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Vitamin K : A Micro-Nutrient with New Perspective

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ABSTRACT

Age-related diseases are becoming more common as people live longer. According to scientific research, a nutritious diet containing beneficial fats, vitamins, minerals, or polyphenols may have antioxidant and antioxidant properties that slow ageing. Studies also show that vitamin K is an essential cofactor in activating many proteins that fight age-related diseases. Vitamin k1 (phylloquinone), which is mainly contained in plants, and vitamin k2 (menaquinone), which is mainly contained in animal foods and dairy products, are both naturally occurring fat-soluble vitamins. Benefits of vitamin K include improved heart disease, bone and cognitive health, and blood clotting. Vitamin K-dependent proteins such as clotting factors (II, VII, IX, X and prothrombin), protein C and protein S, osteocalcin, matrix Gla protein, and periostin support calcium homeostasis and regulate vascular wall mineralization. Inhibits and promotes bone mineralization. Controls and a host of other sequelae. Currently, the demand for vitamin K in health products is increasing. It is found mainly in dairy and meat products, vegetable oils, and green leafy vegetables. Adults need approximately 1 μg of vitamin K per kg of body weight. Vitamin K is popular because it deposits less, needs replenishment, and is difficult to absorb. This review seeks to synthesize information on the origin, metabolism of many forms of vitamin K, deficiency, recommended dietary intake, toxicity, and the role of vitamin K in preventing various therapeutic disorders.

Keywords - Vitamin K, phylloquinone, menaquinones, blood clotting, osteocalcin, homeostasis, calcification, bone mineralization, metabolism, and dairy products.

I. INTRODUCTION

Vitamin K, which was first identified by scientist Karl-Peter Henrik Damm, is a fat-soluble vitamin that affects the body's clotting mechanisms. He gave it the name vitamin K—"clotting" in German—and defined it as a hemostatic vitamin (1, 2). It is menadione, a 2-methyl-1,4-naphthoquinone having a variable side

chain at position 3 in its chemical structure (3). The three primary forms of vitamin K include phylloquinone (vitamin K1), which is the most prevalent form in green leafy greens including spinach, kale, and collards. Some animal species include a second form of menaquinone (vitamin K2) in animal foods and foods that have undergone fermentation. Menadione (vitamin K3), a potential synthetic substance that metabolises to phylloquinone, is a third kind. Menaquinones, with the exception of MK-4, are frequently generated in the human body by the bacteria.(3,4)

Vitamin K is required for protein synthesis involving a number of enzymes and functions as a cofactor for vitamin K-dependent carboxylation. By connecting clotting factors to calcium ions through the process of vitamin K carboxylation, the cascade pathway is further facilitated. In addition, vitamin K is crucial for the health of bones, smooth muscles, and cartilage (1, 3, 4). Uncontrolled bleeding, pancreatic biliary tract illness, cardiovascular disease, and several age-related problems are all made more likely by low vitamin K levels (3, 5, 6). Vitamin K malabsorption, severe malnutrition, drug use that can result in conditions that impact gastrointestinal tract absorption, and vitamin K insufficiency are all examples of this.

Vitamin K is largely transported by lipoproteins and is found in the liver as well as other human tissues like the brain, heart, and bones of the circulatory system (7). The circulation of vitamin K is minimal in comparison to other fat-soluble vitamins due to rapid metabolism and excretion of vitamin K. According to phylloquinone measurements, the body retains only approximately to 40% of the oral physiological dose, whereas around 20% and 40% to 50% are eliminated in the urine, respectively and bile was expelled in the faeces. When compared to the opposite fat-soluble vitamin, vitamin K has a relatively low blood and tissue storage due to its rapid metabolism (7,8). Little is known about how gut bacteria create vitamin K and how that vitamin K is absorbed and transported, although studies show that the large intestine contains significant amounts of long-chain menaquinones (9).

II. METABOLISM OF VITAMIN K

Vitamin K1 is absorbed in the small intestine when bile and pancreatic juice are present (normal biliopancreatic function), whereas vitamin K2 is absorbed in the colon (10,11). Both are carried by the lymphatic system in chylomicrons that are high in triglycerides (12). The majority of K1 remains in the liver, although a little amount returns to the bloodstream and is transported to extrahepatic tissues by very-low-density lipoproteins (VLDL) (12). Low-density lipoproteins (LDL) transport menaquinones (MKs) to extrahepatic tissues. MK-4 is an anomaly, as it can be transported by both high- and low-density lipoproteins (12).

