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Review Article

Impact of nutritional factors on colorectal cancer: implication The molecular mechanisms of vitamins supplementation

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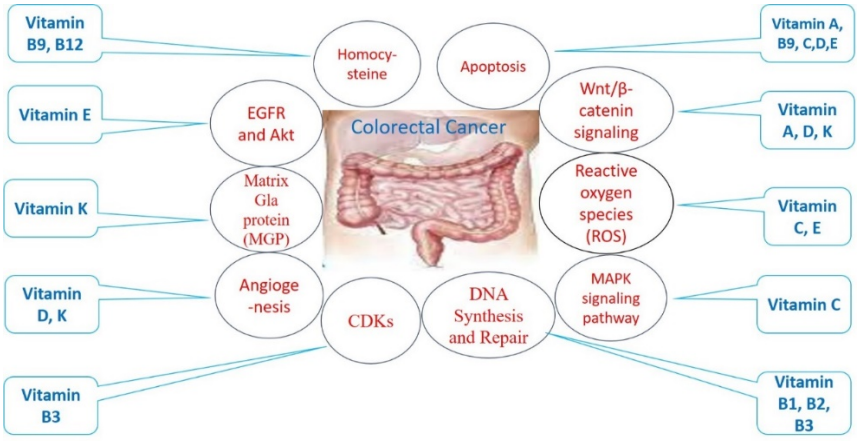
Abstract

Colorectal cancer (CRC) is the leading cause of death from gastrointestinal cancer, the second largest cause of cancer-related death worldwide, and the third most common cancer in both men and women. Bad eating habits, smoking, intestinal inflammatory diseases, polyps, aging, and genetic factors all increase the risk of developing colorectal cancer. More interestingly, vitamin deficiency has been associated with an increased risk of colorectal cancer. We reviewed the published significance of vitamin supplementation on colorectal cancer proliferation, survival, apoptosis, angiogenesis and migration, focusing on the possible molecular mechanisms of water-soluble and fat-soluble vitamins to provide protective suggestions to minimize the occurrence and progression of colorectal cancer.

Keywords: colorectal cancer; nutritional factors; vitamins supplementation



Graphical abstract of the possible molecular mechanisms of vitamins on colorectal cancer.

Introduction

One of the most prevalent cancers in the world is colorectal cancer. It ranks second in terms of cancer-related deaths and third in terms of incidence [1]. In 2018, there were 1.8 million new cases of colorectal cancer worldwide, accounting for nearly 10% of all new cancer cases and deaths worldwide [2]. By 2040, it is predicted that there will be over 1.9 million new cases of colorectal cancer, making it the third most diagnosed cancer worldwide [3]. There could be nearly 2.5 million new cases in 2035. According to data from the USA, the death rate decreased by approximately 50% between 1970 and 2016, from 29.2 per 10,000 patients to 13.7 per 10,000 patients, due to the rapid advancements in screening and treatment procedures. However, this tendency seems only observed in highly developed countries [4].

Meanwhile, the 5-year survival rate for colorectal cancer is roughly 64%, whereas the rate for metastatic colorectal cancer is 12%. Further research is still required to develop effective medical

intervention strategies [5]. The main topic of this review is the role of vitamins in preventing and protecting against colorectal cancer. Moreover, a comprehensive understanding of the underlying molecular mechanisms of vitamin-mediated epigenetic regulation of colorectal cancer genes is required to target therapeutic targets for colorectal cancer prevention and treatment effectively.

Vitamin A

Vitamin A is essential for many physiological functions, such as cellular differentiation regulation and epithelial tissue health maintenance. Numerous molecular mechanisms have been identified as potential means by which vitamin A and its derivatives, including Retinoids, may impact the development of colorectal cancer. Moreover, *Wang* and his colleagues had stated that vitamin E, C, and carotenoid intake did not correlate with the risk of colorectal cancer in either men or women [6].

