Vitamin K and Cancer

RDA: male 120ug, female 90ug

https://ods.od.nih.gov/factsheets/vitaminK-HealthProfessional/

Vitamin K, the generic name for a family of compounds with a common chemical structure of 2-methyl-1,4-naphthoquinone, is a fat-soluble vitamin that is naturally present in some foods and is available as a dietary supplement [1]. These compounds include phylloquinone (vitamin K1) and a series of menaquinones (vitamin K2) [2]. Menaquinones have unsaturated isoprenyl side chains and are designated as MK-4 through MK-13, based on the length of their side chain [1,2]. MK-4, MK-7, and MK-9 are the most well-studied menaquinones.

Menadione, which is sometimes called vitamin K3, is another synthetic form of vitamin K. It was shown to damage hepatic cells in laboratory studies conducted during the 1980s and 1990s, so it is no longer used in dietary supplements or fortified foods [3].

https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/1097-0142(19890301)63:5%3C901::AID-CNCR2820630518%3E3.0.CO;2-G/abstract;jsessionid=E9C4FE55BE79464AB9945EAFA0709A5D.f02t02

Effects of sodium ascorbate (vitamin C) and 2-methyl-1,4-naphthoquinone (vitamin K3) treatment on human tumor cell growth in vitro. I. Synergism of combined vitamin C and K3 action 1989

When given separately, vitamin C or K_3 had a growth inhibiting action only at high concentrations (5.10^3 µmol/1 and 10^5 nmol/1, respectively). Combined administration of both vitamins demonstrated a synergistic inhibition of cell growth at 10 to 50 times lower concentrations. At this level separately given vitamins are not toxic. The sensitivity to this treatment was somewhat different in the three cell lines, being slightly higher for KB line. This tumor cell growth inhibitory effect was completely suppressed by the addition of catalase to the culture medium containing vitamins C and K_3, suggesting an excessive production of hydrogen peroxide as being implied in mechanisms responsible for the above-mentioned effects.

https://pubmed.ncbi.nlm.nih.gov/38927877/

Generation of Hydrogen Peroxide in Cancer Cells: Advancing Therapeutic Approaches for Cancer Treatment 2024

Another possible avenue that could be taken with vitamin C cancer treatment is using it in conjunction with other therapeutics, such as vitamin K3, triethylenetetramine, or other H2O2-responsive chemotherapeutic drugs (i.e., camptothecin) to achieve synergistic anticancer effect while minimizing unwanted side effects [133–135

https://isom.ca/article/vitamin-c-cancer-use-oral-vitamin-c/

Vitamin C and Cancer: Is There A Use For Oral Vitamin C? 2013

Despite this, it is important to remember that vitamin C on its own is a relatively weak anticancer agent. Crucially, however, it can be used as a driver, to supply electrons to synergistic redox agents. Often, such substances combine in a Fenton style reaction, generating hydrogen peroxide which kills cancer cells. Numerous other mechanisms may also be involved, such as inhibition by the combination of vitamin C and alpha-lipoic acid of NF-kappaB, which is involved in the control of DNA copying during cell replication (Flohé, Brigelius-Flohé, Saliou, et al. 1997). When combined with **vitamin K3**, the concentration of vitamin C needed to kill cells is massively reduced – by a factor of 10-50 (Noto, Taper, Jiang, et al. 1989). Similarly, **alpha-lipoic acid** (Casciari, Riordan, Schmidt, et al. 2001), copper (Bram, Froussard, Guichard, et al. 1980), **selenium**, and other redox active supplements greatly increase the selective cytotoxicity of ascorbate (Hickey, Roberts, 2005)

Oral intakes, particularly with combined use of ascorbic acid and liposomal vitamin C, can easily achieve and maintain adequate levels for selective cytotoxicity. Finally, the use of vitamin C as a sole anticancer agent is not recommended, as its anticancer actions are known to be greatly enhanced through use of synergistic supplements, such as **alpha-lipoic acid**.

https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/1097-0142(19890301)63:5%3C901::AID-CNCR2820630518%3E3.0.CO;2-G/abstract;jsessionid=E9C4FE55BE79464AB9945EAFA0709A5D.f02t02