Vitamin K is not kept in large quantities by the body (13). The primary stocks of Phylloquinone (PKs) are located in the liver, heart, and pancreas, whereas long-chain MKs are found in other tissues (14).

III. VITAMIN-K DEPENDENT PROTEINS

Several clotting factors (Factors II, VII, IX, X), circulating anti-coagulants (proteins C, S, and Z), as well as proteins involved in bone and soft-tissue mineralization like osteocalcin (OC) and MGP (MatixGla protein), are among the K dependent Proteins (15). The primary purpose of vitamin K is to work as a cofactor with GGCX to produce proteins that depend on it (VKDP).

Osteocalcin is one of the primary non-collagenous proteins present in bones (OC). Osteoblasts and a few other cells release OC, also known as bone-Gla-protein (16). Ions and hydroxyapatite crystals are both bound by OC. In this manner, it appears that OC is prepared to exercise its regulatory effects on the structure of the bone extracellular matrix and to modify the size and form of the hydroxyapatite crystals (17). There is proof that OC has a function in a number of physiological processes other than bone metabolism, including glucose metabolism (18), energy metabolism (19), fertility, and ectopic calcification (20).

The VKDPs must be carboxylated in order to become biologically active, and they have been shown to play a significant role in angiogenesis, vascular calcification, and vascular cell migration. These findings highlight the part that vitamin K2 plays in the modulation process by activating the VKDPs. Matrix Gla Protein (MGP) is one such VKDP that, when activated, inhibits osteogenic factors, preventing the calcification of vascular and soft tissue (21).

The liver is where a VKDP, S, is mostly synthesised and has a role in anticoagulation. It is also secreted by osteoblasts and has an unknown mechanism of action in bone turnover (22).

Vitamin k dependent Gla protein	Function
Protein C, S and Z	Anticoagulant
Clotting factors Ⅱ Ⅶ X Ⅸ	Procoagulant
Liver	Hepatic carboxylation
Osteocalcin	Bone and calcium metabolism
Transmembrane GLA-protein	Signal transduction
Matrix-Gla-protein	Vascular calcification inhibitor
Periostin	Cell migration, bone metabolism, angiogenesis
Growth-arrest specific gene 6	Apoptosis, phagocytosis, and cell growth (smooth muscle cells, endothelium)
Various tissues	Extra hepatic carboxylation

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4580041/#cit0004

IV. ROLE OF VITAMIN K

Numerous health benefits of vitamin K include treating vitamin k deficiency diseases, enhancing bone and cognitive health, thinning the blood, and reducing heart conditions (23).

1. COAGULATION -The primary vital function of vitamin K is to promote wound healing and counteract the negative effects of blood-thinning medications. It is also used to stop bleeding in babies who have hemorrhagic illness brought on by a lack of vitamin K. (23). Four of the 13 proteins required for blood clotting, which prevents wounds from continuously bleeding so they may heal, are made easier by vitamin K. Vitamin K is frequently mentioned if anticoagulants (also known as blood thinners) are administered to prevent blood clots from developing in the legs, lung, or heart. The effects of blood thinners can be offset by vitamin K. A constant intake of vitamin K from food and supplements may be advised for people taking anticoagulants like warfarin (Coumadin) (24).

2. BONE HEALTH- Protein S, MGP, and osteocalcin are all known to be produced in bone. Osteocalcin has received attention as a potential factor in bone health due to its relative high concentration in bone (25). In order to prevent the weakening of bones, osteocalcin, one of the proteins produced in bone, needs to be present. Vitamin K is involved in this process. Numerous studies have demonstrated a link between higher vitamin K intakes and a decreased risk of hip fractures and low bone density. Low bone density has also been connected with low blood levels of vitamin K. (26). When compared to eating one serving a week, eating a serving of lettuce or other green vegetables every day can reduce the risk of hip fracture in women by half (24). In order to support bone, vitamin K is crucial. It guarantees the calcium-binding action necessary for the healthy operation of the bones and gums when combined with the vitamin D. It improves bone density, strengthens the structure, and lowers the risk of fracture in older women.