Vitamin A is converted into its active form, retinoic acid, which binds to nuclear receptors, such as retinoid X receptors (RXRs) and retinoic acid receptors (RARs) [7]. These receptors control gene transcription, affecting how epithelial cells differentiate. Thus, proper cell differentiation is crucial for maintaining the typical architecture and function of the colorectal epithelium. Dysregulation of this process can contribute to carcinogenesis [8]. Moreover, it has been demonstrated that retinoid affects the expression of cell cycle regulators, which modulate the cell cycle. They can stop cell division and induce cell cycle arrest, which stops the unchecked growth linked to cancer [9]. Furthermore, it has been reported that colorectal cancer cells can undergo apoptosis when exposed to vitamin A and its derivatives [9,10]. This process of programmed cell death removes harmed or aberrant cells, serving as a defence against cancer growth.

Retinoids play a role in modulating the immune system, potentially enhancing the body's ability to recognize and eliminate cancer cells. This includes effects on immune cell function and the production of cytokines [11], as it has been reported that the retinoic acid receptor in the nucleus of bone marrow cells is most likely bound by vitamin A, which controls the population of bone marrow cells. This, in turn, inhibits the expression levels of apoptosis genes, including B-cell lymphoma 2 (Bcl-2) and Fas, where Bcl-2 interfere with apoptosis processing by delaying Fas-induced apoptosis and caspase activation [12]. Furthermore, retinoids may inhibit angiogenesis, the process of creating new blood vessels, which is essential for the growth of tumours. By limiting the blood supply to tumours, Retinoids can suppress tumour progression [13].

The Wnt/Wingless signaling transduction pathway is involved in the development of embryos as well as tumorigenesis. The transcription of Wnt target genes is activated by β-Catenin, a crucial element of the Wnt signaling pathway, through its interaction with the TCF/LEF transcription factor family [14]. *Bian* and his colleagues, demonstrated that The Wnt/β-catenin signaling pathway is thought to be abnormally activated in colorectal cancer because almost all colorectal cancer patients have increased Wnt/β-catenin signaling, which emphasizes the significance of this pathway for therapeutic intervention [15]. Retinoids have been shown to interact with this pathway, influencing the expression of Wnt target genes and preventing aberrant cellular reactions linked to the emergence of cancer [9,16].

Moreover, vitamin A and its derivatives can influence epigenetic modifications, such as DNA methylation and histone acetylation [17]. These epigenetic changes can alter gene expression in colorectal cancer development. In addition to DNA methylation, miRNA expression, and genomic imprinting, histone modification is becoming more widely acknowledged as a crucial mechanism behind the onset and progression of colorectal cancer [18].

Vitamin B1 (Thiamine)

The specific molecular mechanisms underlying the effects of vitamin B1 (thiamine) on colorectal cancer are not as extensively studied and understood as those for some other vitamins. Thiamine is an essential B vitamin critical in energy metabolism, particularly in converting glucose to energy [19].

Thiamine is a cofactor for enzymes involved in the metabolism of carbohydrates, particularly in the tricarboxylic acid (TCA) cycle and the pentose phosphate pathway [19]. Alterations in energy

metabolism are a hallmark of cancer, and maintaining proper energy balance is crucial for normal cell function. Imbalances in energy metabolism could potentially affect the growth and survival of colorectal cancer cells [20].

Thiamine participates in the regeneration of the antioxidant glutathione [21]. Antioxidants protect cells from oxidative stress, which is implicated in cancer development. By contributing to the cellular antioxidant defense system, thiamine may indirectly influence cells' susceptibility to oxidative damage.

Thiamine is involved in nucleotide synthesis, essential for DNA stability and repair. Appropriate mechanisms for DNA repair are also essential for avoiding the build-up of mutations that may aid in the development of cancer [22]. B vitamins, including thiamine, play a role in supporting immune system function. A well-functioning immune system is critical for recognizing and eliminating cancer cells. Thiamine deficiency has been associated with immune system dysfunction, and restoring thiamine levels could potentially support immune responses against colorectal cancer [23].

Vitamin B2 (Riboflavin)

Riboflavin, a water-soluble vitamin B2, is a precursor to the cofactors flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN), which are necessary for many cellular functions, such as energy metabolism [24].