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9413298/

Role of Vitamin K in Selected Malignant Neoplasms in Women 2022

The main function of vitamin K in the human organism is its activity in the blood clotting cascade. Epidemiological studies suggest that reduced intake of vitamin K may contribute to an increased risk of geriatric diseases such as atherosclerosis, dementia, osteoporosis, and osteoarthritis. A growing number of studies also indicate that vitamin K may be involved not only in preventing the development of certain cancers but it may also support classical cancer chemotherapy. Vitamin K_3 inhibited the epithelial-mesenchymal transition (EMT) and Wnt signaling pathway by affecting various molecular targets, such as cadherins, cyclins, and β-catenin [19]. Some other studies have shown that vitamin K leads to depolarization of the mitochondrial membrane and a release of cytochrome c into the cytosol with the generation of apoptosome, which drives the activation of caspase 9, ultimately leading to the activation of caspase 3 and the initiation of apoptosis [20,21,22]. In addition, vitamin K_2 can reduce cyclin D1 expression in cancer cells by inhibiting the binding of the nuclear factor κB (NF-κB) to the cyclin D1 promoter, which occurs by arresting the cell cycle in the G1 phase [23]. Furthermore, vitamin K_2 derivatives showed growth inhibitory effects not only on cancer cells derived from various organs but also on those resistant to radiotherapy by generating ROS [24].

https://pubmed.ncbi.nlm.nih.gov/29805627/

Research progress on the anticancer effects of vitamin K2 2018

Vitamin K2 (VK2), which exerts anticancer effects on a number of cancer cell lines, is considered to be a prospective novel agent for the treatment of cancer. The present review aims to summarize the results of studies in which VK2 was administered either to patients with cancer or animals inoculated with cancerous cells, particularly investigating the inhibitory effects of VK2 on cancerous cells, primarily involving cell-cycle arrest, cell differentiation, apoptosis, autophagy and invasion. The present review summarizes evidence stating that treatment with VK2 could positively inhibit the growth of cancer cells, making it a potentially useful approach for the prevention and clinical treatment of cancer. Additionally, the combination treatment of VK2 and established chemotherapeutics may achieve better results, with fewer side effects. Therefore, more attention should be paid to the effects of micronutrients on tumors.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9509427/

New insights on vitamin K biology with relevance to cancer 2022

Vitamin K intake has been inversely associated with cancer incidence and mortality in observational studies. newly discovered functions of vitamin K in cancer cells include activation of the steroid and xenobiotic receptor (SXR) and regulation of oxidative stress, apoptosis and autophagy. Here we provide an update on vitamin K biology, non-canonical mechanisms of vitamin K actions, potential functions of vitamin K dependent proteins in cancer and observational trials on vitamin K intake and cancer.

There are two naturally occurring substances with vitamin K activity: **phylloquinone** (See Glossary) (PK, or vitamin K1) and **menaquinone** (MK or vitamin K2), and both forms act as co-factors for a unique post-translational protein modification called γ-carboxylation. In γ-carboxylation, glutamate (GLU) residues in target proteins are enzymatically converted to carboxyglutamate (GLA) residues.

https://pubmed.ncbi.nlm.nih.gov/12767595/

The association of vitamins C and K3 kills cancer cells mainly by autoschizis, a novel form of cell death. Basis for their potential use as coadjuvants in anticancer therapy 2003

Deficiency of alkaline and acid DNase is a hallmark in all non-necrotic cancer cells in animals and humans. These enzymes are reactivated at early stages of cancer cell death by vitamin C (acid DNase) and vitamin K(3) (alkaline DNase). Moreover, the coadministration of these vitamins (in a ratio of 100:1, for C and K(3), respectively) produced selective cancer cell death. Detailed morphological studies indicated that cell death is produced mainly by autoschizis, a new type of cancer cell death. Several mechanisms are involved in such a cell death induced by CK(3), they included: formation of H(2)O(2) during vitamins redox cycling, oxidative stress, DNA fragmentation, no caspase-3 activation, and cell membrane injury with progressive loss of organelle-free cytoplasm. Changes in the phosphorylation level of some critical proteins leading to inactivation of NF-kappaB appear as main intracellular signal transduction pathways. The increase knowledge in the mechanisms underlying cancer cells death by CK(3) may ameliorate the techniques of their in vivo administration. The aim is to prepare the introduction of the association of vitamins C and K(3) into human clinics as a new, non-toxic adjuvant cancer therapy.