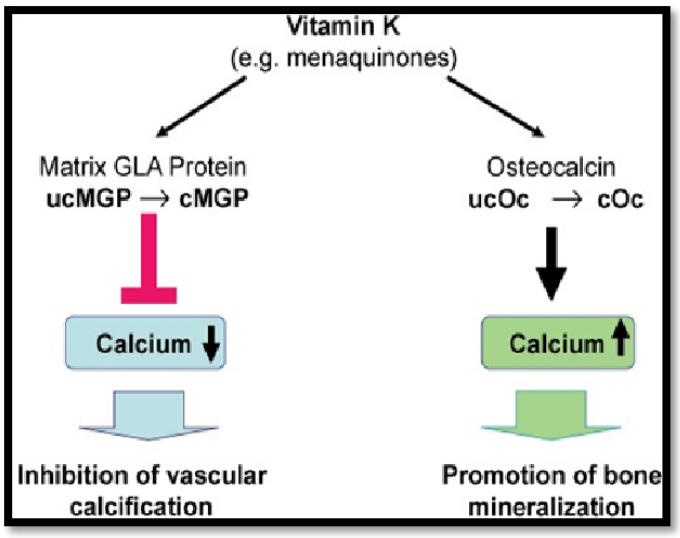
Additionally, osteoporosis and bone loss are successfully treated (23).

3. COGNITIVE HEALTH- According to preliminary study, vitamin K is bad for mental health and sharpness. In one study, it was found that those over 70 who had higher amounts of vitamin K in their bodies performed better overall and remembered verbal episodic information more readily. Two studies used a semi-quantitative frequency approach to assess vitamin K intake (FFQ). They found that senior patients who consumed more vitamin K had much improved cognition, less behavioural problems, and a less severe subjective memory complaint (27, 28). It is generally established that using anticoagulants can lower the incidence of dementia by preventing as many cerebral ischemia episodes in people with AF (29).

4. MINIMIZING THE DANGER OF HEART DISEASE- Numerous academic researches have also discovered a decreased risk of peripheral artery disease in vitamin K users. It promotes overall cardiac health by preventing mineralization inside the artery walls and maintaining the vital signs, letting the heart to circulate blood easily throughout the body (23). The importance of vitamin K for heart health has also been examined in several studies. It involves the creation of matrix Gla proteins (MGP), which aid in preventing the hardening or calcification of heart arteries, a factor in the development of heart disease (24). Some observational studies suggest that vitamin K may be beneficial for cardiovascular health, particularly in people at high risk for and suffering from chronic kidney disease. The majority of clinical research focused on vitamin D + K supplementation, which may have more beneficial effects than vitamin K supplementation. Vitamin D may maintain vitamin K-dependent protein activity, promoting vascular health in the process (30).

5. PREVENT FROM CANCER- One potential new drug for the treatment of cancer is vitamin K2 (VK2), which has anticancer effects on a range of neoplastic cell lines (31). Numerous studies show that VK2 medication can prevent HCC in people with hepatic cirrhosis, and that VK2 consumption can lower the chance of getting cancer in general, especially prostate and carcinoma (32). Quinones are a fundamental component of VK and serve a variety of chemotherapeutic medications, which helps to explain in part why VK is used to treat cancer (33). Quinones frequently undergo one-electron reduction to generate intermediate semi-quinones, which is followed by hydroquinone (two-electron reduction). These reactions consume superoxide radicals, which are typically considered to be cancer-causing, as well as reducing equivalents (NADH, NADPH, glutathione), which are crucial for maintaining the homeostasis of somatic cells (34), thereby establishing an intracellular environment suitable for the induction of apoptosis. VK anticancer action may be partially explained by the VK-modulated redox-cycle (35).

6. PULMONARY DISEASE- The most prevalent chronic respiratory disease is chronic obstructive pulmonary disease (COPD), which includes emphysema and chronic bronchitis. The National Health and Nutrition Examination Survey (NHANES), conducted in the US, found that eating dark green vegetables rich in vitamin K was linked to a 40% lower risk of developing emphysema. Together with vitamin A, vitamin K has shown promise in reducing the progression of emphysema (36). Because pneumonia-related vitamin k depletion reduces MGP and protein S activation, this can worsen pulmonary damage and thrombosis in COVID-19 patients (37).



