bones is absolutely engrained in our society.

However, this widespread and rampant use of calcium fortification and supplements have many hidden dangers; cardiovascular effects of the same being at the forefront in current research. Hence we are further convinced that an effective calcium formulation ensures that calcium is put in the right place (i.e., Bones!) where it is needed, and should ensure that calcium is kept out of the soft tissues and arteries where it is harmful.



Is calcium supplementation a cause for concern?

Large studies over the past 20 years with as much as 12000 participants shows that calcium taken alone can increase the risk of cardiovascular diseases, myocardial infarction and stroke by as much as 30% according to a study published in British Medical Journal. This is called the “Calcium Paradox”.¹

British Medical Journal (BMJ) 2008 “Calcium supplements in healthy post menopausal women are associated with upward trends in cardiovascular event rates. This potentially detrimental effect should be balanced against the likely benefits of calcium on bone.”²

This 5 year study on 1471 postmenopausal women suggests that “women who take calcium supplements may have increased risk of heart attack, stroke or sudden death; because calcium supplements may accelerate the formation of calcium deposits in the arteries by increasing blood calcium levels.

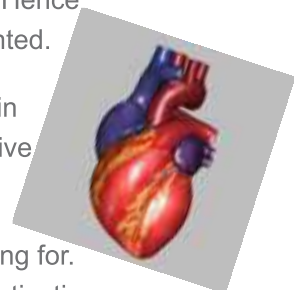
“... A statically significant increase was found in the number of women who had a myocardial infarction in the calcium group compared with placebo....”

Subsequently, 2010 meta-analysis showed calcium supplements (without co-administered Vitamin D) are associated with increased risk for heart attack (BMJ 2010).³ Recently, BMJ (2011) published an update of the meta-analysis of calcium supplements and cardiovascular risk.⁴ It was concluded that calcium supplements with or without Vitamin D increase the risk of cardiovascular events. Hence a reassessment of the role of calcium supplements in osteoporosis management is warranted.



Hence increased calcium intake especially if combined with Vitamin D, results in increased absorption of Calcium. However, Vitamin K2 aids in safe and effective utilization and thus providing a complete formulation.

Vitamin K2-7 may be the answer to what the medical community is now looking for. The natural form as Vitamin K2-7 is a fat soluble vitamin necessary for the activation of Osteocalcin and Matrix Gla-Protein (MGP) for safe and effective calcium utilization for bone and cardiovascular health.



2006 : “Atherosclerotic Vascular disease more commonly seen among women with Osteoporosis than with no Osteoporosis or Osteopenia” Am. J Cardiol 2006; 97 : 1427-1428

2007 : Vascular Calcification and Osteoporosis – from clinical observation towards molecular understanding Osteoporos Int (2007) 18 : 251-259

2008 : “Calcium Supplements in healthy post menopausal women are associated with upward trends in cardiovascular rates” BMJ 2008; 336 : 262-6

2008 : The circulating Inactive form of Matrix Gla Protein (Uc MGP) as a Biomarker for Cardiovascular Calcification J Vasc Res 2008; 45 : 427-436

2010 : “2010 meta-analysis showed that Calcium supplements (with co-administered Vitamin D) are associated with an increased risk of myocardial infarction” BMJ 2010; 341 : c3691

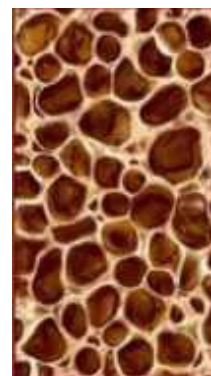
2011 : As an update to the above meta-analysis it was concluded calcium supplements with or without Vitamin D increase the risk of Cardiovascular events BMJ 2011; 342 : d2040

Combating the “calcium paradox”

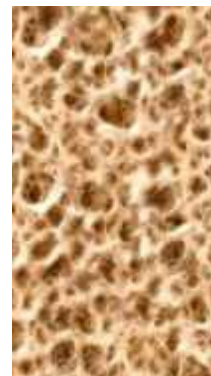
As women enter menopause, they simultaneously lose calcium from bone and increase its deposition in arteries – a negative “double whammy” called the “calcium paradox,” which greatly increases the risk of both osteoporosis and cardiovascular disease. The drop in oestrogen causes both problems, but vitamin K can help rectify them.

