

Vitamin K

"There are in fact two things, science and opinion; the former begets knowledge, the latter ignorance." Hippocrates.

The actions of Vitamin K are less familiar than are those of vitamins C and E: it is essential for blood clotting and is involved in bone metabolism. More importantly, it can also be an effective anti-cancer agent. Unfortunately, this natural and safe substance has tended to be neglected in the fight against cancer. The anti-cancer activity of vitamin K has been investigated for decades,^{841,842} yet its clinical potential remains to be fully realised. Vitamin K provides an introduction into a new world of anticancer agents. Anticancer drugs based on vitamin K may be safe for normal tissues, but deadly for cancer cells.

A Danish researcher, Henrick Dam, won the 1943 Nobel Prize for discovery of vitamin K, which was first isolated in 1939. This substance is needed for blood to clot. Dam named it vitamin K, after *koagulation*, the Danish word for coagulation. Vitamin K exists in several forms, called vitamins K₁, K₂, K₃, and so on. Some of these are natural forms, whereas others, such as K₃, are synthetic.

In this chapter, we describe the properties and pharmacology of this fat-soluble vitamin. Vitamin K is known for its classic action on blood clotting.⁸⁴³ The anticoagulant drug, warfarin, is a vitamin K antagonist. Originally developed as a rat poison, warfarin interferes with the clotting action of vitamin K and has been used for the last fifty years to "thin the blood" of people with heart disease.⁸⁴⁴ As it is both odourless and tasteless, rodents will feed on warfarin-laced food for days, until they accumulate a lethal dose. However, warfarin's effectiveness as a rat poison is declining, as rats have evolved resistance to it.

Warfarin was discovered through observations of a cattle disease, first noticed in the early 1920s. A Canadian veterinary surgeon, Frank Schofield, found that mouldy silage contained an anticoagulant, which made the cattle bleed. About two decades later, chemists from the University of Wisconsin, Karl Link and Harold Campbell, described the toxin as a coumarin derivative. Coumarin is a chemical produced by plants and smelling of freshly mown grass. Link began work on coumarin-based rat poisons, and generated warfarin in 1948.

Vitamin K has other biological functions besides prevention of bleeding.^{845,846} It has been used in the treatment of diseases, including

osteoporosis,^{847,848} vascular calcification and atherosclerosis.⁸⁴⁹ It has also been shown to inhibit the growth of cancer.^{850,851,852,853,854,855,856,857,858} The anticancer effects of vitamin K are accepted by the scientific community.⁸⁵⁹

Requirements and toxicity

In adults, a shortage of vitamin K may result in nosebleeds and haemorrhaging. However, vitamin K deficiency occurs more often in babies; about one percent of infants suffer the tendency to bleed that comes from deficiency. There are many reasons why babies should be short of this vitamin. These include low transfer across the placenta, lack of vitamin K in breast milk and prematurity of the liver. In addition, the relatively sterile newborn gut lacks the bacteria that manufacture the vitamin in adults. The primary deficiency symptom in infants is bleeding, together with easy bruising. Birth defects, such as underdevelopment of the face, nose, bones and fingers, have also been noted.

The US National Institutes of Health have estimated the daily need of vitamin K for adults at 0.08mg per day. Dietary sources include green vegetables, liver, vegetable oils and milk. It is possible to have too much vitamin K, although the different K vitamins differ in their toxicity. Vitamin K₁ is not toxic at doses up to 500 times the recommended daily intake (0.5 mg/kg/day).⁸⁶⁰ However, vitamin K₃ is more toxic: it should not be used to treat deficiency. In infants, an overdose of K₃ can cause haemolytic anaemia, in which the red blood cells are destroyed, or jaundice, when excess bilirubin builds up in the blood and brain, turning the skin yellow.

Mechanism for killing cancer

Although the physiology of vitamin K is interesting, we are mainly concerned with its actions against cancer. Vitamin K is reversibly oxidised and reduced inside cancer cells, which suggests a mechanism by which it might destroy the cells.^{844,845,a} In the presence of iron and other metals, vitamin K takes part in a Fenton reaction, generating free radicals or oxidants that are believed to induce DNA breakage and cell death. However, vitamin K may also kill cancer cells in the absence of iron.⁸⁶¹

^a For chemists: vitamin K (a hydroquinone) cycles from an epoxide to a quinone and back to the hydroquinone for another gamma-carboxylation reaction.