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V. RECOMMENDED DIETARY INTAKE

- Dietary Reference Intakes, created by the Food and Nutrition Board, the Institute of Medicine of the National Academies, offer intake guidelines for vitamin K and other micro or macro nutrients (38).
- These values are age- and gender-specific.
- In accordance with FAO/WHO recommendations, people should consume 55 g of vitamin K each day (39).

Adequate Intake of Vitamin K

Age	Female (mcg)	Male (mcg)	Pregnancy (mcg)	Lactation (mcg)
Birth to 6 months	2.0	2.0		
7-12 months	2.5	2.5		
1-3 years	30	30		
4-8 years	55	55		
9-13 years	60	60		
14-18 years	75	75	75	75
19+ years	90	120	90	90

https://ods.od.nih.gov/factsheets/VitaminK-HealthProfessional/#en3

RICH FOOD SOURCES OF VITMAIN K

Leafy vegetables are the main source of vitamin K1 (phyroquinone) and have been shown to contain 400-700g per 100g, with dark green leafy vegetables being the most abundant. Vegetable oils with a vitamin K1 level of 50-200g per 100g also make an important contribution. Fermented dairy products are the main source of vitamin K2 (menaquinone) in the Western diet. Soft cheeses and blue cheeses are especially high levels and may be related to the species of lactic acid bacteria that inhabit them. Kale, spinach, and broccoli contained the highest levels of vitamin K1 from 156 to 817 g per 100 g (40).

TYPE OF VITAMIN K	DIETARY FIBER	SUPPLEMENTATION TRIAL EFFECTS
VITAMIN K1 (Phylloquinone)	Leafy vegetables like, kale, spinach, broccoli, etc. and vegetable oils	Increased insulin sensitivity in prediabetes women.(44) Decreased insulin resistance in nondiabetic adults.(45)
VITAMIN K2 (Menaquinones)	Pork and poultry products like, goose liver paste, egg yolk and fermented foods like, cheese, Japanese specially natto	Positive effects on bone health in osteoporotic subject.(46) Positive effects on cardiovascular health in renal transplant patients.(40)
VITAMIN K3 (menadione)	Synthetic form, used in animals feed	Cytotoxic, may be used in cancer therapy.

https://lucris.lub.lu.se/ws/portalfiles/portal/48792396/1532502121article_pdf555035515.pdf

Some animal-based meals include MK4, and some tissues convert phylloquinone to MK4 (47). Some bacteria produce menaquinones 5 to 13 which are found in fermented dairy products, meat, and vegetables (48). Menaquinones are also produced by colonic bacteria, but because they are poorly absorbed from the colon, they do not significantly improve vitamin K nutritional status.

About 80% of phylloquinone is absorbed while it is in its free morpheme, but this percentage is much lower when it is consumed through food (49). Because plant foods are almost certain to contain chloroplasts, the phylloquinone they contain is less accessible than that found in oils or dietary supplements (50). For instance, the body absorbs phylloquinone from spinach only 4 to 17 percent as well as it would from a pill (49). Although the amount of phylloquinone absorbed from veggies is improved when eaten alongside some fat, it is still less than that from oils. Only a little amount of data suggests that phylloquinone from green vegetables may not be as readily absorbed as long-chain MKs (51).

GREEN VEGETABLES- kale, spinach, green turnip, parsley, lettuce, cauliflower, broccoli, Brussel, cabbage, etc.
DAIRY SOURCES- cheese, milk and yogurt.
FRUITS- kiwi, avocado, blueberry, etc.
OTHER SOURCES- Fermented food, sauerkraut, eggs and meat.

https://www.netmeds.com/health-library/post/vitamin-k-functions-food-sources-deficiencies-and-toxicity

VI. DEFICIENCY OF VITAMIN K

In India, vitamin K insufficiency is not a significant cause for concern. Conditions that can limit the absorption of vitamin K, such as gastrointestinal illnesses such fat malabsorption, disease, gallbladder or biliary disease, or Crohn's disease, can result in vitamin K shortage. Additionally, taking some

antibiotics and oral blood thinners can interfere with vitamin K absorption (42).

