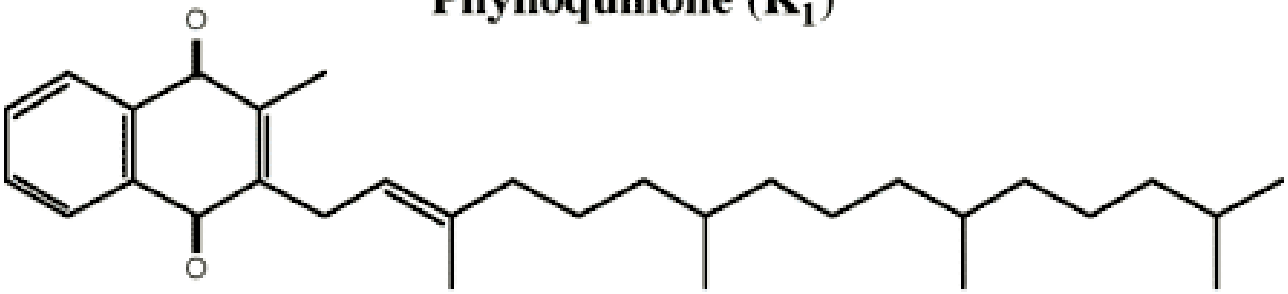
Sultan Qaboos University

College of Agricultural & Marine Sciences

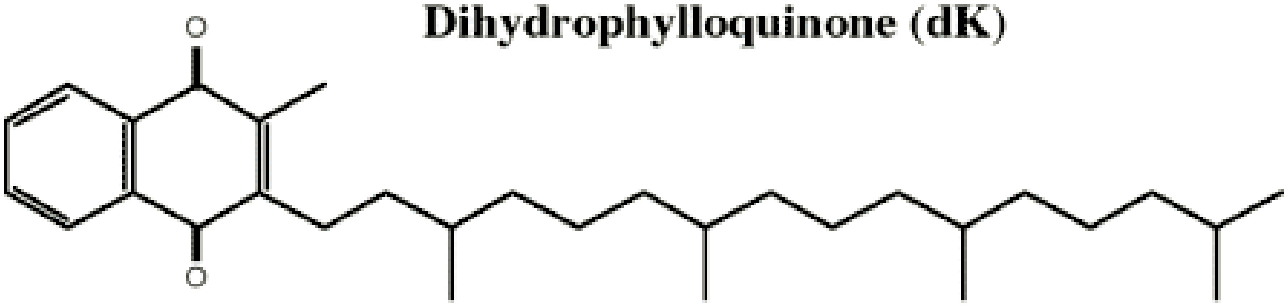
Vitamin K

Lecture Summary

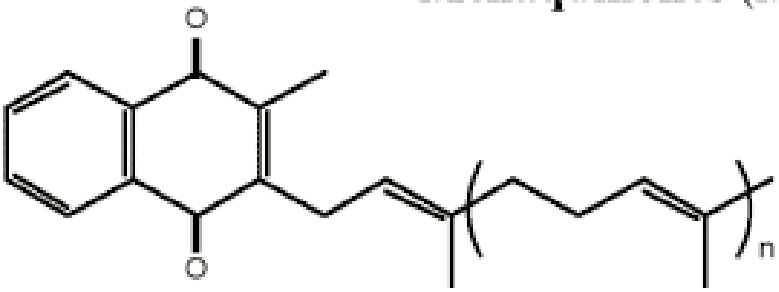
Phylloquinone (K_1)



Dihydrophylloquinone (dK)



Menaquinones (MK-n)



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Introduction:

Vitamin K is a group of structurally similar of two naturally occurring fat-soluble vitamins, vitamin K1 and vitamin K2. Vitamin K1 is also known as phylloquinone (2-methyl 3-phytyl 1, 4-naphthoquinone) or phytomenadione (phytonadione), while vitamin K2 includes menaquinone (MK) and menatetrenone. Vitamin K1 is made by plants. However, vitamin K2 is typically produced in the large intestine by bacteria. Vitamins K3, K4 and K5 also exist - they are synthetic forms and are used to inhibit fungal growth as well as by the pet food industry. Compounds with vitamin K activity all have a 2-methyl-1, 4-naphthoquinone ring.

Vitamin K is crucial for proper blood coagulation - it helps make 4 of the 13 proteins required for blood clotting such as prothrombin (factor VII), Christmas Factor (factor IX) and Stuart-Prower factor (factor X). It facilitates the incorporation of sugars in the proteins at a post-ribosomal stage. Thus it's important in preventing the hemorrhagic disease. It is also involved in maintaining good bone health (calcification) with aid of vitamin D as we age and can reduce the risk for hip fracture women. The known bone protein called collagen is vitamin K dependent. Vitamin k dependent carboxylation of glutamic acid is required to produce Y-carboxyglutamic acid. But do not have any anti-oxidant activities. The natural products are all fat soluble but water soluble derivatives showing most of the activity of the natural substances.

Osteoporosis and coronary heart disease are strongly associated with lower levels of vitamin K2. Menaquinone is not inhibited by salicylates as happens with K1, so menaquinone supplementation can alleviate the chronic vitamin K deficiency caused by long term aspirin use.