https://pubmed.ncbi.nlm.nih.gov/31238027/

Vitamin K3 (menadione) suppresses epithelial-mesenchymal-transition and Wnt signaling pathway in human colorectal cancer cells 2019

Tumor recurrence and metastasis decrease the survival rate of colorectal cancer (CRC) patients. Menadione reduces the numbers and incidences of 1,2-dimethylhydrazine induced colon tumors in mouse but the mechanism of anticancer activity of menadione in colorectal cancer is not very clear. Since Wnt signaling is constitutively active in CRC and it aggravates the epithelial mesenchymal transition (EMT), the regulation of EMT and Wnt signaling by menadione (vitamin K3) was investigated in CRC cells. Menadione showed cytotoxicity against human CRC cells (SW480 and SW620) and human primary colon cancer cells but was relatively ineffective against the cells from human normal colon (CRL-1790) and human primary colon epithelial cells.

https://www.clinicalnutritionjournal.com/article/S0261-5614(20)30613-0/abstract

Vitamin K intake and breast cancer incidence and death: results from a prospective cohort study 2021

Neither dietary vitamin K1 nor total vitamin K was associated with breast cancer incidence and mortality.

Dietary vitamin K2 was associated with breast cancer incidence and mortality.

Reducing dietary intake of menaquinones may offer a novel strategy for breast cancer prevention.

https://pubmed.ncbi.nlm.nih.gov/24175842/

Menadione (Vitamin K3) induces apoptosis of human oral cancer cells and reduces their metastatic potential by modulating the expression of epithelial to mesenchymal transition markers and inhibiting migration 2013

Oral cancer is one of the most commonly occurring cancers worldwide, decreasing the patient's survival rate due to tumor recurrence and metastasis. Menadione (Vitamin K3) is known to exhibit cytotoxicity in various cancer cells but the present study focused on its effects on viability, apoptosis, epithelial to mesenchymal transition (EMT), anchorage independent growth and migration of oral cancer cells. The results show that menadione is more cytotoxic to SAS (oral squamous carcinoma) cells but not to non-tumorigenic HEK293 and HaCaT cells. Menadione treatment increased the expression of pro-apoptotic proteins, Bax and p53, with a concurrent decrease in anti-apoptotic proteins, Bcl-2 and p65. Menadione induced the expression of E-cadherin but reduced the expression of EMT markers, vimentin and fibronectin. Menadione also inhibited anchorage independent growth and migration in SAS cells. These findings reveal and confirm that menadione is a potential candidate in oral cancer therapy as it exhibits cytotoxic, antineoplastic and antimigratory effects besides effectively blocking EMT in oral cancer cells.

https://iubmb.onlinelibrary.wiley.com/doi/10.1002/bab.2312

Vitamin K: A novel cancer chemosensitizer 2022

Vitamin K is an essential nutrient and has recently been investigated as a potential anticancer agent. The combination of vitamin K analogs, such as vitamins K1, K2, K3, and K5, with other chemotherapeutic drugs have demonstrated a safe, cost-effective, and most efficient way to overcome drug resistance and improved the outcomes of prevailing chemotherapy. Published reports have shown that vitamin K in combination therapy improved the efficacy of clinical drugs by promoting apoptosis and cell cycle arrest and overcoming drug resistance by inhibiting P-glycoprotein. In this review, we discuss the mechanism, cellular targets, and possible ways to develop vitamin K subtypes into effective cancer chemosensitizers. Finally, this review will provide a scientific basis for exploiting vitamin K as a potential agent to improve the efficacy of chemotherapeutic drugs.

https://pubmed.ncbi.nlm.nih.gov/17611688/

Vitamins K2, K3 and K5 exert antitumor effects on established colorectal cancer in mice by inducing apoptotic death of tumor cells 2007

Although a number of studies have shown that vitamin K possesses antitumor activities on various neoplastic cell lines, there are few reports demonstrating in vivo antitumor effects of vitamin K, and the antitumor effect on colorectal cancer (CRC) remains to be examined. Therefore, antitumor effects of vitamin K on CRC were examined both in vitro and in vivo.