Receptors

Many drugs and hormones act via specific receptors on the surface of cells. They bind with the receptors, stimulating the cell to perform a biochemical action. Vitamin K interacts with such receptors, influencing

cell signalling. Vitamin K dependent signalling is involved in cell death, transformation to a state of unlimited growth, and replication.^{862,863} These processes are central to the development of cancer cells. Vitamin K influences a gene called Gas6,^b which prevents cell division. When Gas6 is expressed highly, cell growth is inhibited.^{863,864,865,866} One function of this growth-limiting gene is to increase cell survival under conditions where cell division and proliferation are restricted.⁸⁶⁷

Vitamin K may act as a physiological anti-inflammatory agent, disposing of dead or dying cells by helping phagocytic cells to recognize them.^{868,869} Its actions may help regulate cell growth and tumour formation, including multiple myeloma and lung cancer.^{870,871}

Vitamin K₁

The most abundant member of the family is vitamin K₁, which is involved in the fundamental chemistry of life.^c It occurs in green plants and algae, and is associated with photosynthesis. Leafy, green vegetables provide vitamin K₁ in the diet.⁸⁷² Vitamin K₁'s anticancer activity is a good reason to eat your greens.

Several studies have established Vitamin K₁ as an anticancer agent. It can diminish growth in a number of cell lines, including cancer of the breast, liver, colon, lung, nasopharynx, stomach, oral cancer and leukaemia. The concentration of K₁ needed to halve cell growth in these cancers ranges from 2-10 mM/L.⁸⁵⁰ However, other cancers may respond to lower physiological concentrations; these include cell lines from brain tumours,⁸⁵¹ other forms of leukaemia,⁸⁹¹ and liver cancer.⁸⁵⁸ Clinical trials have supported the anticancer effects of vitamin K₁ in humans.^{873,874,875} The fact that vitamin K₁ can slow the growth of tumour cells has been demonstrated, but the concentrations necessary to achieve the effect are high, compared with those of other forms of the vitamin.

^b Gas6 is a Growth Arrest Specific gene.

^c Vitamin K₁ is also known as phyloquinone, phytonadione or menaphthone.

Vitamin K₂

Vitamin K₂ also has anticancer activity.^d This second form is chemically similar to K₁ and occurs naturally. It is produced by bacteria, rather than plants, and was originally isolated from putrefied fishmeal. It is possible that it is synthesised in some animals.^{876,877,878} In animals, K₂ is the most common form of vitamin K. Intestinal bacteria provide a consistent source for adult humans.

Vitamin K₂ has widespread anticancer actions. Experiments, in both humans and mice, have shown that it is effective against several cancer cell types.^{.879,930} As with vitamin K₁, a number of cancer cell lines are sensitive to vitamin K₂, including breast, colon, liver, leukaemia, lung, stomach, lymphocyte, nasopharynx, and oral cancers. Vitamin K₂ is effective at lower concentrations than vitamin K₁ (0.8-2 mM/L), but much higher than required with vitamin K₃ (18-45 µM/L).^{.850}

Vitamin K₂ reduces cancer growth by stopping cells dividing or by killing them; the extent of this action varies with the dose.^{.880,921,881} Some leukaemic cell lines resist K₂ induced cell death; however, they change to become more like healthy cells.^{.881} Researchers in Japan claim that culturing cancer cells with 1 µM/L of vitamin K₂, but not K₁, induces cellular differentiation. This suggests K₂ causes cancer cells to revert to a healthier state. Other chemicals that induce differentiation are synergistic with vitamin K₂,^e and increase its effectiveness.^{.882,883}

At concentrations as low as 10 µM/L, vitamin K₂ induces cell death in leukaemic cells, within 48 hours.^{.883} Furthermore, chemicals similar to vitamin K₂, which occur naturally, cause 90% of leukaemic cells to commit suicide, while having little effect on healthy bone marrow cells.^{.883,884} These results illustrate the selective killing of cancer cells. Case studies confirm the potential of vitamin K₂ as a therapy. In one study, an eighty-year-old female patient, whose bone marrow did not produce enough blood cells,^f was given an oral dose of 45 mg per day. After 14 months of treatment, her regular blood transfusions were no longer needed and her blood counts improved.^{.885} In a second study, a 72-year-old female, with acute leukaemia, went into remission after one week of conventional treatment and retinoic acid

^d Vitamin K₂ is also known as menaquinone.

