

Vitamin K: food composition and dietary intakes

Sarah L. Booth*

Vitamin K Laboratory, USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA, USA

Abstract

Vitamin K is present in the diet in the forms of phylloquinone and menaquinones. Phylloquinone, which is the major dietary source, is concentrated in leafy plants and is the vitamin K form best characterized in terms of food composition and dietary intakes. In contrast, menaquinones are the product of bacterial production or conversion from dietary phylloquinone. Food composition databases are limited for menaquinones and their presence in foods varies by region. Dietary intakes of all forms of vitamin K vary widely among age groups and population subgroups. Similarly, the utilization of vitamin K from different forms and food sources appear to vary, although our understanding of vitamin K is still rudimentary in light of new developments regarding the menaquinones.

Keywords: *vitamin K; phylloquinone; menaquinones; food composition; dietary intake*

The term ‘vitamin K’ represents a family of compounds with a common chemical structure, 2-methyl-1,4-naphthoquinone (Fig. 1).

Food sources

Phylloquinone

Phylloquinone, also referred to as vitamin K₁, is a compound present in all photosynthetic plants (1). Phylloquinone is the primary dietary source of vitamin K. In general, green, leafy vegetables contain the highest known phylloquinone concentrations and contribute approximately 60% of total phylloquinone intake (2, 3). As indicated in Table 1, spinach and collards, which have concomitant high concentrations of chlorophyll associated with the photosynthetic process, hence, dark leaf color have substantially higher concentrations of phylloquinone compared to the more commonly consumed iceberg lettuce, which is substantially paler, hence, lower chlorophyll concentrations. The other plant sources of phylloquinone are certain plant oils including soybean, canola (also known as rapeseed), cottonseed, and olive (Table 1). Margarine, spreads, and salad dressings derived from these plant oils are important dietary sources of phylloquinone (4, 5). Plant oils are used for preparation of multiple mixed dishes, hence many commercially prepared foods including baked goods also contain small amounts of phylloquinone. Although multiple databases now exist that contain

some phylloquinone contents of foods (6, 7), the most extensive analysis of phylloquinone in common foods using established food sampling protocols (8) are found in the United States Department of Agriculture (USDA) Nutrient Database for Standard Reference (<http://www.ars.usda.gov/SP2UserFiles/Place/12354500/Data/SR22/nutrilistsr22a430.pdf>; accessed 05.22.10).

2',3'-Dihydrophylloquinone

The commercial hydrogenation of phylloquinone-rich oils results in a transformation of phylloquinone into a hydrogenated form, 2',3'-dihydrophylloquinone (9). As expected, *trans* fatty acid concentrations are highly correlated with dihydrophylloquinone concentrations (10). In the US food supply commercial hydrogenation of plant oils was a common practice that prolonged shelf life of the oil-based products. Many foods sold in fast-food restaurants and frozen prepared products such as fast-food French fries, doughnuts, and breaded fish sticks contained high concentrations of 2',3'-dihydrophylloquinone (5) (Table 1). However, with current controversy regarding the health consequences of *trans* fatty acid intake (11), there have been regional trans fat bans in the US food supply. It is anticipated that the decrease in hydrogenation of plant oils will also reduce the presence of dihydrophylloquinone in the US food supply, hence monitoring of this form of vitamin K in the food supply is warranted. Unlike *trans* fatty acids, dihydrophylloquinone is only present in hydrogenated

