

### An Interview with Dr. Ralph Holsworth, D.O. and Dr. Mark Swanson, N.D.

*I appreciate the expertise you will share with us today. Can you tell us a little about your backgrounds?*

**Dr. Swanson:** I received my naturopathic degree from Bastyr University in 1984. I have spent 20 years in a nutritionally-oriented private practice in Washington state. I am also a former Acquisitions Editor for the AANP Journal of Naturopathic Medicine. I have been a Pure Encapsulations customer and consultant for almost 15 years.

**Dr. Holsworth:** I am a board-certified family medicine osteopathic physician and have clinically researched enzymes for the last 10 years. I was the first U.S. physician to introduce nattokinase, specifically NSK-SD™, to the medical community in 2001. The significance of this is that vitamin K<sub>2</sub> is removed from NSK-SD™ by the manufacturer, Japan BioScience Laboratories, Inc. The resulting vitamin K<sub>2</sub>, specifically MK-7, is perhaps the most beneficial form of vitamin K.

*Vitamin K's role in blood coagulation is well recognized. Can you comment about the emerging interests of vitamin K in bone and arterial health?*

**Dr. Swanson:** Osteocalcin, the most abundant non-collagen protein found in bone, is carboxylated by vitamin K. This produces the active form of osteocalcin, which helps to deposit calcium into bones. Increased undercarboxylated osteocalcin serum concentration is an undesirable indicator of excess bone turnover. That's why, especially as we age, it is important to maintain optimal carboxylation and activation of osteocalcin with vitamin K. When it comes to arteries, carboxylation by vitamin K catalyzes the biosynthesis of Matrix Gla Protein (MGP) in the arterial wall, which maintains healthy soft tissue calcium metabolism. Healthy vitamin K status minimizes the amount of serum undercarboxylated MGP.

**Dr. Holsworth:** Unfortunately, vitamin K requirements to date have only been estimated for the liver and not for extra-hepatic tissues. Vitamin K dependent proteins in the liver are responsible for maintaining healthy blood coagulation and platelet function.

As recognition for the role of vitamin K in extra-hepatic tissues increases, so will the utilization of vitamin K<sub>2</sub> (MK-7), which has a specific affinity for these tissues. This will certainly help to better address concerns related to bone and vascular health.

*What is the difference between vitamin K<sub>1</sub> and two forms of vitamin K<sub>2</sub>, MK-4 and MK-7?*

**Dr. Swanson:** Vitamin K<sub>1</sub> (phylloquinone) is the most common form and is found in green vegetables like brussels sprouts, spinach, chard, peas and green beans in addition to soybean and olive oils. Meat, egg yolk, and dairy are typical sources of vitamin K<sub>2</sub> (menaquinones) as menaquinone-4, or MK-4. Fermented food like Japanese natto is a source of menaquinone-7, or MK-7. MK-4 is also the form of vitamin K naturally produced by bacteria in the gastrointestinal tract. The synergy of vitamin K forms should be looked upon similarly to the benefits of using mixed tocopherol vitamin E as opposed to using alpha tocopherol alone.

**Dr. Holsworth:** The chemical differences between vitamin K<sub>1</sub>, MK-4 and MK-7 involve varying side chains on their ring structure. This does in fact provide them with different properties. After vitamin K is absorbed in the intestines, it is distributed to the liver, bones, arterial vessels and other tissues. Where it is most likely to concentrate depends on the form. Vitamin K<sub>1</sub> and MK-4 are primarily concentrated in the liver. Once the liver becomes saturated with these forms, only then do they typically work to support other tissues, like bone. MK-7, on the other hand, concentrates in extra-hepatic tissues, especially vascular tissues. It appears that vitamin K<sub>1</sub> may be most supportive for bone health but may require higher doses than MK-4 or MK-7 to do so. MK-4 and MK-7 may be most supportive for arterial health, with MK-7 believed to be the more advanced and effective of the forms. MK-7 also has a longer half-life, about 48 hours compared to 1 hour for



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vitamin K<sub>1</sub> and 1½ hours for MK-4. It is also better absorbed—90% compared to as low as 10% or less of vitamin K<sub>1</sub>. That is why you typically need less MK-7 for the health benefits of vitamin K.