These results suggest that vitamins K2, K3 and K5 exerted effective antitumor effects on CRC in vitro and in vivo by inducing caspase-dependent apoptotic death of tumor cells, suggesting that these K vitamins may be promising agents for the treatment of patients with CRC.

https://pubmed.ncbi.nlm.nih.gov/28915711/

Vitamin K and its analogs: Potential avenues for prostate cancer management 2017

Especially intake of certain essential nutrients like vitamins has been shown to be beneficial in experimental studies and some clinical trials. Vitamin K (VK) is an essential nutrient involved in the blood clotting cascade, and there are considerable experimental data demonstrating its potential anticancer activity in several cancer types including prostate cancer.

https://pubmed.ncbi.nlm.nih.gov/30624568/

Vitamin K intake and prostate cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Screening Trial 2019

Background: Vitamin K inhibits prostate cancer cells, and an altered expression of vitamin K-dependent proteins in prostate tumors has been linked to their aggressiveness and progression. However, little is known about the effect of vitamin K intake on prostate cancer in human populations.

Objectives: We evaluated the associations of dietary intake of phylloquinone (vitamin K-1), menaquinones (vitamin K-2), and total vitamin K with the development of prostate cancer among participants in the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Screening Trial.

Conclusions: The present study does not suggest that vitamin K intake influences the occurrence of total and advanced prostate cancer in the general US population.

https://pubmed.ncbi.nlm.nih.gov/30703479/

The combination of ascorbate and menadione causes cancer cell death by oxidative stress and replicative stress 2019

The combination of ascorbate and menadione (VC:VK3 = 100:1) is an investigational treatment for cancer under clinical trials.

The mechanism of cell death induced by VC/VK3 was also elucidated. We found that VC/VK3 inhibited glutathione peroxidase activity and led to an elevated level of lipid peroxidation, which triggered apoptosis-inducing factor (AIF) mediated cell death pathway. Therefore, the combination not only induced replicative stress by inhibiting RNR, but also oxidative stress by targeting anti-oxidant systems and triggered AIF-mediated cancer cell death.

https://pmc.ncbi.nlm.nih.gov/articles/PMC4687332/

PRX1 knockdown potentiates vitamin K3 toxicity in cancer cells: a potential new therapeutic perspective for an old drug 2015

Vitamin K3 (vitK3) is a synthetic naphthoquinone exhibiting significant in vitro and in vivo anticancer activity against multiple human cancers, and has therapeutic potential when combined with other anticancer molecules. The major mechanism for the anticancer activity of vitK3 is the generation of cytotoxic reactive oxygen species (ROS). We thus reasoned that a rational redox modulation of cancer cells could enhance vitK3 anticancer efficiency.

Vitamin K3 (2-methyl-1, 4 naphthoquinone, also known as menadione) is a form of vitamin K that does not participate in the synthesis of coagulation proteins [1, 2]. Rather, vitamin K3 (vitK3) is readily redox cycled, thereby generating reactive oxygen species (ROS) and consuming NADPH. VitK3 exhibits anticancer activity against a variety of human cancer cell lines [3–6].

https://pubmed.ncbi.nlm.nih.gov/23590997/

A biophysical approach to menadione membrane interactions: relevance for menadione-induced mitochondria dysfunction and related deleterious/therapeutic effects 2013

Menadione (MEN), a polycyclic aromatic ketone, was shown to promote cell injury by imposing massive oxidative stress and has been proposed as a promising chemotherapeutic agent for the treatment of cancer diseases.

https://pmc.ncbi.nlm.nih.gov/articles/PMC3171656/

Pankiller effect of prolonged exposure to menadione on glioma cells: potentiation by vitamin C 2010

Menadione (Vitamin K3) has anti-tumoral effects against a wide range of cancer cells. Its potential toxicity to normal cells and narrow therapeutic range limit its use as single agent but in combination with radiation or other anti-neoplastic agents can be of therapeutic use.