Riboflavin is a critical component of the electron transport chain, where it participates in oxidative phosphorylation within the mitochondria. Proper mitochondrial function is essential for cellular energy production [25]. Dysregulation of energy metabolism is a common feature of cancer cells, and riboflavin's role in this process could indirectly impact colorectal cancer cells [26].

Riboflavin synthesizes the antioxidant cofactors FMN and FAD, which are essential for the activity of antioxidant enzymes [24,25]. Antioxidants help protect cells from oxidative stress, and maintaining an adequate supply of riboflavin may contribute to cellular defence mechanisms against oxidative damage, which is associated with cancer development [27].

Riboflavin is involved in nucleotide metabolism, crucial for DNA synthesis and repair [28]. Proper DNA repair mechanisms are crucial to stopping the accumulation of mutations that might lead to the development of colorectal cancer [29].

Chronic inflammation is a known risk factor for cancer development, including colorectal cancer [30]. Some B vitamins, including riboflavin, may have anti-inflammatory effects, potentially contributing to a lower risk of cancer [31]. Riboflavin is essential for the normal functioning of the immune system [32]. A well-functioning immune system is crucial for recognizing and eliminating cancer cells. Adequate riboflavin levels may support immune responses against colorectal cancer [32].

Vitamin B3 (Niacin)

Vitamin B3, also known as niacin, is a water-soluble vitamin that plays essential roles in cellular metabolism and DNA repair. The effects of vitamin B3 on colorectal cancer involve several molecular mechanisms [33]. Nicotinamide adenine dinucleotide (NAD+) is a coenzyme involved in energy metabolism, DNA repair, and cell signaling, as well as Niacin is a precursor for NAD+. For cellular health and function to be maintained, adequate levels of NAD+ are essential [34]. Moreover, NAD+ is a cofactor for several enzymes involved in energy metabolism, such as those in the glycolytic pathway and the tricarboxylic acid (TCA) cycle [35].

Also, Poly (ADP-ribose) polymerase (PARP) enzymes, which utilize NAD+ as a substrate, play a role in DNA repair [36]. Niacin supplementation may impact DNA repair processes, contributing to genomic stability and reducing the risk of mutations leading to colorectal cancer. Moreover, NAD+-dependent sirtuin enzymes have been implicated in regulating angiogenesis and blood vessel formation [37]. Tumor growth requires proper control of angiogenesis, and niacin's effect on sirtuin activity may impact this process [38]. Most interestingly, it has been proposed that niacin affects the function of cyclin-dependent kinases (CDKs), which control the cell cycle [39].

Vitamin B5 (Pantothenic acid)

Vitamin B5 is an essential water-soluble vitamin that is a coenzyme A (CoA) component, which plays a critical role in various cellular processes, including energy metabolism and the synthesis of fatty acids and cholesterol. Pantothenic acid is a precursor to CoA, which is essential for acetyl-CoA synthesis. Acetyl-CoA is a critical intermediate in energy metabolism, linking the breakdown of carbohydrates, fats, and proteins to producing ATP, the cell's primary energy source. Dysregulation of energy metabolism is a hallmark of cancer, and alterations in these pathways could impact colorectal cancer cells [40].

More interestingly, CoA is involved in various mitochondrial reactions, maintaining cellular redox balance [41]. Moreover, vitamin B5's role in supporting mitochondrial function may affect colorectal cancer. Furthermore, Acetyl-CoA, generated from vitamin B5-derived CoA, is involved in acetylation reactions that regulate gene expression and cellular signaling [42]. Aberrant acetylation patterns have been observed in cancer cells, and Vitamin B5 may indirectly influence these processes [41,42].

Vitamin B6 (Pyridoxine)

Vitamin B6 is a water-soluble vitamin in several forms, including pyridoxine, pyridoxal, and pyridoxamine. The active coenzyme forms of vitamin B6, pyridoxal 5'-phosphate (PLP) and pyridoxamine 5'-phosphate (PMP) play crucial roles in various biological processes [43]. Vitamin B6 is involved in one-carbon metabolism, including converting homocysteine to cysteine [44]. The regulation of homocysteine levels is essential for DNA methylation and synthesis, and disturbances in this process have been associated with cancer, including colorectal cancer [45].