^e Retinoic acid, interferon-gamma and camptothecin.

^f The women had MDS - myelodysplastic syndrome.

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(a derivative of vitamin A).^{.g} Eight months later, she relapsed. Her initial treatment was repeated, with the addition of vitamin K₂ (20 mg/day), which produced measurable improvements in her white blood cells, after two months. Her bone marrow was examined and was found to suggest complete remission,^{.886} a result that would normally be unexpected. Finally, a 65-year-old man with acute myeloid leukaemia was treated with oral vitamin K₂ (90 mg/day). Six weeks later, he showed a significant decrease in his immature white blood cell count, and an increase in platelets. After 10 months of treatment, the dose was reduced to 45 mg/day and the good response was maintained, without side effects.^{.880} These encouraging results from vitamin K₂ led to cancer

therapy trials in Japan.^{887,888} Vitamin K₃ is still more effective and its clinical promise is potentially even greater.

Vitamin K₃

Vitamin K₃, or menadione, is an effective killer of cancer. It is considered a synthetic chemical, which acts as a provitamin, and is converted to a vitamin by the body. It has a simpler structure than vitamins K₁ or K₂. It may also be formed from K₁, by bacteria in the gut.^{877,889} Although it does not provide the full nutritional benefits of the natural vitamin (K₁ and K₂),⁸⁹⁰ K₃ is a more powerful anticancer agent. Laboratory experiments have demonstrated the anticancer activity of vitamin K₃ in both animal^{851,891,892,893,894} and human^{852,853,895,896,925,937} cancer cells. This vitamin has been reported as effective against multidrug resistant leukaemia cells.⁹²⁵ In rats, vitamin K₃ is active against leukaemia cells that are resistant to a conventional drug.^{897, h} Researchers have demonstrated the anticancer activity of Vitamin K₃ in laboratory, animal and human experiments. Intravenous K₃ has increased the survival time of lung cancer patients, also receiving radiation therapy, from 3.77 months to 5.42 months.⁸⁹⁸ Injections of vitamin K₃ in rats with malignant liver cancer increased their survival period to 60 days, compared to 17 days for control animals.⁸⁵⁶ In mice with transplanted liver tumours, radiation treatment was more effective if the mice were given oral or intraperitoneal injections of vitamins K₃ and C.⁸⁹⁹

^g The women received all-trans-retinoic acid (60 mg/day), enocitabine (200 mg/day), and daunorubicin (40 mg/day).

^h Adriamycin.

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Vitamin K₃ has been shown to work in combination with conventional chemotherapy. It increases the effectiveness of 5-fluorouracil against liver cancer cells.⁸⁹⁴ In a culture of human oral cancer cells, it was shown to be synergistic with conventional cancer agents.^{925,i} This beneficial action of vitamin K₃ has been also demonstrated in cells from cancer of the upper throat.⁹⁰⁰ Vitamin K₃ allows a 10- to 50-fold reduction in the levels of the anticancer drug, mitomycin C, needed to kill cancer cells.⁹⁰¹ Pre-treatment with vitamin K₃ also increases the toxicity of standard chemotherapy treatments against breast cancer cells.⁹⁰³ The promising results of these experiments with vitamin K₃ have resulted in a number of trials, in both animals and humans. Studies in rats indicate that vitamin K₃, at blood levels less than 1 µM/L, increases the action of the anticancer drug, methotrexate, without increasing its toxicity. The combination of methotrexate with vitamin K₃ led to a massive reduction in cancer growth, supporting K₃'s potential to increase

the effectiveness of this form of chemotherapy.⁸⁵⁷ Results from human studies with vitamin K₃ and a different anticancer drug have been less consistent,^{i,j,901,902,903} which may indicate that the drugs have differing mechanisms of action.