In this long-term assay, menadione:vitamin C at a ratio 1:100 showed higher anti-proliferative activity when compared to each drug alone and allowed to reduce each drug concentration between 2.5 to 5-fold. Similar anti-proliferative effect was demonstrated in 8 patient derived glioblastoma cell cultures. Our data should be able to encourage further advanced studies on animal models to evaluate the potential use of this combination therapy for glioma treatment.

https://www.sciencedirect.com/science/article/abs/pii/S0304419X23002068

Vitamin K: New insights related to senescence and cancer metastasis 2024

Highlights

- •Vitamin K has not only coagulation effects but also anti-inflammatory, antioxidant, and anticancer effects.
- •The close relationship between vitamin K, cellular senescence, and cancer metastasis.
- •Vitamin K has anti-cancer activity and can inhibit cancer metastasis through various mechanisms, including direct inhibition through anti-inflammatory and antioxidant pathways, and indirect inhibition through combating cellular senescence.
- •Vitamin K as an adjuvant therapy for cancer metastasis has potential application prospects.
- •Clinicians customize vitamin K supplementation based on the specific situation of patients in order to provide the best strategy for preventing or treating cancer.

https://pmc.ncbi.nlm.nih.gov/articles/PMC10483107/

Vitamin K Intake and Risk of Lung Cancer: The Japan Collaborative Cohort Study 2023

We investigated the associations between total vitamin K intake from food and the development of lung cancer based on this large prospective cohort study

A validated food frequency questionnaire was used to examine vitamin K intake among 42,166 (16,341 men and 25,825 women) at the Japan Collaborative Cohort Study's baseline (1988–1990). Hazard ratios (HRs) and 95% confidence intervals (CIs) of incident lung cancer were calculated using the Cox proportional hazard regression method based on vitamin K consumption quartiles.

430 cases (308 males and 122 women) of lung cancer were documented during a total of 564,127 person-years of follow-up (median follow-up, 14.6 years). Vitamin K consumption was shown to be inversely related to lung cancer risk; the multivariable hazard ratio [HR] for the highest versus lowest quartiles was 0.67 (95% confidence interval [CI], 0.46–0.96; *P* for trend = 0.010).

One prospective study from Germany, which included 24,340 participants during a median follow-up of 10.2 years, reported an inverse association between total vitamin K intake and the incidence of lung cancer.[21]

https://pubmed.ncbi.nlm.nih.gov/12946240/

The anticancer effects of vitamin K 2003

Vitamin K, an essential nutrient often associated with the clotting cascade, has been the focus of considerable research demonstrating an anticancer potential. Much of this research has focused on vitamin K3, although vitamins K2 and K1 have also been shown to have anticancer effects. Early studies of vitamin K3 employed an oxidative model to explain the anticancer effects seen in both in vitro and in vivo studies; however, this model does not adequately address the action of vitamins K1 and K2. Recent research has demonstrated the anticancer action of vitamin K may act at the level of tyrosine kinases and phosphatases, modulating various transcription factors such as Myc and Fos. Tyrosine kinases associated with cyclins have also been shown to be affected by vitamin K, which can lead to cell cycle arrest and cell death.

https://cancerci.biomedcentral.com/articles/10.1186/1475-2867-11-19

Vitamin K3 and vitamin C alone or in combination induced apoptosis in leukemia cells by a similar oxidative stress signalling mechanism 2011

It is shown that vitamin K3- or vitamin C- induced apoptosis in leukemia cells by oxidative stress mechanism involving superoxide anion radical and hydrogen peroxide generation, activation of NF-κB, p53, c-Jun, protease caspase-3 activation and mitochondria depolarization leading to nuclei fragmentation. Cell death was more prominent when Jurkat and K562 cells are exposed to VC and VK3 in a ratio 1000:1 (10 mM: 10 μM) or 100:1 (300 μM: 3 μM), respectively.

