

## Vitamin K in Calcium Supplements

Vitamin K1 has recently been added to Caltrate Plus and Caltrate Plus Chewable, which are both available without a prescription. (See Table 1) The label on these products now includes a caution to check with a healthcare professional if taking an anticoagulant.<sup>1</sup> What are the risks and benefits of these new formulations?

### Bottom line:

- The evidence of benefit for routine vitamin K supplementation is weak.
- Few if any patients should require more than one Caltrate Plus daily. Counsel on recommended daily calcium and vitamin D intake.
- For patients on warfarin with a stable INR, the amount of vitamin K in one or two Caltrate Plus tablets taken daily poses very little risk. Adhering to the dosing regimen will help ensure consistent levels and a more stable INR. Warfarin requirements to maintain a therapeutic INR may increase or decrease when starting or stopping vitamin K, and thus, increased monitoring may be required during these transitions
- Ask about other supplements which could also contain vitamin K such as multivitamins and meal replacements.
- The new oral anticoagulants do not interact with vitamin K, therefore there is no increased risk for patients on these drugs.

**Table 1: Ingredients in Caltrate Plus / Caltrate Plus Chewable**

Ingredient	Amount
Calcium	600 mg
Copper	1 mg
Magnesium	50 mg
Manganese	1.8 mg
Vitamin D	400 IU
Vitamin K1	20 mcg
Zinc	7.5 mg

### What is the rationale for adding vitamin K to calcium supplements?

Vitamin K has a role in the maintenance of bone health.<sup>2</sup> It is a cofactor required for the synthesis of certain proteins which facilitate bone mineralization.<sup>3</sup> Deficiency in normal healthy adults is very rare, however, because it is widely available in food, synthesized in the gut and recycled in the body.<sup>3,4</sup> Deficiency could be a concern in the following situations:

- Conditions causing fat malabsorption e.g. celiac disease, inflammatory bowel disease, biliary disorders, etc. (Note: vitamin K is a fat-soluble vitamin)
- Long-term use of broad spectrum antibiotics which disrupt the normal flora in the gut
- Prolonged fasting, starvation<sup>3,4</sup>

There is conflicting evidence as to whether or not vitamin K supplements help to prevent osteoporosis and bone fracture. Only Trials among Japanese subjects have shown a positive effect on bone mineral density but trials involving North American subjects have not reported any benefit.<sup>5</sup> Solitary vitamin K supplements are not readily available in most pharmacies but can be found in health food stores. If a patient chooses to take a vitamin K supplement, recommend a product with a Natural Product Number (“NPN”) to increase the likelihood that the product they are ingesting matches the information on the label.

### What are the safety concerns with supplemental vitamin K?

**Too much vitamin K:** There are no reports of toxicity due to vitamin K1 overdose; a tolerable upper limit for daily intake has not been determined.<sup>3,4</sup>

## Interactions with anticoagulants:

*Warfarin and acenocoumarol* act by inhibiting vitamin K-dependent clotting factors. High amounts of dietary or supplementary vitamin K can antagonize their effects, decrease INR and increase the risk of clots.<sup>4,5</sup> In a study of healthy subjects, a minimum dose of 150 mcg of vitamin K taken once daily for 7 days was required to cause a clinically significant decrease in INR.<sup>6</sup>

Deficiency of vitamin K is a concern because patients may have an exaggerated response to warfarin and difficulty in stabilizing their INR.<sup>7</sup> Patients should ensure they consume at least the recommended adequate daily intake of vitamin K (Table 2).<sup>8</sup> Consistency in vitamin K intake rather than limitation in the amount consumed is appropriate advice.<sup>7</sup> Information on the vitamin K content of food can be found online at:

[clotcare.com/include/vitaminkcontent.pdf](http://clotcare.com/include/vitaminkcontent.pdf) or  
[ars.usda.gov/SP2UserFiles/Place/12354500/Data/SR24/nutrlist/sr24w430.pdf](http://ars.usda.gov/SP2UserFiles/Place/12354500/Data/SR24/nutrlist/sr24w430.pdf)

The new oral anticoagulants - *dabigatran, rivaroxaban and apixaban* - have different mechanisms of action than warfarin and do not interact with vitamin K. Supplements containing vitamin K are not a concern with these drugs.<sup>9</sup>

## What are the safety concerns with calcium?

Excess dietary calcium does not appear to be harmful but excess supplementary calcium has been associated with a number of potential adverse effects including kidney stones, prostate cancer, constipation, dyspepsia<sup>10</sup> and most recently, concern about increased risk of cardiovascular events.<sup>11,12</sup> Patients taking supplements should ensure their total daily calcium intake does not exceed the tolerable upper limit for their age group.<sup>10</sup> (Table 2) The calcium content of common foods are listed online at [www.osteoporosis.ca/osteoporosis-and-you/nutrition/calcium-requirements](http://www.osteoporosis.ca/osteoporosis-and-you/nutrition/calcium-requirements).

Current Health Canada recommendations for daily intake of calcium are 1000 – 1200 mg elemental calcium daily. Calcium should preferably be obtained from dietary sources. If this is not possible, supplements in the form of calcium carbonate or calcium citrate can be taken to bring the daily calcium total including dietary sources up to the recommended amount.<sup>10</sup> A tool to calculate calcium intake and requirements is available on the Osteoporosis Canada website at <http://www.osteoporosis.ca/osteoporosis-and-you/nutrition/calculate-my-calcium>. Smaller doses (500 mg or less) taken two or three time daily rather than one large daily dose improve absorption and may be safer.<sup>10</sup>

Vitamin D is necessary for absorption of calcium. Patients should ensure they are ingesting the recommended daily intake of vitamin D (Table 2) especially during the fall and winter months or year round if exposure to sunlight is limited.<sup>11</sup>

**Table 2: Reference Values for Vitamin K, Calcium, and Vitamin D**

Population Group	Adequate Intake	Upper Limit
<b>Vitamin K</b>		
Adults greater than 19 years		
Men	120 mcg	Not defined
Women	90 mcg	Not defined
<b>Calcium</b>		
Adults 19-50 years	1000 mg	2500 mg
Adults 51-70 years		
Men	1000 mg	2000 mg
Women	1200 mg	2000 mg
Adults greater than 70 years	1200 mg	2000 mg
<b>Vitamin D</b>		
Children and Adults 9-70 years	600 IU (15 mcg)	4000 IU (100 mcg)
Adults greater than 70 years	800 IU (20 mcg)	4000 IU (100 mcg)

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