
Available online through
http://jprsolutions.info

Vitamin K₁ (Phylloquinone) – A review

Department of Pharmacognosy, Sree Vidyanikethan College of Pharmacy, Tirupathi 517 102, (A.P) India.

Received on:15-07-2013; Revised on:19-08-2013; Accepted on:23-09-2013

ABSTRACT
Phylloquinone known as vitamin K₁ is considered as essential fat-soluble micronutrient. It is the major dietary source of vitamin K, which is concentrated in leafy vegetables and it is the best available form of vitamin K in terms of food composition and dietary intakes. The present review is on vitamin K₁ which involves introduction, structure, function, beneficial effects, deficiency effects on human health and dietary sources of phylloquinone.

Key words: Phylloquinone, Vitamin K₁, Functions, Dietary sources, Deficiency.

1. INTRODUCTION:
Vitamin K₁, also known as phylloquinone, phytomenadione or phytomenadione is synthesized by plants. It is distributed mostly in green leafy vegetables (normally in 400–700 µg/100 g) because it is directly involved in photosynthesis. It is also called as the “plant form” of vitamin K. The next best sources of vitamin K are certain vegetable oils (e.g., soybean, rapeseed, and olive oils) which contain 50–200 µg/100 g. Some vegetable oils, such as peanut, corn, sunflower and safflower oils, have lower phylloquinone content (1–10 µg/100 g) 1. The chief source of vitamin K is synthesis by bacteria in the large intestine. The phylloquinone content of human milk was between 1 and 4 µg/l 2.

1.1 HISTORY:
Dam et al (1935) proposed that the anti-haemorrhagic vitamin of the chick was a new fat-soluble vitamin, and he called it as “vitamin K” 3. Edward Adelbert Doisy of Saint Louis University discovered the structure and chemical nature of vitamin K 4. Phylloquinone (a purified form of vitamin K) was isolated from plants in 1939 and used to treat nutritional deficiency characterized by decreased prothrombin levels. Unlike other nutrients, vitamin K₁ is stored in small amounts in the body suppressing its deficiency. Therefore, regular intake of vitamin k will boost up coagulation vitamin levels in body 5. As the vitamin in body is found in soft tissues, cartilage and bones where it plays an important role in protein synthesis without which, normal bone growth and development would not be possible.

1.2 STRUCTURE:
Vitamin K₁ (phylloquinone) contains a functional naphthoquinone ring, an aliphatic side-chain and a phytol side-chain containing four isoprenoid residues, one of which is unsaturated.

Nomenclature – 2-Methyl-3 Phytol-1, 4- naphthoquinone.

Fig: 1. Structure of phylloquinone

2. FUNCTION:
The function of vitamin K involves a post-translational modification of the protein. The vitamin K acts as a cofactor in a specific carboxylation reaction, which transforms selective glutamate (Glu) residues to γ-carboxyglutamate (Gla) residues. Vitamin K – dependent carboxylation or γ-glutamyl, a microsomal enzyme catalyses the reaction, which is linked to a cyclic pathway known as the vitamin K epoxide cycle. The carboxylation reaction converts vitamin K quinol to vitamin K 2, 3-epoxide 6. Vitamin K 2, 3-epoxide is reduced to the quinone and then to the quinol by vitamin K epoxide reductase. The reductase activity is dithiol dependent which is inhibited by coumarin anticoagulants like warfarin. Dietary vitamin K may enter the cycle through NAD (P) H-dependent vitamin K reductase activity, which is not inhibited by warfarin. The vitamin K cycle involves reduction and subsequent reoxidation of vitamin K coupled with carboxylation of Glu 7.