#### *Who is at risk for vitamin K deficiency?*

**Dr. Swanson:** Of course, individuals who don't obtain enough vitamin K from consuming a healthy diet are at risk. Consumption from a varied diet may reach about 300-500 mcg per day of vitamin K but many individuals fall short of this. Still, deficiency is more likely in people with fat malabsorption conditions, including Crohn's disease, celiac disease, cystic fibrosis, chronic pancreatitis, and liver disease. People with impaired kidney function or those who use antibiotics for extended periods of time may also be at greater risk. Of major clinical significance is recognizing that there is a widespread vitamin K insufficiency, which has a profound impact on bone mineralization, joint and cartilage composition, and vascular function.

**Dr. Holsworth:** It is also important to remember that the majority of individuals deficient in vitamin K have a deficiency in the extra-hepatic tissues, not in the liver. This realization is why MK-7 is fast gaining the attention of the medical community.

#### *Why is vitamin D an important cofactor for vitamin K formulations?*

**Dr. Swanson:** Recent studies indicate that vitamin D enhances the activity of MGP and that the combination of vitamin K and D provides synergistic support for healthy arterial calcium metabolism and blood vessel function. In addition, the synthesis of osteocalcin by osteoblasts in bone is regulated by vitamin D. In general, the consequences of suboptimal levels of either vitamin are the same.

**Dr. Holsworth:** Dr. Vermeer, a scientist at the Cardiovascular Research Institute Maastricht with whom I have worked closely with, has investigated the beneficial effects of vitamins D and K on the elastic properties of blood vessels in postmenopausal women. The study also supports that MK-4 and MK-7 are in fact the most beneficial forms of vitamin K for heart health.

#### *Why do a number of studies utilize 45 mg per day vitamin K?*

**Dr. Holsworth:** These studies are based on pharmacological doses used in Japan, involving 3 capsules per day of 15 mg MK-4, about 500 times the recommended daily allowance. We know that vitamin K<sub>1</sub> at levels of 500–1,000 mcg is supportive of bone health and that vitamin K<sub>2</sub>, because of its better absorption, longer half life, and concentration in extra-hepatic tissues, may be even more helpful for bone and heart health at lower concentrations.

**Dr. Swanson:** The intestinal synthesis of MK-4 occurs in the colon with limited absorption compared to oral vitamin K<sub>1</sub> or MK-7, which is absorbed in the small intestine. This may be a reason why large supra-physiological amounts of MK-4 are given therapeutically by the Japanese researchers. It's also very expensive. The synergistic combination of physiological dosages of MK-4, natto MK-7, K<sub>1</sub> and D may provide equal health benefits at a more affordable cost.

#### *What recommendations do you have for testing individuals for vitamin K status?*

**Dr. Swanson:** In general, testing vitamin K status routinely will not be as clinically relevant compared to testing vitamin D levels, using 25 (OH) vitamin D. The classic measure of vitamin K deficiency involves prothrombin and clotting time, but this is of little value for determining vitamin K status in bones or arteries. For bones, the percentage of undercarboxylated osteocalcin (ucOC) in the serum may provide a helpful indication of vitamin K status while the percentage of undercarboxylated MGP (ucMGP) in the serum may reveal vitamin K status in the arteries. In fact blood coagulation tests may appear normal in individuals with undercarboxylated osteocalcin or MGP.

#### *What complementary support products do you recommend with vitamin K?*

**Dr. Swanson:** For bone support, the combination of vitamin K, strontium, magnesium, boron, vitamin D<sub>3</sub>, fish oils, B vitamins and calcium are essential. Excellent choices are Synergy K, Cal/Mag w/Cofactors or OsteoBalance™, Nutrient 950® and EPA/DHA essentials. Many people don't make the connection between fish oil and bone health, but studies have suggested its role in calcium absorption and bone mineralization. For cardiovascular health, I would also emphasize the combination of Nutrient 950, vitamin K and fish oils as a base.

#### *What is the safety profile of vitamin K? Drug interactions?*

**Dr. Swanson:** There is no toxicity associated with vitamin K. Only small amounts of it are stored in body tissues. Even in high doses, with as much as 45 mg being used in some studies, vitamin K has not produced symptoms of toxicity. There has been no upper limit established by the Institute of Medicine at the National Academy of Sciences.

Individuals taking Coumadin/warfarin should avoid vitamin K unless it is specifically recommended by their health care professional. A number of medications increase the need for vitamin K, including antibiotics, anticonvulsants, bile acid sequestrants and others. Pregnant or lactating women should not take vitamin K supplements exceeding the daily allowance of 65 mcg.

The information contained herein is for informational purposes only and does not establish a doctor-patient relationship. Please be sure to consult your physician before taking this or any other product. Consult your physician for any health problems.

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