Conclusion

We provide for the first time in vitro evidence supporting a causative role for oxidative stress in VK3- and VC-induced apoptosis in Jurkat and K562 cells in a domino-like mechanism. Altogether these data suggest that VK3 and VC should be useful in the treatment of leukemia.

https://pmc.ncbi.nlm.nih.gov/articles/PMC6481349/

Divergent effects of vitamins K1 and K2 on triple negative breast cancer cells 2019

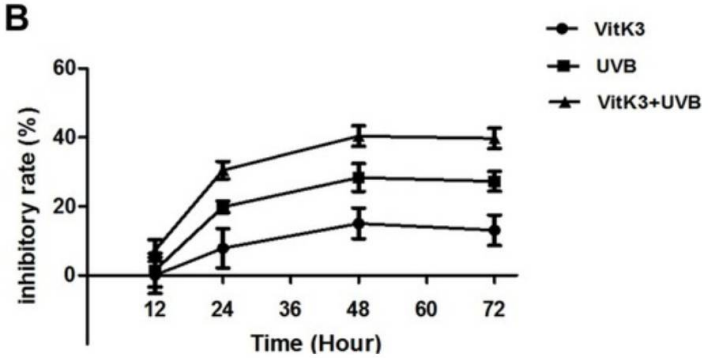
These studies show that TNBC cells express a functional vitamin K pathway and that K1 and K2 exert distinct phenotypic effects. Clarification of the mechanisms by which K1 and K2 induce these effects may lead to relevant therapeutic strategies for manipulating this pathway in TNBC patients .

https://www.tandfonline.com/doi/full/10.2147/ott.s228792

Effects of Vitamin K3 Combined with UVB on the Proliferation and Apoptosis of Cutaneous Squamous Cell Carcinoma A431 Cells 2020

Cutaneous squamous cell carcinoma (cSCC) is the second most common form of skin cancer and its incidence continues to rise yearly. Photodynamic therapy (PDT) is a non-invasive form of cancer therapy, which utilizes the combined action of a photosensitizer, light, and oxygen molecules to selectively cause cellular damage to tumor cells. Vitamin K3 (VitK3) has been shown to induce apoptosis and inhibit the growth of tumor cells in humans. The purpose of this study was to determine the effect of VitK3 and ultraviolet radiation B (UVB) on oxidative damage, proliferation and apoptosis of A431 cells.

We found that the co-treatment of VitK3 combined with UVB more significantly inhibited the growth and proliferation of A431 cells than either VitK3 or UVB alone.



Treatment with different concentrations (0, 30, 45, 60, and 100 μmol/L) of VitK3 for 24 h reduced cell growth in a dose-dependent manner. The median inhibitory concentration (IC50) of VitK3 was 40 μmol/L in A431 cells producing a corresponding inhibition rate of 50.7% ± 2.88% (Supplementary Figure A). Similarly, cell irradiation with different doses of UVB (0, 0.5, 1.0, 1.5, and 2.0 J/cm^2) for 24 h also showed a reduction in tumor cell growth in a dose-dependent manner. The half inhibitory dose of UVB was 0.8 J/cm^2, yielding an inhibition rate of 49.85% ± 3.02% in A431 cells. The inhibition rate was moderate at 1.5 J/cm^2 (Supplementary Figure B). These results indicated that VitK3 and UVB reduced tumor cell viability in a dose-dependent manner.

https://pubmed.ncbi.nlm.nih.gov/12470246/

Potential therapeutic application of the association of vitamins C and K3 in cancer treatment 2002

Combined vitamin C and K(3) administration in vitro and in vivo produced tumor growth inhibition and increased the life-span of tumor-bearing mice. CK(3)-treatment selectively potentiated tumor chemotherapy, produced sensitization of tumors resistant to some drugs, potentiated cancer radiotherapy and caused inhibition of the development of cancer metastases without inducing toxicity in the host. We propose the association of vitamins C and K(3) as an adjuvant cancer therapy which may be introduced into human cancer therapy without any change in the classical anticancer protocols, and without any supplementary risk for patients.

https://acsjournals.onlinelibrary.wiley.com/doi/abs/10.1002/1097-0142%2819890301%2963%3A5%3C901%3A%3AAID-CNCR2820630518%3E3.0.CO%3B2-G

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https://ar.iiarjournals.org/content/38/3/1407