Moreover**,** PLP, the active form of vitamin B6, is a cofactor for various enzymes involved in amino acid metabolism [46]. These enzymes synthesize and break amino acids, which are essential for cell growth and proliferation. Furthermore, PLP is a cofactor for enzymes involved in heme synthesis. Heme is an essential component of haemoglobin and other hemoproteins [47]. Alterations in heme metabolism may influence oxygen transport and cellular respiration, potentially impacting cancer cells.

More interestingly, PLP synthesizes neurotransmitters such as dopamine, serotonin, and gamma-aminobutyric acid (GABA). Neurotransmitters can influence cellular signaling, and disturbances in neurotransmitter balance may impact cancer progression [48].

Vitamin B7 (Biotin)

Vitamin B7, known as biotin, is a water-soluble cofactor for several carboxylase enzymes involved in various metabolic pathways [49]. Carboxylase enzymes, such as pyruvate carboxylase, acetyl-CoA carboxylase, and propionyl-CoA carboxylase, require biotin as a cofactor [50]. These enzymes play crucial roles in fatty acid synthesis, gluconeogenesis, and amino acid metabolism. Dysregulation of these metabolic pathways has been linked to cancer, and biotin's role in supporting carboxylase function may indirectly impact these processes. Moreover, Biotin can modulate gene expression, and some studies suggest it may play a role in cell proliferation and growth [51]. Uncontrolled cell proliferation is a hallmark of cancer, and factors that regulate cell cycle progression are of interest in cancer research.

Biotin has been suggested to modulate immune responses, and a well-functioning immune system is critical for recognizing and eliminating cancer cells [52]. The influence of biotin on immune function may have implications for colorectal cancer.

Vitamin B9 (Folic acid)

Vitamin B9 also called folic acid, is the synthetic form of folate or folate, a water-soluble vitamin that plays a crucial role in various cellular processes, including DNA synthesis, repair, and methylation [53]. Folate is essential for normal cell function and development, and its status has been implicated in developing and preventing colorectal cancer [54]. Folate is involved in synthesising thymidylate, a DNA synthesis precursor. Thymidylate is necessary to produce thymine, one of the four nucleotide bases that make up DNA [55]. Adequate folate levels support normal DNA synthesis and repair, which is crucial

for preventing mutations that can lead to cancer [56]. Moreover, folate is a crucial donor of methyl groups essential for DNA methylation. DNA methylation is an epigenetic modification that regulates gene expression [57].

Most interestingly, Folate, along with vitamins B6 and B12, is involved in converting homocysteine to methionine [58]. Elevated levels of homocysteine are associated with an increased risk of colorectal cancer, and folate supplementation has been shown to help lower homocysteine levels [59]. Folate plays a role in regulating cell proliferation and apoptosis (programmed cell death). Adequate folate levels are necessary for maintaining a balance between cell growth and cell death. Dysregulation of these processes can contribute to cancer development [60]. Folate deficiency has been linked to chromosomal instability, a hallmark of cancer. Adequate folate levels are essential for maintaining chromosomal integrity and preventing structural abnormalities that can contribute to cancer development [61].

Moreover, folate status may influence the expression of microRNAs, small RNA molecules that play a role in post-transcriptional gene regulation. Changes in microRNA expression patterns have been observed in colorectal cancer [62]. Furthermore, folate supplementation has been associated with reducing DNA strand breaks, providing protection against DNA damage [63]. This is important for preventing the accumulation of genetic alterations that can contribute to colorectal cancer.

Vitamin B12 (Cobalamin)

Cobalamin, another name for vitamin B12, is a water-soluble vitamin essential for many cellular functions, such as DNA synthesis, red blood cell production, and neurological function [64]. Vitamin B12 is involved in the conversion of homocysteine to methionine, a process that also requires the participation of folate and vitamin B6. Methionine is crucial for synthesizing thymidylate, a nucleotide necessary for DNA replication and repair [65]. Most interestingly, vitamin B12 is involved in the methylation of DNA through its role in providing methyl groups for one-carbon metabolism [66]. Moreover, vitamin B12 is involved in the normal functioning of the immune system [67]. A well-functioning immune system is critical for recognizing and eliminating cancer cells. Adequate vitamin B12 levels may support immune responses against colorectal cancer [68].