2.1 BLOOD CLOTTING:
The vitamin K₁ is an anti-haemorrhagic factor that is needed for the synthesis of four vitamin K-dependent pro-coagulants (factor II or
prothrombin, and factors VII, IX, and X) like serine proteases. They are synthesized in the liver and then released into the circulation as inactive forms (zymogens). When coagulation is initiated, the zymogens of the vitamin K dependent clotting factors are cleaved to yield the active protease clotting factors. The activity of this protease depends on their normal complement of Gla residues, which are efficient chelators of calcium ions. Vitamin K-dependent gamma-carboxylation of specific glutamic acid residues in those proteins makes it possible for them to bind calcium. In the presence of Gla and calcium ions these proteins bind to the surface membrane phospholipids of platelets and endothelial cells together with other cofactors, which form membrane-bound enzyme complexes.

Two other vitamin K-dependent proteins called protein C and protein S play a regulatory role in the inhibition of coagulation. The function of protein C is to degrade phospholipid-bound activated factors V and VIII in the presence of calcium. Protein S acts as synergistic cofactor while protein C act by enhancing the binding of activated and VIII in the presence of calcium. Protein S acts as synergistic cofactor while protein C acts by enhancing the binding of activated protein C to negatively charged phospholipids and another vitamin K-dependent plasma protein (protein Z) is suspected to have a function.

2.2 PROCESS OF BONE MINERALIZATION:

Apart from coagulation proteins, three other vitamin K-dependent proteins have been isolated they are Osteocalcin, Matrix Gla Protein (MGP) and Protein S from bone, cartilage, kidney, lungs, and other tissues, in which only two, osteocalcin and matrix Gla protein (MGP), have been well characterised. Both are found in bone but MGP also occurs in cartilage, blood vessel walls, and other soft tissues. The capacity of osteocalcin in mineral-binding requires vitamin K-dependent gamma-carboxylation of three glutamic acid residues. The function of osteocalcin is thought to be related to bone mineralization. MGP has been found in bone, cartilage, and soft tissue, including blood vessels and prevents the calcification of soft tissue and cartilage, while facilitating normal bone growth and development. The anticoagulant protein S is also synthesized by osteoblasts, but its role in bone metabolism is not clear. Children with inherited protein S deficiency suffer from problems related to increased blood clotting and decreased bone density.

2.3 CELL REGULATION

In 1993, Growth Arrest-Specific protein 6 (Gas6), a vitamin K-dependent protein was identified which has been found throughout the nervous system, as well in the heart, lungs, stomach, kidneys, and cartilage. The exact mechanism of its action is not clear, but it appears to be a cellular growth regulation factor with cell-signaling activities. Gas6 is important in diverse cellular functions, including cell adhesion, cell proliferation and protection against apoptosis. It also plays important roles in the developing and aging nervous system. Further, it appears to regulate the platelet signaling and vascular homeostasis.