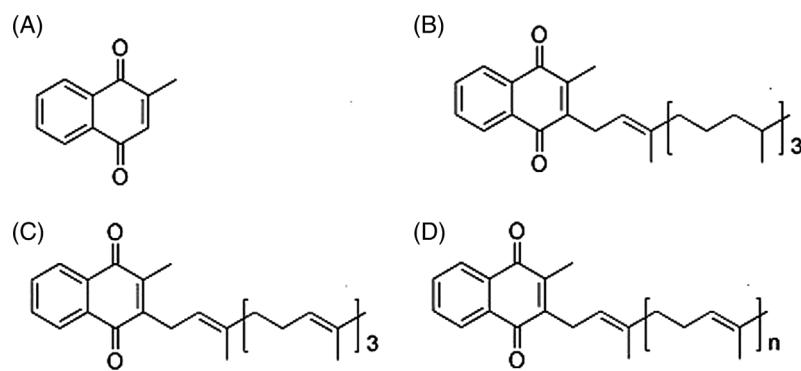


Fig. 1. Forms of vitamin K. (A) Menadione, which is present in animal feed; (B) phylloquinone, which is the primary dietary source; (C) menaquinone-4, which is a conversion product from menadione or phylloquinone; and (D) menaquinones, which can vary in length from MK-4 to MK-13.

plant oils, hence monitoring this form of vitamin K in the food supply is a robust approach to monitoring the practice of commercial hydrogenation of plant oils.

Menaquinones

Menaquinones are the other category of vitamin K present in the food supply (Fig. 1). Menaquinones are often referred to as Vitamin K₂, which is somewhat misleading given that all menaquinones are not alike in their origin or their function. Menaquinones are primarily of

bacterial origin, and differ in structure from phylloquinone in their 3-substituted lipophilic side chain. The major menaquinones contain 4–10 repeating isoprenoid units indicated by MK-4 to MK-10; forms up to 13 isoprenoid groups have been identified.

Menaquinone-4 (MK-4) (Fig. 1) is unique among the menaquinones in that it is not of bacterial origin. Instead, MK-4 is formed by a realkylation step from menadione present in animal feeds or is the product of tissue-specific conversion directly from dietary phylloquinone (12, 13).

Table 1. Vitamin K content of common foods

Food	Major form of vitamin K	Concentration ($\mu\text{g}/100 \text{ g}$)	References ^a
Vegetables			
Collards	Phylloquinone	440	(39)
Spinach	Phylloquinone	380	(39)
Broccoli	Phylloquinone	180	(39)
Cabbage	Phylloquinone	145	(39)
Iceberg lettuce	Phylloquinone	35	(39)
Fats and oils			
Soybean oil	Phylloquinone	193	(5)
Canola oil	Phylloquinone	127	(5)
Cottonseed oil	Phylloquinone	60	(5)
Olive oil	Phylloquinone	55	(5)
Mixed dishes ^b			
Fast food french fries	Dihydrophylloquinone	59	(40)
Fast food nachos	Dihydrophylloquinone	60	(40)
Frozen, breaded fish sticks	Dihydrophylloquinone	16	(40)
Margarine with hydrogenated oil	Dihydrophylloquinone	102	(5)
Other foods			
Natto	Menaquinone-7	998	(6)
Hard cheeses	Menaquinone-9	51.1	(6)
Soft cheeses	Menaquinone-9	39.5	(6)

^aReferences are the primary data source. However, numbers in this table are indicative of median concentrations of all analysis for a given food in the author's laboratory and may differ from reference because of the inclusion of unpublished data.

^bThese data reflect the content when hydrogenated phylloquinone-rich oils are used. When non-hydrogenated oils are used, the predominant form would be phylloquinone.

In the United States, menadione is the synthetic form of vitamin K used in poultry feed. As such, MK-4 formed from menadione is present in poultry products in the US food supply (14). However, MK-4 formed from phylloquinone is limited to organs not commonly consumed in the diet including kidney. The exceptions are dairy products with MK-4 found in milk, butter, and cheese, albeit in modest amounts. Therefore it is unlikely that MK-4 is an important dietary source of vitamin K in food supplies that do not use menadione for poultry feed nor are rich in dairy products.