Vitamins C and K3: A Powerful Redox System for Sensitizing Leukemia Lymphocytes to Everolimus and Barasertib 2018

Results: Combined administration of 300 μM vitamin C plus 3 μM pro-vitamin K3 reduced the viability of leukemia lymphocytes by ~20%, but did not influence the viability of normal lymphocytes. All combinations of anticancer drug plus vitamins C and K3 were characterized by synergistic cytotoxicity towards Jurkat cells, compared to cells treated with drug alone for 24 h. In the case of barasertib and everolimus, this synergistic cytotoxicity increased within 72 hours. It was accompanied by strong induction of apoptosis, but a reduction of level of hydroperoxides and moderately increased protein–carbonyl products in leukemia cells. Conclusion: Leukemia lymphocytes were more sensitive to combined administration of anticancer drug (everolimus or barasertib) plus vitamins C and K3, compared to normal lymphocytes. The combination of vitamin C plus K3 seems to be a powerful redox system that could specifically influence redox homeostasis of leukemia cells and sensitize them to conventional chemotherapy.

https://pubmed.ncbi.nlm.nih.gov/23272231/

Alpha-tocopheryl succinate inhibits autophagic survival of prostate cancer cells induced by vitamin K3 and ascorbate to trigger cell death 2012

The redox-silent vitamin E analog α-tocopheryl succinate (α-TOS) was found to synergistically cooperate with vitamin K3 (VK3) plus ascorbic acid (AA) in the induction of cancer cell-selective apoptosis via a caspase-independent pathway.

Conclusions/significance: α-TOS, a mitochondria-targeting apoptotic agent, switches at sub-apoptotic doses from autophagy-dependent survival of cancer cells

to their demise by promoting the induction of apoptosis.

https://pubmed.ncbi.nlm.nih.gov/32798378/

Photodynamic Effects of Vitamin K3 on Cervical Carcinoma Cells Activating Mitochondrial Apoptosis Pathways 2021

Photodynamic Therapy (PDT) is a photoactivation or photosensitization process, wherein vitamin K3 (Vit K3) serves as a photosensitizer to produce Reactive Oxygen Species (ROS) against bacteria at appropriate wavelengths. In this study, we used Vit K3 treatment combined with Ultraviolet radiation A (UVA) to produce photodynamic effects on cervical cancer.

Results: Vit K3 treatment plus UVA reduced tumor cell viability in a dose-dependent manner. Further studies indicated that Vit K3 treatment plus UVA can inhibit tumor growth and enhance the apoptosis of cervical cancer cells.

Conclusion: Our results showed that Vit K3 treatment combined with UVA exerted photodynamic effects on cervical cancer cells by activating mitochondrial apoptosis pathways.

https://iubmb.onlinelibrary.wiley.com/doi/abs/10.1002/biof.2117

Vitamin K3 derivative inhibits androgen receptor signaling in targeting aggressive prostate cancer cells 2024

The effect of micronutrients, including Vitamin K, on various cancer cell lines has been widely studied, but the potential anticancer effect of VK3-OCH3, an analog of vitamin K3 (Menadione), on African American prostate cancer has not been evaluated. In this study, we compared the anticancer effect of VK3-OCH3 on targeting African American derived PCa cell lines namely RC77-T and MDA-PCa-2b. Our results show that VK3-OCH3 significantly inhibits the proliferation of both RC77-T and MDA-PCa-2b African American PCa cells and promotes apoptosis, and the underlying mechanism of cell death appears to be similar in both the cell lines. Notably, VK3-OCH3 inhibits colony-forming ability and induces apoptosis by blocking the cell cycle at G0 in African American PCa cells. VK3-OCH3 also acts as an anti-metastatic agent by inhibiting the migration ability of the metastatic properties of African American PCa cells. The cell death of African American PCa cells mediated by VK3-OCH3 is associated with the production of free radicals, such as intracellular and mitochondrial reactive oxygen species (ROS). Interestingly, antioxidants such as N-Acetylcysteine (NAC) and Glutathione (GSH) effectively negated the oxidative stress induced by VK3-OCH3 on PCa cell lines derived from African American patients.