3. DIETARY SOURCES:

Phylloquinone dietary sources and the amount present are given in the table 1, which is based on USDA (US Department of Agriculture) National Nutrient Database Release 22 (SR22). The values are mean nutrient values per 100 grams of the edible portion.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Plant Name</th>
<th>Common Name</th>
<th>Family</th>
<th>Part of plant</th>
<th>Amount present per 100 gms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Ocimum sanctum</td>
<td>Basil</td>
<td>Lamiaceae</td>
<td>Seeds</td>
<td>1,714.5 mcg</td>
</tr>
<tr>
<td>2.</td>
<td>Salvia officinalis</td>
<td>Sage</td>
<td>Polygonaceae</td>
<td>Leaves</td>
<td>1,714.5 mcg</td>
</tr>
<tr>
<td>3.</td>
<td>Thymus vulgaris</td>
<td>Thyme</td>
<td>Lamiaceae</td>
<td>Seeds</td>
<td>1,714.5 mcg</td>
</tr>
<tr>
<td>4.</td>
<td>Coriandrum sativum</td>
<td>Coriander</td>
<td>Apioaceae</td>
<td>Leaves</td>
<td>1,359.5 mcg</td>
</tr>
<tr>
<td>5.</td>
<td>Petroselinum crispum</td>
<td>Parsley</td>
<td>Apioaceae</td>
<td>Leaves</td>
<td>1,359.5 mcg</td>
</tr>
<tr>
<td>6.</td>
<td>Amaranthus caudatus</td>
<td>Amaranth</td>
<td>Amaranthaceae</td>
<td>Leaves</td>
<td>1,140.0 mcg</td>
</tr>
<tr>
<td>7.</td>
<td>Beta vulgaris</td>
<td>Chard, swiss</td>
<td>Amaranthaceae</td>
<td>Leaves</td>
<td>830.0 mcg</td>
</tr>
<tr>
<td>8.</td>
<td>Brassica oleracea</td>
<td>Kale</td>
<td>Brassicaceae</td>
<td>Leaves</td>
<td>817.0 mcg</td>
</tr>
<tr>
<td>9.</td>
<td>Origanum vulgare</td>
<td>Marjoram</td>
<td>Lamiaceae</td>
<td>Leaves</td>
<td>621.7 mcg</td>
</tr>
<tr>
<td>10.</td>
<td>Lepidium sativum</td>
<td>Cress</td>
<td>Brassicaceae</td>
<td>Leaves</td>
<td>541.9 mcg</td>
</tr>
<tr>
<td>11.</td>
<td>Spinacia oleracea</td>
<td>Spinach</td>
<td>Amaranthaceae</td>
<td>Leaves</td>
<td>482.9 mcg</td>
</tr>
<tr>
<td>12.</td>
<td>Chrysanthemum coronarium</td>
<td>Chrysanthemum</td>
<td>Astereaceae</td>
<td>Leaves</td>
<td>350.0 mcg</td>
</tr>
<tr>
<td>13.</td>
<td>Cichorium intybus</td>
<td>Chicory greens</td>
<td>Astereaceae</td>
<td>Leaves, roots</td>
<td>297.6 mcg</td>
</tr>
<tr>
<td>14.</td>
<td>Brassica rapa</td>
<td>Turnip greens</td>
<td>Brassicaceae</td>
<td>Roots</td>
<td>251.0 mcg</td>
</tr>
<tr>
<td>15.</td>
<td>Nasturtium officinale</td>
<td>Watercress</td>
<td>Brassicaceae</td>
<td>Leaves</td>
<td>250.0 mcg</td>
</tr>
<tr>
<td>16.</td>
<td>Cichorium endivia</td>
<td>Endive</td>
<td>Astereaceae</td>
<td>Leaves</td>
<td>231.0 mcg</td>
</tr>
<tr>
<td>17.</td>
<td>Allium schoenoprasum</td>
<td>Chives</td>
<td>Amaryllidaceae</td>
<td>Leaves</td>
<td>212.7 mcg</td>
</tr>
<tr>
<td>18.</td>
<td>Glycine max</td>
<td>Soybean</td>
<td>Fabaceae</td>
<td>Oil of seeds</td>
<td>183.9 mcg</td>
</tr>
<tr>
<td>19.</td>
<td>Lactuca sativa</td>
<td>Lettuce</td>
<td>Astereaceae</td>
<td>Leaves</td>
<td>173.6 mcg</td>
</tr>
<tr>
<td>20.</td>
<td>Piper nigrum</td>
<td>Pepper</td>
<td>Piperaceae</td>
<td>Seeds</td>
<td>163.7 mcg</td>
</tr>
<tr>
<td>21.</td>
<td>Syzygium aromaticum</td>
<td>Clove</td>
<td>Myrtaceae</td>
<td>Flower buds</td>
<td>141.8 mcg</td>
</tr>
<tr>
<td>22.</td>
<td>Colocasia esculenta</td>
<td>Taro</td>
<td>Araceae</td>
<td>Leaves</td>
<td>108.6 mcg</td>
</tr>
<tr>
<td>23.</td>
<td>Eruca sativa</td>
<td>Arugula</td>
<td>Brassicaceae</td>
<td>Leaves</td>
<td>108.6 mcg</td>
</tr>
</tbody>
</table>
4. BENEFICIAL EFFECTS:

- Both physiological and observational evidence suggest that vitamin K, plays a role in bone growth and the maintenance of bone density. Vitamin K supplementation promotes osteotrophic processes and slows osteoclastic processes through calcium bonding. The primary function is to prevent over calcification of the bone and cartilage. Studies suggested that an inverse relationship between dietary vitamin K and the risk of hip fracture.