Among postmenopausal women not using oestrogen replacement, low levels of vitamin K or high levels of undercarboxylated (vitamin K-dependent) osteocalcin are associated with low spine BMD, but a 3-year study of 325 postmenopausal women, receiving either K2 or placebo, shows that supplementation with K2 can prevent bone loss associated with oestrogen decline. In the women given K2, bone mineral content increased, and hip and bone strength remained unchanged, whereas in the placebo group, bone mineral content and bone strength decreased significantly.

Vitamin K-dependent MGP (Matrix Gla Proteins) inhibits vascular calcification and also helps maintain the elasticity of postmenopausal women's blood vessels, thus improving cardiovascular health.⁵



Osteoporosis



Normal Bone

Vitamin K2

Vitamin K2 is arguably the most interesting vitamin of this decade. Its function is unique and its beneficial effects on bone and cardiovascular health have been clearly documented.

Osteoporosis and cardiovascular disease are closely linked: the lack of calcium in bones correlates strongly with calcium build up in arteries. This is called the “Calcium paradox” and Vitamin K2 plays a vital role in this “double-jeopardy” situation by activating crucial proteins responsible for bone mineralization and vascular calcification.

Vitamin K2 is needed for the activation of specific proteins which perform a number of essential activities throughout the body, including regulating blood clotting and effective calcium utilization. Inadequate vitamin K2 results in these key proteins being “inactive” and thus “ineffective”.

K1 is the form used in the liver to activate clotting factors, while K2 is the form used in the rest of the body to activate Vitamin K-dependent proteins, including osteocalcin, which is essential for bone health, and matrix-Gla protein (MGP), which prevents calcification of blood vessels and organs.

MenaquinGold® contains natural Vitamin K2 in the highly bioavailable form of Vitamin K2-7 (menaquinone-7, MK-7). This long chained vitamin K2 molecule offers superior bioavailability and health effects in low doses.

Only Vitamin K2-7 has been tied to both bone health and cardiovascular health, and MenaquinGold® is the safe, natural, non synthetic source of Vitamin K2-7.



K2 For Healthy Bones.....

Calcium has been the focus of attention for decades for improvement of bone health and is needed to build the hydroxyapatite matrix in our bones. However, several human studies have shown that this is not enough to prevent osteopenia, osteoporosis or fractures. Why? There are 2 vitamins known to be involved with calcium metabolism vitamin D and vitamin K. Increased calcium intake, especially if combined with vitamin D, results in increased absorption of calcium. However, without Vitamin K2, our bodies cannot use Calcium effectively.



Vitamin K2 is needed to activate a specific bone protein called osteocalcin, which is essential to bind calcium effectively to the bone matrix, keeping bones dense and strong.⁶

In the absence of Vitamin K2, osteocalcin remains inactive and thus not effective. As a result, very little Calcium is deposited and this calcium is lost into the blood stream ... simultaneously increasing the risk of Osteoporosis and calcification of the arteries (arterial calcification). Vitamin K2 also stimulates the creation of osteoblasts (bone-forming cells) and restrains the creation of osteoclasts (bone-destroying cells).

Industry experts are now strongly recommending vitamin K2 supplementation to help ensure bone and heart health: “the goal should be to provide supplements that help put calcium in the bones where it is needed, and keep it out of the soft tissues and arteries, where it can be harmful. Recent research has shown that vitamin K2 plays a vital role in calcium utilization, and we believe it should be included in all calcium supplements”.

K2 For Healthy Heart

Excess Calcium build-up in our cardiovascular system may lead to arterial calcification, and the calcium content of arteries is now proven to be more dangerous than elevated cholesterol.

Vitamin K2 is also required for activation of the vascular protein MGP, which is a potent inhibitor of vascular wall and heart valve calcification.⁷

Lack of sufficient amounts of vitamin K2 strongly influences how the body tackles calcium. Bones get depleted of calcium while arteries and cartilage become calcified. At age 80 the average calcium content in the aorta is 140 times greater than the levels of aortic calcification at age 40. This may relate to a long period of unrecognized Vitamin K2 deficiency.

The Rotterdam Study⁸

Another large epidemiological population-based study published in 2004 – The “Rotterdam study” with 4473 subjects with no history of Myocardial infarction, over a period of 10 years showed a significant 50% reduction in Coronary Heart Disease (CHD), mortality and aortic calcification CHD mortality for those who were in the 45 mcg per day of dietary intake of vitamin K2-7 in the upper tertile and 25% reduction in 24 mcg per mid tertile compared to the 12.5 mcg per day lower tertile. Such dose-response relationship in a population was impressive for the new role of vitamin K2-7. Their findings did not show any correlation between vitamin K1 intakes to the CHD outcome.