There is growing interest in the health benefits of longer-chain menaquinones, which are limited to certain foods in the food supply. Menaquinone-7 (MK-7) is primarily the product of fermentation using *bacillus subtilis natto* and is present in a traditional Japanese soybean-based product called *natto*. *Natto* contains approximately 2.5 times more MK-7 compared to the phylloquinone content of spinach (Table 1). *Natto* also contains MK-8 and phylloquinone (84 and 35 µg/100 g, respectively), although both are modest in concentration compared to MK-7 (6). Some cheeses also contain MK-8 and MK-9 (6), but these are dependent on cheese production practices, hence the food composition databases are limited in their ability to characterize menaquinone intake across different food supplies.

Dietary intakes

The current US dietary guidelines for intakes of vitamin K are 90 and 120 µg/day for women and men, respectively (15). These guidelines are termed adequate intakes (AI) because the Institute of Medicine concluded in 2001 that there were insufficient data available to generate a precise recommendation for vitamin K. The AI values for vitamin K were generated from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) and based on the median phylloquinone intake in the United States for each age and gender category (15). In the absence of abnormal bleeding associated with low vitamin K intakes among adults, it was assumed that the current intakes are adequate. However, the adequacy of intake defined by an absence of bleeding is controversial. Furthermore, the elderly report median intakes below the current AI for adults. As reviewed elsewhere (16), there is controversy regarding biochemical measures of subclinical vitamin K deficiency and as a consequence, the true dietary requirement of vitamin K is unknown. For the purpose of this review, dietary intakes of vitamin K will be presented relative to the current AI. By comparison, the guidelines in the United Kingdom are 1 µg/kg body/day (17) and are set at 75 µg/day for adult men, 60 µg/day for women, aged 18–29 year, and 65 µg/day for women 30 years and over in Japan (18).

Estimates of phylloquinone intake in various populations are probably more accurate than intakes of other forms of vitamin K and there is a substantial difference in the reported intakes from a number of countries, which seems to be related to food consumption practices in different areas (18–23). For example, the mean reported vitamin K intake of young Japanese women (mean 21.2 years, $n=124$) was about 230 µg/day (18). The estimated phylloquinone intakes in northern China, England, and Scotland were 247, 103, and 70 µg/day, respectively (23, 24). Of note, phylloquinone intakes have been decreasing over the last two decades in the United Kingdom, consistent with a concomitant decline in leafy green vegetable consumption (25). Based on the NHANES III data, the elderly (defined as older as 71 years of age) have median phylloquinone intakes lower than the current AI (89 and 79 µg/day for women and men, respectively). This observation supports the findings of others who have reported very low phylloquinone intakes among those in nursing homes (26) and those with Alzheimer's disease (27). Given emerging association of low vitamin K intakes with risk of certain diseases such as cardiovascular disease and osteoarthritis (16), the elderly present a potentially vulnerable subgroup of the population with respect to vitamin K.

Very little is known about the contribution of dietary menaquinones to overall vitamin K nutrition and although it has been stated that approximately 50% of the daily requirement for vitamin K is supplied by the gut flora through the production of menaquinones, there is little evidence to support this estimate (28). In one study among adults with acute bacterial overgrowth as induced by omeprazole, menaquinones produced by these bacteria had some contribution to vitamin K status during dietary phylloquinone restriction, but not enough to restore biochemical measures of vitamin back to normal range (29).

As previously indicated, there are regional differences in the forms and content of menaquinones in the food supply. For example, *natto* is unique to a traditional Japanese diet whereas the cheeses that contain high concentrations of MK-8 and MK-9 appear to be most prevalent in European dairy producing food supplies. Although there are reported menaquinone intakes, these are limited to studies from Japan (18) and the Netherlands (21), and are low compared to phylloquinone intakes. In the United States, menaquinones are limited in the food supply and have not been systematically assessed.

Are all forms of vitamin K the same?

There are surprisingly little data on the relative biological availability of different forms of vitamin K among different food sources. Furthermore, there is a growing body of literature to suggest that our understanding of

vitamin K is still rudimentary in light of new developments regarding different forms.