Vitamin C (Ascorbic acid)

Vitamin C, or ascorbic acid, is a water-soluble vitamin with antioxidant properties. While its role in preventing and treating colorectal cancer is a topic of ongoing research, several potential molecular mechanisms through which vitamin C may influence it exist. Vitamin C is a potent antioxidant that can neutralize reactive oxygen species (ROS) and free radicals [69]. Colorectal cancer development is associated with oxidative stress, and the antioxidant properties of vitamin C may help reduce DNA damage and genomic instability [70]. Also, vitamin C is essential for collagen synthesis, which is crucial for maintaining the integrity of the extracellular matrix. The extracellular matrix plays a role in cell adhesion, migration, and invasion, which are relevant to cancer progression [71,72]. Moreover, vitamin C is involved in the function of immune cells, including lymphocytes and phagocytes. Adequate vitamin C levels may enhance immune response against colorectal cancer cells [73]. Most interestingly, vitamin C is a cofactor for dioxygenase enzymes, such as the ten-eleven translocation (TET) enzyme involved in DNA demethylation. DNA methylation patterns are altered in cancer, and vitamin C's role in epigenetic regulation may impact gene expression and cellular behaviour [74,75].

Vitamin C disrupts the mitogen-activated protein kinase (MAPK) signaling pathway, which is involved in cell division, survival, and apoptosis [76,77]. Modulation of these signaling pathways may impact the behaviour of colorectal cancer cells. Recent studies show that vitamin C has pro-oxidant effects in cancer cells, leading to selective cytotoxicity. This is thought to be due to the generation of hydrogen peroxide in the presence of transition metal ions [78]. Furthermore, vitamin C has been investigated for its potential to enhance the effectiveness of chemotherapy. Some studies suggest that vitamin C may sensitize colorectal cancer cells to the effects of specific chemotherapeutic agents [79,80].

Vitamin D (Cholecalciferol)

Vitamin D is a fat-soluble vitamin that plays a crucial role in calcium homeostasis, bone health, and immune function [81]. Emerging evidence suggests that vitamin D may also prevent colorectal cancer, as demonstrated in Figure 2 [82].

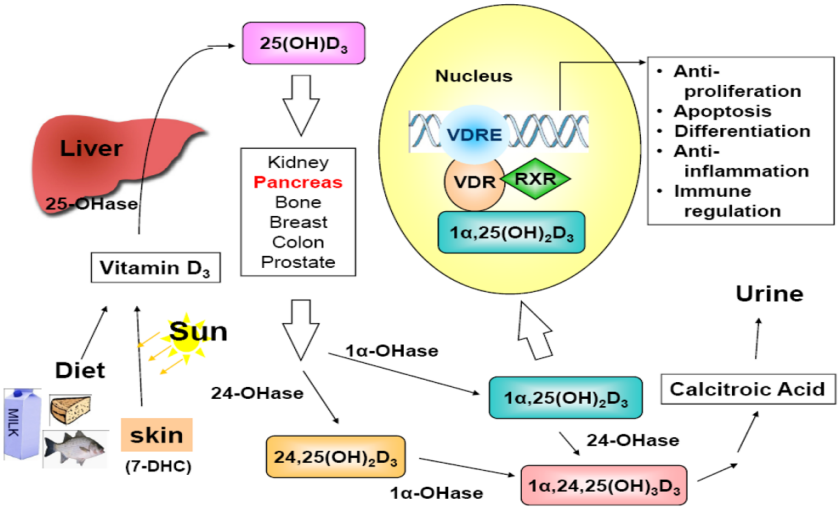


Figure 2. Vitamin D sources, metabolism, mechanism of action and biological activities [101].