Related compounds

We have no information about the anticancer activity of vitamin K₄. A recent study has shown that vitamin K₅ has antitumour activity.⁹⁰⁴ We suggest that numerous other natural substances, which are chemically related to vitamin K, especially quinones,^{905,906,907,908} could prove to have non-toxic anticancer activity.⁹⁰⁹

The selective actions of vitamin K₃ and other, non-toxic, cancer agents are closely related to biochemical mechanisms occurring in standard chemotherapy. Some synthetic anticancer drugs have redoxactive quinone forms, although they are more toxic than vitamin K.^{910,911} Such drugs can undergo redox cycling, to generate free radicals.⁹¹² Their anticancer mechanisms have some degree of specificity for diseased cells. Like vitamin K, such drugs can be influenced by ascorbate and other antioxidants.⁹¹³

The idea of using this relatively safe supplement to augment toxic chemotherapy and radiotherapy seems superficially reasonable. If lower

i 5-FU, bleomycin, cisplatin, dacarbazine, mercaptopurine, cytarabine, hydroxyurea, VP-16, vincristine, doxorubicin, mitoxanthine, mitomycin C, actinomycin D, and thiotepa.

j Mitomycin 3.

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doses of these conventional therapies produce the same effects when combined with the vitamin, the reductions in side effects are likely to be significant. However, such an approach indicates a failure of imagination. Surely, it would be more appropriate to carry out research to discover the mechanism of action that allows vitamin K to kill cancer cells, without harming normal cells. Physicians could then use this knowledge as the basis for treatments that do not poison their patients.

How does it work?

Vitamin K's cytotoxic effects and cancer growth inhibition have been demonstrated in isolated cell lines, in animals and in humans. Scientists do not yet fully understand how the vitamin works against cancer cells. There are several possible mechanisms, of which the primary model depends on vitamin K's ability to affect cell oxidation and generate free radicals. This production of free radicals could explain how vitamin K₃ can kill cancer cells directly. Some of the effects of vitamins

K₁ and K₂, such as redifferentiation and inhibition of the cell cycle, may involve additional mechanisms.

The primary action of vitamin K₃ against cancer is a result of redox cycling.⁹¹⁴ Vitamin K₃ is oxidised and reduced, in a repeated cycle that releases free radicals. This redox cycle is similar to that for vitamin C, described previously. If redox cycling produces more free radicals than a cell can quench by generating antioxidant electrons, the free radicals damage the cell, which eventually dies. At higher doses, vitamin K₃ kills cancer cells more effectively than other forms of vitamin K.^k Vitamins K₁ and K₂ are less effective at generating free radicals.^l

Vitamin K₃ can exist in three different forms: a quinone, a semiquinone and a hydroquinone. It switches between these states by oxidation (losing electrons) and reduction (gaining electrons). In its oxidized form, vitamin K₃ is a quinone. Quinones can be reduced, gaining one electron to generate semiquinone radicals, or two electrons to become hydroquinones. In moving from the quinone form to the hydroquinone, K₃ gains two electrons. In the return section of the cycle, the hydroquinone is oxidised by the loss an electron to form a semiquinone. Loss of another electron returns it to its original quinone state.

^k Vitamin K₃ can arylate nucleophiles, such as glutathione, and thus initiate rapid one- or two-electron redox cycling.

^l K₁ and K₂ have lower rates of redox cycling and a higher proportion of two-electron transfers than vitamin K₃.

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Vitamin K₃'s redox cycling increases oxidative stress in malignant cells,^{915,916,917,918} and can produce the highly reactive hydroxyl radical, •OH. This damaging free radical derives from superoxide by way of a Fenton reaction, involving transition metals such as iron. Antioxidants, such as glutathione, can quench superoxide and hydrogen peroxide, decreasing the oxidative stress caused by vitamin K₃.^{919,920} The antioxidant enzymes catalase and superoxide dismutase have a similar effect. Vitamin K₃'s anticancer effect is decreased if oxidative stress is lower, in the presence of some antioxidants, for example.⁸⁵⁸ Despite this, vitamin C increases the ability of vitamin K₃ to kill cancer cells. It may be that only antioxidants that are able to reduce quinones directly, as opposed to general antioxidants, have protective effects for the cancer cell.⁹²¹ At high doses, vitamin C may act as an additional oxidant, driving the oxidation-reduction cycle and generating even greater amounts of hydrogen peroxide, which kill the cancer cell.