As previously stated, phylloquinone is of plant origin, with absolute intakes being predominantly from green leafy vegetables. Phylloquinone is tightly bound to the membranes of plant chloroplasts, and is less bioavailable compared to phylloquinone obtained from plant oils and/or dietary supplements (30). Some estimates place the absorption of phylloquinone to be 10% from plants compared to supplements (31). However there appear to be differences in absorption compared to the plant species, with phylloquinone obtained from broccoli and collards having greater absorption compared to spinach (31, 32). Similarly, and not unexpected because vitamin K is lipophilic, addition of a fat source to the meal results in higher absorption. For a more comprehensive review of vitamin K absorption, the readers are referred elsewhere (33).

Phylloquinone differs from 2',3'-dihydrophylloquinone by a saturation of a single bond at the 2',3' position of the side chain (9). Surprisingly this single substitution results in a lower absorption of dihydrophylloquinone compared to an equimolar amount of phylloquinone (34). There is also indirect evidence of lower activity of dihydrophylloquinone as an enzyme cofactor, which currently is the only known function of vitamin K. The implications of this poor bioavailability and activity are currently unknown, although at least one study suggests a detrimental effect on bone mineral density among older adults in a community-based cohort (35). The potential impact of poor utilization of dihydrophylloquinone on bone health will be of little importance in the future should hydrogenated oils be removed from the food supply.

The menaquinones are poorly understood in terms of vitamin K absorption and utilization. MK-7, when administered in the form of *natto* in equimolar amounts to phylloquinone administered in the form of spinach, has a peak height difference of more than 10-fold compared to phylloquinone, with a half-life of 56 hours, compared to 7.5 hours for phylloquinone (36). Whereas all forms of vitamin K appear to be initially associated with triglyceride-rich lipoproteins (TRL), the longer chain menaquinones including MK-7 and MK-9 are also associated with low-density lipoprotein (LDL). MK-4 has been reported in TRL, LDL, and high density lipoproteins. These preliminary data suggest that the menaquinones have different transport pathways and distribution, which has implications for transport to extra-hepatic tissue such as bone (33).

Emerging studies on MK-4 challenge our current understanding of vitamin K. As demonstrated using stable isotopes, MK-4 is a conversion product of phylloquinone via the intermediate, menadione (37). There appears to be both local and systemic conversion to MK-4, with the local conversion being the predominant

pathway. The implications of this conversion are still the topic of speculation. To add complexity to the interpretation is the observation that this conversion does not occur in all tissues. Whereas the liver contains primarily phylloquinone and very long-chain menaquinones, MK-4 is the predominant form in the brain, pancreas, and glands (38). In terms of dietary intakes, MK-4 intakes are low compared to other forms of vitamin K. However, dietary phylloquinone converts to MK-4 in those tissues where MK-4 appears to be required so it is likely that low MK-4 intakes are of little consequence to health when there is adequate dietary phylloquinone available for conversion to MK-4.

In conclusion, much of our understanding of vitamin K nutrition has focused on the primary dietary source, phylloquinone. There are comprehensive databases available that contain phylloquinone contents of a variety of foods. Dietary assessment of phylloquinone reveals variation in intakes by age and population subgroups. In contrast, the menaquinones are present in the food supply, but there are limited food composition data available. As a corollary, estimates of intakes of menaquinones are very limited and our understanding of their role in vitamin K nutrition is not well understood.

Conflict of interest and funding

Based upon work supported by the US Department of Agriculture, Agricultural Research Service under Cooperative Agreement No. 58-1950-7-707, and National Institutes of Health DK069341. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the view of the US Department of Agriculture.

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*Sarah L. Booth

USDA Human Nutrition Research Center on Aging at Tufts University
711 Washington St.
Boston, MA 02111
Tel: 617 556 3231
Fax: 617 556 3149
Email: sarah.booth@tufts.edu