“... A statistically significant reduction of cardiovascular diseases and death by 50%...”

The Gast Study⁹

The Gast study published in 2009 with 16057 participants over 8.1 years confirmed the Rotterdam study and conclude a 9% reduction in risk of developing CHD for every 10 mcg of natural vitamin K2 consumed. The highest average consumption was >36 mcg K2/day. This study could not confirm a protective effect of Vitamin K1 for coronary calcification and CHD similar to the conclusions of Rotterdam study. The need for a higher dose of vitamin K2-7 was obvious.

“...9% reduction of risk of Coronary Heart Disease for every 10 mcg natural K2-7 a day...”

Vitamin K2 and K1

Vitamin K refers to a group of chemically similar fat soluble compounds called naphthaquinones. These compounds have a common 2-methyl-1, 4-Naphthaquinone ring but differ in the structure of the side chain at the three position.



The naturally occurring forms of Vitamin K include Vitamin K1 and Vitamin K2. Vitamin K1 (Phylloquinone, phytonadione) is regarded as the major dietary source of Vitamin K, occurring naturally in plants, algae, and photosynthetic bacteria¹⁰, green leafy vegetables, and vegetable oils.

Vitamin K2 or Menaquinone includes a range of related forms generally designated as menaquinone-n (MK-n) where n is the number of isoprenyl groups. Vitamin K2 compounds are also made by bacteria in the human gut, and provide a smaller amount of the human Vitamin K requirement.^{11,12}

Vitamin K2-4 (MK-4) which is a short chain menaquinone is found predominately in meat, but can also be found in fermented products, certain types of cheese, butter, chicken egg yolk and natto. Vitamin K2-7 (MK-7) is among the most popular long chain menaquinones and is primarily derived from our gut bacteria, in addition, it can be found in certain types of cheese, butter and natto.¹³

Vitamin K3 or menadione is a synthetic version, not recommended for human use due to its toxicity. Menadione is not considered a natural Vitamin K, but a synthetic analogue that acts as a provitamin. Vitamin K3 cannot exert all the functions of natural Vitamin K because of limited transformation into the fat soluble Vitamin K forms.^{14,15}



Natural Vitamin K2-7



Fermented soybean product Natto is a natural source of MK-7. Natto is a Japanese breakfast food that has been traditionally eaten for over 1000 years. Studies in Japan have linked vitamin K2 to a reduction of cardiovascular disease and could explain lower levels of heart diseases in Japan. Additionally, several Japanese studies have been published on the effect of nutritional MK-7 intake and bone health.



Vitamin K2, and particularly Vitamin K2-7 (MK-7) has a better bioavailability and longer half life, and studies show that this molecule remains in the body for a longer period and is more effective at lower doses, hence is much more bio-effective than K1.

During prolonged intake the long half life permits accumulation of K2 to levels 7-8 fold higher than that seen after one dose.¹⁶ Vitamin K2 (MK-7) is 6 times more potent than Vitamin K1, and is also the form in which vitamin K has been found to protect against arterial calcification.

Human cells are not able to synthesize vitamin K2 and present knowledge strongly indicates that western diets do not contain enough Vitamin K2. Even if you eat a lot of green vegetables, you do not get enough vitamin K1 or K2. This is due to several factors, most important of which is that vitamin K1 is not effectively released (only about 5-20%) for absorption in the intestines, and secondly because the amount ingested is rapidly cleared by the liver and excreted. Consequently, vitamin K1 will not stay long enough in the circulation to reach peripheral arteries or bone cells in sufficient amounts for optimal action. K1 is the form used in the liver to activate clotting factors, while K2 is the form used in the rest of the body to activate other vitamin K-dependent Gla-proteins, including osteocalcin, which is essential for bone health, and matrix-Gla protein, which prevents calcification of blood vessels and organs.

Studies have shown that natural vitamin K2 as menaquinone-7 (MK-7) was significantly better as compared to vitamin K1 in several important areas, including better absorption, much longer bioavailability and higher efficacy levels in the body. The primary reason for MK-7's superiority appears to be its very long half life in the blood, compared to the half-life of K1, which results in more stable blood levels and significantly greater accumulation of vitamin K2 in the blood. This results in K2 being supplied to ALL tissues 24 hours a day, reaching a steady-state level in 2 weeks. Research data show that MK-7 is redistributed by the liver and made available for extra-hepatic tissues like bones and arteries. This is not the case for K1, which remains in the liver.¹⁶

Hence, Natural Vitamin K2 as Vitamin K2-7 is the optimal vitamin K product because it is the most bio-available, has the longest half life and is most bioactive form of vitamin K.