Vitamin D can inhibit cell proliferation by inducing cell cycle arrest. It exerts its effects through interactions with the vitamin D receptor (VDR), leading to the regulation of genes involved in cell cycle control [83,84]. Dysregulation of cell cycle progression is a hallmark of cancer, and vitamin D's influence on this process may contribute to its anti-cancer effects [85,86]. Moreover, vitamin D's ability to promote apoptosis may help prevent cancer cell survival and proliferation [87]. It can also inhibit angiogenesis, forming new blood vessels. Inhibition of angiogenesis is considered a strategy to limit the blood supply to tumours, thereby restricting their growth and metastasis [88,89]. Also, vitamin D may enhance DNA repair mechanisms, contributing to the maintenance of genomic stability [90]. This is important for preventing the accumulation of mutations that can lead to the initiation and progression of colorectal cancer. Vitamin D can modulate immune responses by influencing the function of immune cells, including T cells and macrophages. A well-functioning immune system is critical for recognizing and eliminating cancer cells [91]. Furthermore, vitamin D exerts its biological effects by binding to the Vitamin D receptor (VDR). VDR activation leads to gene expression regulation, affecting various cellular processes. Alterations in VDR expression and function have been associated with colorectal cancer risk [92,93]. Vitamin D has been shown to downregulate the Wnt signaling pathway, which plays a crucial role in colorectal carcinogenesis. Dysregulation of Wnt signaling is common in colorectal cancer [94,95]. Also, several recent studies demonstrate that vitamin D has been shown to suppress the Wnt/β-catenin signaling pathway, a critical pathway involved in colorectal carcinogenesis. Vitamin D's inhibitory effects on this pathway may contribute to its anti-cancer properties [96-101].

Vitamin E (Tocopherol)

Vitamin E is a group of fat-soluble antioxidants, including tocopherols and tocotrienols, each with distinct molecular structures and potential health effects. Vitamin E, as an antioxidant, can neutralize ROS and free radicals [102]. ROS are implicated in DNA damage, inflammation, and cellular stress, all of which can contribute to cancer development. By scavenging ROS, vitamin E may help protect cells from oxidative damage. Most importantly, Vitamin E can influence various signalling pathways in cell growth, survival, and apoptosis. These pathways include those related to the epidermal growth factor receptor (EGFR) and protein kinase B (Akt), which play roles in colorectal cancer development [103-106]. Furthermore, vitamin E, especially alpha-tocopherol, is known for protecting cell membranes from lipid peroxidation. This preservation of cell membrane integrity may affect cellular function and survival [107].

Vitamin K

As a fat-soluble vitamin, vitamin K is essential for bone metabolism and blood clotting. Vitamin K comes in two primary forms: K1 (phylloquinone) and K2 (menaquinone) [108]. Vitamin K is essential for the gamma-carboxylation of specific proteins, including clotting factors involved in blood coagulation. Beyond coagulation, vitamin K-dependent proteins (VKDPs) play roles in processes such as bone metabolism and may have implications for cancer [109]. The Wnt signaling pathway is frequently dysregulated in colorectal cancer. Some studies suggest that vitamin K may modulate the Wnt signaling pathway, influencing cell differentiation, proliferation, and survival [110-112]. Moreover, vitamin K has demonstrated anti-angiogenic properties, which may inhibit the formation of new blood vessels that supply nutrients to tumours. Limiting angiogenesis can impede the growth and spread of colorectal cancer [113]. Moreover, Matrix Gla-protein (MGP) is a vitamin K-dependent protein inhibiting vascular calcification. The regulation of MGP may have implications for vascular health, which is relevant to colorectal cancer progression [114-118]. Moreover, vitamin K has been suggested to play a role in epigenetic regulation, potentially affecting gene expression patterns. Epigenetic changes are involved in cancer development, and vitamin K's impact on this process may contribute to its anti-cancer effects [119].