Vitamin K and similar molecules inhibit cancer growth. This inhibition is blocked by sulphur containing antioxidants, but not by other reducing agents, such as vitamin C.⁹²¹ Vitamin K₃ may lower the activity of critical cell-growth enzymes, by reacting with sulphur-containing

amino acids.⁹²² Vitamin K₃ can combine directly with sulphur-containing molecules, in a process called arylation.^{921,923,924} This refers to the addition of aromatic groups, such as those contained in vitamin K₃, to a sulphur-containing molecule, such as the antioxidant glutathione. Adding glutathione to cancer cells inhibits the anti-cancer actions of vitamin K₃.^{925,914,915,926,927}

Vitamin K₃ causes oxidative stress in cancer cells, generating a cascade of events, which leads to cell shrinkage, DNA fragmentation and cell death. It does this mainly by oxidation and through combination with sulphur-containing molecules, lowering the activity of cell growth enzymes. It also stops the cell dividing by a separate mechanism, which may be unrelated to its redox cycling.⁹²⁸ However, the increased chemotoxicity of K₃ when used in combination with electron donors, such as vitamin C, suggests that the redox cycle is a primary factor in K₃'s cancer killing role.¹⁵

The enzyme catalase, which destroys hydrogen peroxide, inhibits the anticancer effect of K₃, but has less effect on the actions of vitamins K₁ and K₂.^{858,929} Both K₁ and K₂ appear to act through additional mechanisms, which do not involve generation of hydrogen peroxide.

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Vitamins K₁ and K₂ do not take part in the same redox cycling and may induce cell death using additional, non-oxidative mechanisms. Low concentrations (20 µM/L) of vitamin K₃ result in limited cell death, whereas higher concentrations (60-150 µM/L) can lead to necrosis. In necrosis, cells die abruptly, in a relatively uncontrolled fashion. Vitamin K₂ has similar effects, but at higher concentrations. Concentrations of K₂ as high as 150 µM/L, for example, may bring about a low frequency of cell death, with no necrosis.⁹³⁰

Vitamin K₃ may kill cancer cells by two different mechanisms. At higher levels, oxidation induced by the vitamin leads to necrosis, or another form of cell death, autoschizis.^{931,932,933,934} During autoschizis, the cell's internal fluid or cytoplasm is extruded from the cell, leaving an intact nucleus.⁹³⁵ This involves substantial membrane damage. The cell bleeds cytoplasm, leaving behind the sub-cellular particles and structures. The cell becomes smaller, until its membranes surround a shrunken nucleus and a narrow ring of cytoplasm, which contains the internal particles or organelles. The mitochondria also shrink, but the cell does not appear to die from lack of energy. The process of autoschizis depends on a reduction in DNA synthesis.⁹³⁶ Moreover, addition of the enzyme catalase can prevent the cell from dying,⁸⁵³ which indicates the involvement of oxidation.

At lower levels, Vitamin K₃ can prevent cell division and induce cell death by influencing gene transcription factors.^{937,938,939,940} This method probably forms the basis for its non-oxidative anticancer action. Transcription factors can induce cell cycle arrest and apoptosis, and alter the expression of oncogenes.^{855,941,942,943,944,945,946}

Combining vitamins C and K

Since both vitamins K and C use related mechanisms to kill cancer cells preferentially, it makes sense to ask if they might work in combination. Researchers have shown that vitamin K increases the anticancer properties of ascorbate. Vitamin C, combined with a much smaller amount of vitamin K₃, will kill cancer cells more effectively than either substance alone.^{947,948,949,950,951} A combination of vitamins C and K₃ could be used for treatment of cancer,^{952,953} even with oral dosing. In experiments on mice with tumours, researchers found that treatment with oral vitamin C and vitamin K₃ increased the lifespan of the treated mice, whose tumours grew less quickly. Human prostate tumours implanted into mice were found to be selectively sensitive to

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these vitamins.⁹⁵⁴ Oral doses of vitamin C and K₃ (15g/L ascorbate with 0.15g/L K₃, in drinking water) have been shown to be effective in mice with metastatic cancer. The controls had greater numbers of tumours of the lung (19, in 14 of 33 mice) and local lymph nodes (9 in 33 mice). The treated mice had fewer tumours of the lung (10, in just 3 of 19 mice) and less lymph node involvement (3 in 29 mice). Microscopic examination confirmed that, in the treated animals, many tumour cells were undergoing autschizitic cell death. These results demonstrate clearly that oral vitamin C and K₃ significantly inhibit and kill tumour cells. Mice are not ideal animals for vitamin C studies, as they synthesise the vitamin internally and do not need it in their diet. The effect may be greater in vitamin C dependent species, such as humans or guinea pigs. Preliminary results in human patients with prostate cancer are consistent with the experimental and animal studies.⁹⁵⁵