Why You Never Heard This Before?

Because the focus has been on how much Vitamin K it takes to make blood clot, the issue of how much a person needs to maintain solid bone and clear arteries hasn't been adequately researched.

The RDA is roughly based on how much vitamin K is required to maintain clotting factors. According to evidence, this amount is dangerously inadequate for bone and arteries.

Safety

Vitamin K is not stored in the body, and is therefore nontoxic in high amounts. Vitamin K has been approved in Japan for the treatment of osteoporosis since 1995 and no upper limit for K2 dosage is established internationally.

The Vitamin K2 dose needed to have a significant effect is 45 to 90 mcg per day. At this dose it is unlikely to interfere with anticoagulant treatment with Coumadin/Warfarin and does not provoke any additional risk of clot formation inside blood vessels.

MenaquinGold®

MenaquinGold is natural Vitamin K2 known as menaquinone (MK-7, Vitamin K2-7). It is manufactured by Synergia Life Sciences a subsidiary of Viridis Biopharma in Mumbai, India, using proprietary fermentation technology in a dedicated GMP facility. Decades of testing and hundreds of published studies prove that Vitamin K2 is an essential nutrient. Without sufficient Vitamin K2 intake, the population will suffer from cardiovascular disease, osteoporosis, prostate cancer, etc. It is, in addition, an essential nutrient to supplement as our dietary intake of this compound is dangerously low. Vitamin K2 thus embodies the purpose and the spirit of the Dietary Supplement industry itself, it is essential for health and supplementation is required.

MenaquinGold® is EU approved, GRAS, Kosher and Halal certified. It is supported by extensive stability studies and validated analytical methods. It has been extensively studied for safety and is used in several leading brands.



Calcium, Vitamin D and Vitamin K2 a synergistic approach for effective calcium utilization



These three ingredients work synergistically, which may assist with:

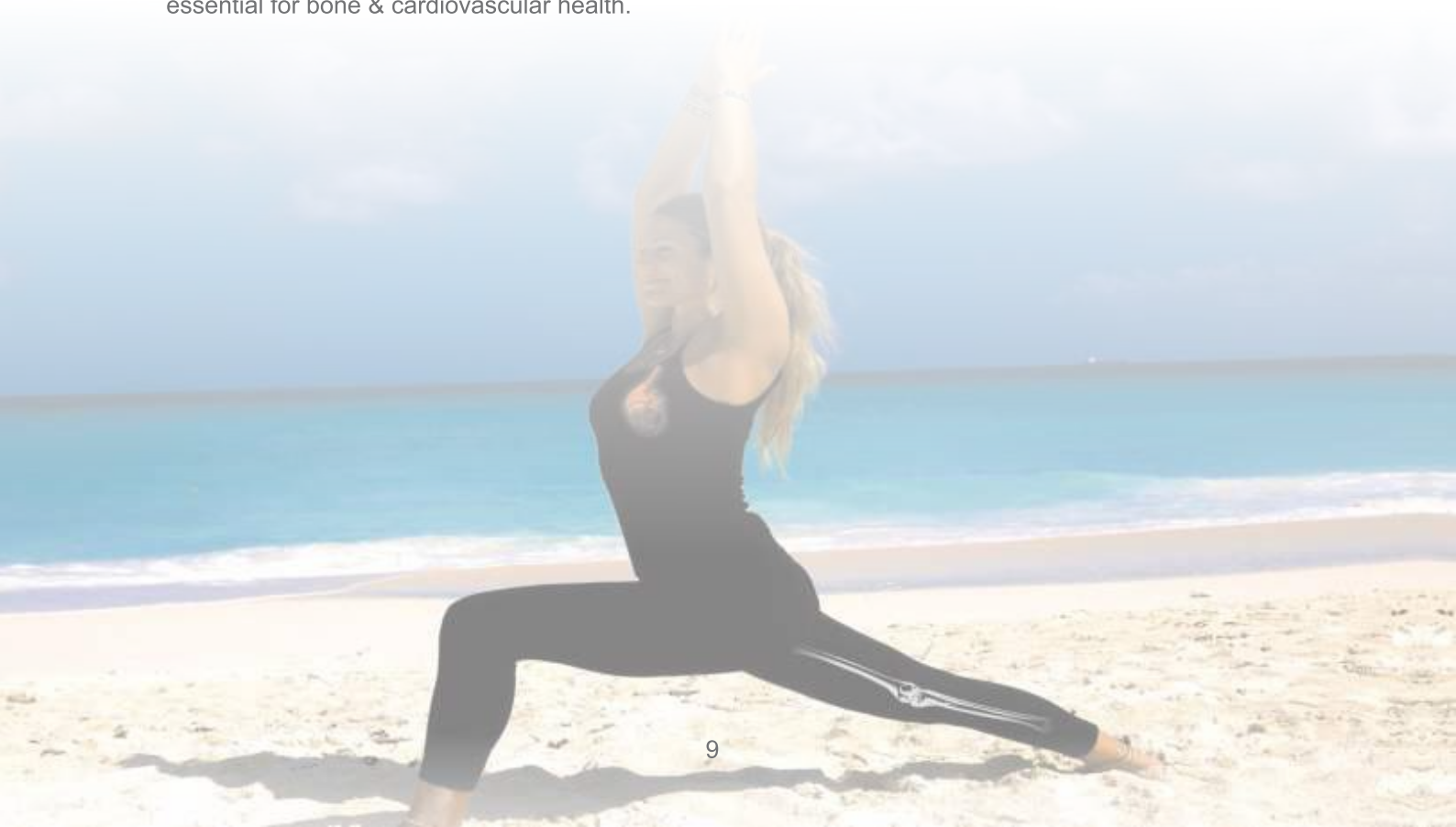
- Building and maintaining strong bones.
- Preventing the calcification of arteries.
- Promoting blood vessel elasticity.