- Human studies showed that high vitamin K intake is associated with reduced coronary artery calcification and reduced risk of CVD. These effects are thought to be mediated by increased activation of MGP.

- Alzheimer’s disease: In brain, vitamin K participates in the synthesis of sphingolipids, an important class of lipids present in high concentrations in brain cell membranes. Studies suggest that vitamin K has the potential to influence psychomotor behavior and cognition. Alterations in sphingolipid metabolism results to age-related cognitive decline and neurodegenerative diseases such as Alzheimer’s disease (AD).

- Cancer: Researchers studied the role of vitamin K in the prevention of bone loss in females with liver disease and proved that women supplemented with vitamin K were 90% less likely to develop liver cancer.

- Diabetes, a research showed that total diabetes risk of individual who have highest circulating levels of vitamin K were 51% lower than those with the lowest levels. The researchers reported that dietary phylloquinone intake is associated with reduced risk of type 2 diabetes.

- Non-Hodgkin lymphoma, research showed that the risk of developing non-Hodgkin lymphoma was decreased by 45 percent in the study participants who had the highest vitamin K levels compared to participants with the lowest levels of the vitamin.

- To reverse the effects of “blood thinning” medications when taken at high doses;

- To prevent clotting problems in newborns;

- To treat bleeding caused by medications including salicylates, sulfonamides, quinine, quinidine, or antibiotics.

- To treat and prevent vitamin K deficiency,

- To prevent and treat weak bones (osteoporosis);

- To relieve itching that often accompanies a liver disease called biliary cirrhosis,

- To remove spider veins, bruises, scars, stretch marks, burns and also to treat rosacea, a skin condition that causes redness and pimples on the face. After surgery, vitamin K is used to speed up skin healing and reduce bruising and swelling.

5. DEFICIENCY:

Deficient is rare because, vitamin K is continuously recycled in cells. Primary deficiency occurs in new born infants and those who suffer from liver damage or disease (e.g. alcoholics), cystic fibrosis, inflammatory bowel diseases and person recently had abdominal surgeries. Secondary vitamin K deficiency occurs in bulimics, those on stringent diets, and those taking anticoagulants. Drugs causing vitamin K deficiency include salicylates, barbiturates and cefamandole.

Vitamin K deficiency can result in coagulopathy, a bleeding disorder.
and decrease in bone density. Symptoms of K_1 deficiency include anaemia, bruising, and bleeding of the gums or nose in both sexes, and heavy menstrual bleeding in women. Vitamin K deficiency bleeding occurs in the first week of the infant’s life is estimated at 0.25 to 1.7%, with two to 10 cases per 100,000 births. Premature babies have even lower levels of the vitamin, leading to hospitalizations, blood transfusions, brain damage, and death, which can be prevented by Intramuscular administration effectively than oral administration.

CONCLUSION:

Vitamin K_1 plays a major role in our metabolic processes. It is used to reverse the effects of “blood thinning” medications when given in high doses. It prevents clotting problems in newborns and to treat bleeding caused by medications including salicylates, sulfonamides, quinine, quinidine, or antibiotics. It is also given to treat and prevent its deficiency, used to prevent and treat weak bones (osteoporosis). After surgery, vitamin K_1 is used to speed up skin healing and reduce bruising and swelling. An increased understanding of the role of vitamin K in the body beyond blood clotting led some researchers to suggest that the recommended amounts for dietary intake of vitamin K_1 be increased.

REFERENCES:


Source of support: Nil, Conflict of interest: None Declared