Sources:

Good sources of vitamin K1 are spinach, cabbage, kale, cauliflower, broccoli, avocado, kiwifruit and grapes. Vegetable oil is a rich source of this kind of vitamin (142-200 ug/100g). Good sources of vitamin K2 are meat, and eggs.

Food	Serving Size	Vitamin K (µg)	Food	Serving Size	Vitamin K (µg)
Kale, cooked	1/2 cup	531	Parsley, raw	1/4 cup	246
Spinach, cooked	1/2 cup	444	Spinach, raw	1 cup	145
Collards, cooked	1/2 cup	418	Collards, raw	1 cup	184
Swiss chard, cooked	1/2 cup	287	Swiss chard, raw	1 cup	299
Mustard greens, cooked	1/2 cup	210	Mustard greens, raw	1 cup	279
Turnip greens, cooked	1/2 cup	265	Turnip greens, raw	1 cup	138
Broccoli, cooked	1 cup	220	Broccoli, raw	1 cup	89
Brussels sprouts, cooked	1 cup	219	Endive, raw	1 cup	116
Cabbage, cooked	1/2 cup	82	Green leaf lettuce	1 cup	71
Asparagus	4 spears	48	Romaine lettuce, raw	1 cup	57

Table: Clinical Center, National Institutes of Health Drug Nutrient Interaction Task Force.

Absorption, Transportation and Metabolism:

Vitamin K1 is absorbed in the jejunum by energy dependent transport mechanism. Moreover; vitamin K2 is absorbed in both small distil intestine and colon by passive diffusion. Since they are fat soluble so its absorption is enhance through bile salt and pancreatic juice. Once absorbed they are incorporated into chylomicrons and enters lymphatic system. In the liver it has a short life and once entered they are incorporated into VLDL. Then carried out to various tissues like lung and kidney in LDL and HDL. Vitamin K turnover is 50-100 ug and assume to be the least if compared to other vitamins. The transmission across the placenta is poor and the neonate has low levels. Very little is stored and rapid depletion occurs with reduced intake.

Warfarin and other drugs block the action of the vitamin K epoxide reductase. This results in decreased concentrations of vitamin K and vitamin K hydroquinone in the tissues, such that the carboxylation reaction catalyzed by the glutamyl carboxylase is inefficient. This results in the production of clotting factors with inadequate Gla. Without Gla on the amino termini of these factors, they no longer bind stably to the blood vessel endothelium and cannot activate clotting to

allow formation of a clot during tissue injury. As it is impossible to predict what dose of warfarin will give the desired degree of suppression of the clotting, warfarin treatment must be carefully monitored to avoid over-dosing.

Recommendation:

Due to sterile condition of the intestine tract during the infant birth who may lack the bacteria which synthesizing the vitamin K inside the human. Lower concentration of vitamin K during this period may cause low prothrombin level. Thus to prevent uncontrolled bleeding in the newborn, the American Academy of pediatrics (AAP) recommends that a single dose of vitamin K be given at birth.

In 2001 the adequate intake level for vitamin K in men was recommended as 120 ug/day and in women as 90 ug/day. A normal diet can contain from 300 to 500 ug/day of vitamin k sources. The bacteria inside the intestine provide about 1-1.5 mg of vitamin K daily. Due to lack of adequate evidence no national authority defines a specific RDA but there are many suggestions.

Vitamin K status is assessed by the determination of the specific clotting factors. It is also possible to measure serum phylloquinone level.

Deficiency:

Vitamin K deficiency is extremely rare in healthy adults but could fatal if not noticed for so long. Newborn infants may have a higher risk until their intestinal bacteria start production. Vitamin K deficiency among infants is potentially dangerous because it can lead to bleeding (hemorrhage) in the brain and other vital organs. Patients with liver damage, alcoholics, those with cystic fibrosis, inflammatory bowel disease, as well as those who have had surgical procedures in their abdomen have a higher risk of vitamin K deficiency. Some people with eating disorders, such as bulimia have a higher risk of vitamin K deficiency, as well as individuals on very severe or strict diets. Patients who are taking anticoagulants, salicylates, barbiturates, or cefamandole may also have a higher risk of bleeding because it’s interfering with metabolism and activity of the vitamin K. Deficiency may lead also to poor skeletal mineralization and fat mal-absorption.

Signs and symptoms of vitamin K deficiency may include:

- Heavy menstrual bleeding
- Anemia
- Nose bleeds
- Bleeding gums
- Osteoporosis is strongly linked to low vitamin K2 levels
- Coronary heart disease is strongly linked to low vitamin K2 levels

Vitamin K1 is degraded much slowly than vitamin K2 and metabolites are excreted in urine and feces as “glucuronides”.

Toxicity:

As the deficiency, toxicity is also very rare and high doses reduce effectiveness of anticoagulant. It’s noticed in infants and pregnant women more once the supplementation of vitamin K is exceeding the normal limits. Effects like hemolytic anaemia and jaundice is more common. Red blood cell lysis thus high bilirubin concentration will be in human plasma sample (yellowish coloring of the skin). Hyperbilirubinaemia may cause serious brain damage. The side effect of vitamin K1 such as sensation of heat in the head, dyspnoea and pain in the chest.

References:

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