Several studies show that supplementing with calcium is not enough for optimal bone health. Adding vitamin D and vitamin K significantly improved bone health. The scientific rationale and documentation is that vitamin D stimulates the synthesis of osteocalcin, while vitamin K2 is needed for the activation of osteocalcin. Only the vitamin K2 activated osteocalcin will bind calcium optimally. In this way both vitamin D and vitamin K2 work in synergies to make the body able to use calcium efficiently for improved bone health.

British Medical Journal (BMJ 2005): "Prevention of fractures with Calcium and Vitamin D is not enough....combining Vitamin K, Vitamin D and Calcium seems ideal....."¹⁷

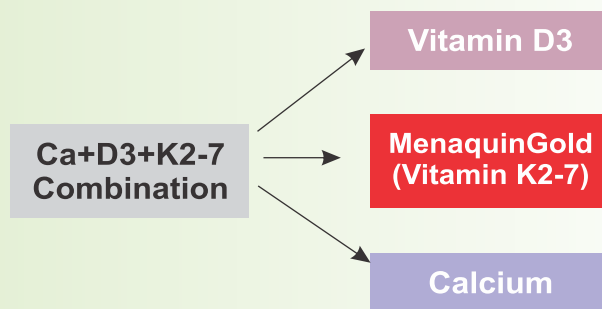
Vitamin K2 may be the solution to keeping Calcium in its place!

Ca+D3+K2-7 Combination will thus help to keep calcium in bones and out of arteries essential for bone & cardiovascular health.

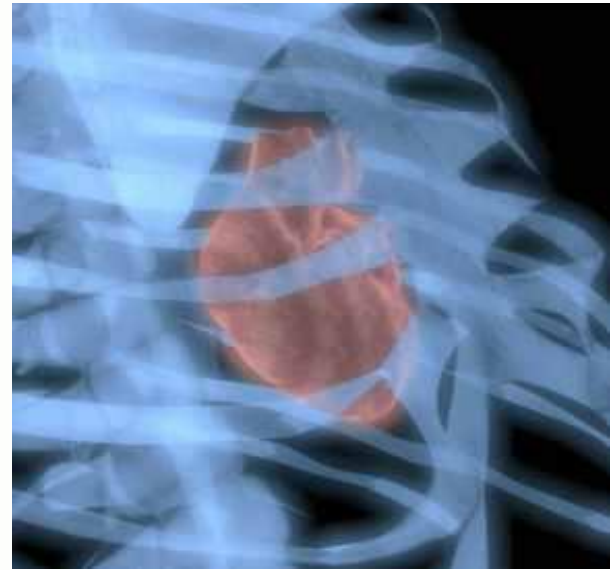




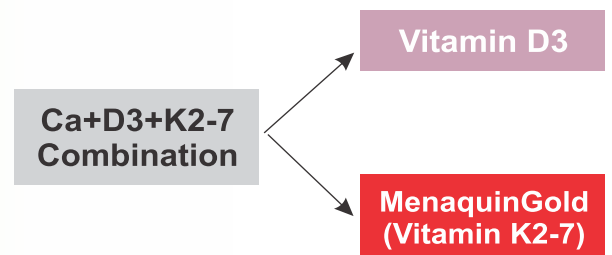
How does Ca+D3+K2-7 Combination aim to strengthen bones?