Human bladder cancer cells are sensitive to the combined action of vitamins C and K₃.⁹⁵⁶ These vitamins also increase the effects of standard anti-cancer chemotherapeutic drugs.^{957,958} A Chinese research group carried out laboratory studies, confirming that vitamins C and K₃ kill a range of cancer cells.⁹⁵⁹ In these experiments, two types of human cancer were shown to be more sensitive to the vitamins than were normal cells. A Japanese group has demonstrated that the cytotoxic activity of both vitamin C and K₃ can be enhanced by using a plant extract, lignin F.⁹⁶⁰ Vitamins C and K₃ have shown anticancer effects both *in vitro* and *in vivo*. In combination with vitamin C, (dose ratio of 100(C):1(K₃)) vitamin K₃ is cytotoxic in doses 10-50 times less than when administered

alone.⁸⁵³ In laboratory experiments, researchers demonstrated a 50% inhibition of growth of oral carcinoma cells with high concentrations of vitamin K₃ (100 µM/L).⁸⁵⁹ However, when combined with vitamin C (5 mM/L), a lower concentration of K₃ (8 µM/L) resulted in an equivalent level of growth inhibition. Thus, the synergistic inhibition of cell growth from combined administration required much less vitamin K₃. When the concentrations were increased, 100% inhibition of cancer cell growth was achieved. Similar results were found using human endometrial adenocarcinoma cells.⁸⁵³ High concentrations of vitamins C (10 mM/L) and K (100 µM/L) were even more effective, producing a 93% inhibition. In another short experiment, vitamin K₃ at 8 µM/L, when given with vitamin C (500 µM/L), gave 74% inhibition. The combination of vitamins C and K₃ (dose ratio of 100:1) has been shown to inhibit a number of urological cancer cell lines.^{961,962} Two

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groups of cell lines were selected, to test their sensitivity. The first group contained cell lines covering several grades of cancer of the kidney and bladder. A combination of vitamin C (89 µM/L) and vitamin K₃ (0.9 µM/L) produced a 10-20 fold increase in toxicity, compared to the individual agents. The second group of cell lines included prostate, bladder and testicular cancer. The combination of vitamin C (212 µM/L) and vitamin K₃ (2.13 µM/L) produced a 7-22 fold increase in potency, compared to either vitamin alone.^{961,962} Oral doses can sustain plasma levels of vitamin C indefinitely at up to 250 µM/L.¹⁵ These results indicate that oral treatments may be effective in humans, since tumours absorb ascorbate preferentially.

In a further study on prostate cancer, human tumours implanted into nude mice were treated with vitamins C and K₃, resulting in cell death.⁹⁵⁴ Nude mice are a form of hairless mouse, which are unable to generate mature T lymphocytes and therefore cannot mount a full immune response. The mice were implanted with human prostate cancer and then given vitamins K₃ and C, orally or by injection. Treated mice were found to survive 25% longer than controls.⁹⁶³

Numerous studies illustrate the combined effects of vitamins K₃ and C in cancer treatment. Mice with liver tumours and abdominal fluid, known as ascites, were resistant to the anticancer drug oncovin. When pretreated with the combination of vitamins K and C, the mice regained sensitivity to the drug, without additional organ toxicity.⁹⁵⁸ Furthermore, the combination of vitamins C and K₃ is toxic to oral cancer and human leukaemia, but not to healthy cells, such as fibroblasts or pulp cells.⁹⁵⁴

Conclusions

Vitamin K clearly has anticancer activity. Its most direct mechanism is cell oxidation, caused by the redox cycling of vitamin K₃. This exceeds the cancer cells' capacity for production of antioxidants and leads to cell death.

At this stage of the chapter, you might be wondering why vitamin K, or a derivative of it, is not a central feature of cancer research. There is no scientific answer to this question. The vitamin, which is normally present in the body, has a powerful anticancer action and relatively low toxicity. Any new drug with such properties would surely be vigorously promoted and researched. Such a compound would add greatly to the share price of the company that held the patent.

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In practice, the use of vitamin K may have been limited by its inability to be patented and thereby to generate profits. Considering the promise of vitamin K as an anticancer agent, with a high degree of safety, it is disappointing that more research has not been performed on this nutrient.