To avoid vitamin K-deficient bleeding that could occur otherwise because vitamin K does not penetrate the placenta, newborns are given vitamin K at birth (41). A well-known risk of vitamin K deficiency, which can cause skull haemorrhage in the first few weeks of life, is particularly present in the susceptible demographic group of newborn newborns. Infants who are breastfed in particular have low vitamin K levels due to poor placental transfer of the vitamin and low vitamin K levels in human milk. Consequently, all babies are frequently given vitamin K as a preventative measure in many places (42).

A lack of vitamin K in the diet is only one cause of vitamin K insufficiency. Other causes include illness, biliopancreatic disorders, CF, alcoholism, and enteric conditions that cause malabsorption (inflammatory bowel disease, short bowel syndrome, etc). (43)

Blood may start leaking from the mouth or nostrils as a result of a vitamin K deficiency, which can cause excessive bleeding (also known as haemorrhage) (42)

Antibiotics have the potential to kill the bacteria in the gut that produce vitamin K, which could lower vitamin K levels, especially if taken for longer than a few weeks. Long-term antibiotic users who have weak appetites may be more susceptible to a deficiency and might benefit from taking a vitamin K supplement (24).

Lack of vitamin K will eventually result in various chronic diseases, including:

Coagulopathy is a fatal bleeding disorder where excessive bleeding occurs after surgery or other procedures because the blood's ability to clot is impaired.

Anaemia is a blood condition characterised by a decrease in haemoglobin and red blood cell counts, which affects the body's ability to carry oxygen.

Hematoma Localized bruising outside of the blood vessels, caused by trauma, or blood leaking from broken capillaries.

Petechia A skin condition in which the affected area develops red or purple spots as a result of burst capillaries.

Calcification The vitamin K-dependent protein known as matrix Gla, which is present in bone and cartilages, is important for calcification. This substance, which may be a powerful vascular inhibitor, needs to be carboxylated by vitamin K in order to inhibit calcification. Long-term lack of this can lead to calcification, which may result in bone loss.

Vitamin K Bleeding Newborn babies that experience excessive bleeding due to vitamin K deficient bleeding, also known as VKDB, have insufficient vitamin K levels in their blood. It may be fatal if there is bleeding on the inside or outside of the body.

Obstructive Jaundice The small intestine can receive waste products from the liver and gallbladder thanks to ducts, which are tiny tubes. If there is an obstruction in the duct, not enough enzymes are produced to enable the body to absorb nutrients from food, which results in Vitamin K depletion. Blood bilirubin levels rise as a result, which may develop chronic liver disorders or obstructive jaundice.

TOXICITY

Extremely little vitamin K poisoning occurs. Menadione, which is useless to humans, has been reported to be the only poisonous substance. Its water-soluble qualities are thought to be related to its toxicity. When poisoning does occur, it shows up as infantile kernicterus, hemolytic anaemia, hyperbilirubinemia, and jaundice.

The increased oxygen intake in the liver, which leads to a considerable rise in lipid peroxidation, which ultimately results in cell destruction and death, is the mechanism through which menadione poisoning occurs. The related symptoms of vitamin K poisoning are caused by hepatocyte destruction. (1)

VII. CONCLUSION

In addition to being a micronutrient that sustains the body, vitamin K also functions as a therapeutic dietary

strategy for illness prevention. In addition to acting as an anticoagulant, vitamin K is crucial for the health of bones. Similar to the surge in vitamin D, menaquinones, or vitamin K2, are also experiencing a significant boom in the health products industry. Especially in at-risk patient groups with a high frequency of calcification or vitamin K insufficiency, vitamin K2 has the potential to be utilized as a therapy or preventative measure for the occurrence of vascular calcification. The most recent RDA for adults is 55 g of vitamin K per day. Since vitamin K is fat soluble, it is advisable to eat foods containing it together with some fat to increase absorption. So, add chopped avocado or vegetable oil to your preferred leafy green salad. Any dosage that is too high may be poisonous and result in side effects like decreased appetite, enlarged liver, breathing issues, muscular stiffness, pallor, and bodily edema. Therefore, have a diversified diet to obtain the ideal amount of Vitamin K needed by the body to fend against numerous diseases and lead a healthy lifestyle.

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