- **Vitamin D3:** Increases the production of Osteocalcin by the Osteoblasts (bone-forming cells)
- **MenaquinGold®:** Is necessary to “activate” osteocalcin that binds Calcium effectively to the bone.
- **MenaquinGold®:** Inhibits the production of osteoclasts (bone-destroying cells)
- **Calcium:** To be deposited effectively into the bone.



How does Ca+D3+K2-7 Combination aim to promote cardiovascular health?



- **Vitamin D3:** Increases the production of Matrix Gla-Protein (MGP).
- **MenaquinGold®:** Is necessary to “activate” MGP to inhibit calcification of the arteries.
- **MenaquinGold®:** Promotes blood vessel elasticity by safeguarding elastin, the protein responsible for the elasticity of the arterial wall.
- **MenaquinGold®:** Ensures that calcium is deposited into the bone and doesn't leak into the bloodstream where it may deposit into the arteries.

Ca+D3+K2-7 Combination is the simple solution to putting calcium in its place...

Viridis – A Reliable Supplier

Synergia Life Sciences (A Viridis Group Company) manufactures and supplies Vitamin K2-7 (**MenaquinGold®**) as raw material in powder, granules or oil, for use in Food Supplement, Fortified Food and Animal Food in global markets.

MenaquinGold® – A unique and well documented ingredient

- Novel Food Approval (EC Notified List)
- Self-affirmed GRAS
- Extensive Safety & Toxicity Studies

Acute Toxicity Study

Chronic Toxicity Study

Genotoxicity Protection Study

Genotoxicity Study

Ames Test

LD₅₀ Study

- cGMP & NSF GMP Certified
- Kosher & Halal Certified
- HACCP & ISO 22000 Certified
- Extensive Stability Studies for all Grades
- Equivalent DMF - CTD
- Water Dispersible and Oil Soluble forms of the product for Food and Drinks use
- Production is both cGMP and Pharma Grade
- Product is used in Pharmaceutical formulations
- Continuous Innovation and Technical Support
- Flexibility in response to customer inquiries
- Inventory maintained as per customer requirements



MenaquinGold® – For People at all Ages

- Modern lifestyles require Vitamin K2 supplementation for various extra-hepatic tissues (outside the liver) as not enough is available for them through our diet and hence the majority of children and adults are Vitamin K deficient
- Children should take MenaquinGold® daily to develop strong bones so they reach maximum peak bone mass before by the age of 30-35 years (see figure1)
- Women should take MenaquinGold® daily to maintain strong bones before and during menopause to prevent Osteoporosis, improve bone density, reduce the risk of getting Cardiovascular Diseases, Myocardial Infarction and Stroke
- Men should MenaquinGold® daily to prevent Cardiovascular Diseases, and at the same time reach optimal bone strength



Viridis BioPharma Pvt. Ltd.

Viridis BioPharma is a reputed Indian BioPharmaceutical company involved in research, manufacturing, techno-marketing and distribution of innovative active ingredients for the management of chronic metabolic disorders and various health care applications including wound healing. Our areas of application are ever expanding with breakthrough solutions for diverse industries and applications. Through our strategic association with research organizations and pharma companies of international repute, we are well positioned to identify and commercialize products with efficacy and growth potential. We are the techno marketers for Pharmaceuticals, Nutraceuticals, Cosmeceuticals, Medical Devices, Animal Nutrition and Synthetic Chemicals.

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Manufactured by :

Synergia **SYNERGIA LIFE SCIENCES PVT. LTD.**
Life Sciences (A Viridis Group Company)

VIRIDIS
THE ACTIVEedge

6/10, Jogani Industrial Complex, V. N. Purav Marg,
Chunabhatti, Mumbai - 400 022. (India)
Tel. : (91-22) 2405 5607-09 Fax : (91-22) 2405 5952
Email : info@viridisbiopharma.com
Web: www.viridisbiopharma.com