Colorectal cancer risk factors related to vitamin deficiency

Numerous studies have investigated the relationship between vitamin deficiency and colorectal cancer occurrence and progression. Vitamin D deficiency has been extensively studied for colorectal cancer. Several epidemiological studies have shown an inverse association between vitamin D levels and colorectal cancer risk [120]. Lower circulating levels of vitamin D have been associated with an increased risk of colorectal cancer incidence and mortality. Additionally, vitamin D deficiency has been implicated in colorectal cancer progression, including tumour growth, invasion, and metastasis [121]. Moreover, vitamin A and its derivatives, including retinoids, have been implicated in colorectal cancer prevention and progression. Animal studies have shown that vitamin A deficiency increases susceptibility to colorectal cancer development, while dietary supplementation with vitamin A or retinoids can inhibit tumour growth and progression [122]. Furthermore, studies examining the association between vitamin E levels and colorectal cancer risk have yielded mixed results. Some studies have reported an association between vitamin E intake or serum levels and colorectal cancer risk [123]. More research is needed to clarify the role of vitamin E in colorectal cancer prevention and progression. Vitamin C is a potent antioxidant that may protect against colorectal cancer by scavenging free radicals and reducing oxidative stress. Some epidemiological studies have suggested an inverse association between vitamin C intake or serum levels and colorectal cancer risk, although results have been inconsistent [124].

Moreover, vitamin C deficiency has been associated with colorectal cancer progression, including tumour growth and metastasis, possibly due to impaired antioxidant defence mechanisms and increased oxidative stress. Finally, vitamin K, particularly vitamin K2 (menaquinone), has been studied for its potential role in colorectal cancer prevention and treatment. Vitamin K deficiency has been associated with an increased risk of colorectal cancer incidence and mortality in some observational studies [125]. Additionally, preclinical studies have shown that vitamin K2 supplementation inhibits colorectal cancer cell proliferation, invasion, and metastasis, possibly by regulating cell signaling pathways, including the MAPK pathway [126].

Summary and Conclusion

The risk of colorectal cancer is increased by several environmental lifestyle factors that are primarily modifiable, including smoking, drinking too much alcohol, and gaining weight. More interestingly, there are some modifiable nutritional risk factors such as consuming red and processed meat, low fibre intake, low vitamin D level and consuming a high-fat diet; vitamin deficiency may increase the risk of colorectal cancer. In this review, we focus on the molecular mechanisms of vitamins on colorectal cancer tumorigenesis and progression and demonstrate, based on the previous studies, that all vitamin

supplementation may protect against colorectal cancer. However, some vitamins have precise molecular mechanisms on molecular pathways involved in cancer proliferation, survival, angiogenesis migration and metastasis, such as vitamins A, B3, B9, C, D, E and K.

Future directions

Examining the impact of nutritional factors, particularly vitamins, on colorectal cancer through molecular mechanisms presents a rich avenue for research. Thus, we suggest the following future directions:

- Further elucidating the molecular mechanisms by which vitamins influence colorectal cancer development and progression involves investigating their effects on key signaling pathways, such as the MAPK pathway, Wnt/β-catenin pathway, PI3K/AKT pathway, and NF-κB pathway, which are dysregulated in colorectal cancer.
- Identifying specific genes, proteins, and metabolites modulated by vitamins and their implications for colorectal cancer pathogenesis.
- Investigating the potential interactions and synergies between different vitamins and other dietary factors in colorectal cancer prevention and treatment. This involves examining how combinations of vitamins or vitamins with other bioactive compounds (e.g., phytochemicals, minerals) may exert additive or synergistic effects on colorectal cancer-related molecular pathways.
- Translating findings from preclinical studies into clinical settings by conducting well-designed clinical trials to evaluate the efficacy and safety of vitamin supplementation as adjuvant therapy or preventive intervention for colorectal cancer.
- Investigating the potential of nutritional interventions, including vitamin supplementation, in high-risk populations for colorectal cancer, such as individuals with a family history of colorectal cancer, inflammatory bowel disease (IBD), or genetic predisposition to colorectal cancer (e.g., Lynch syndrome). This involves assessing such interventions' feasibility, acceptability, and efficacy in real-world settings.
- Assessment of the long-term outcomes and survivorship benefits of vitamin supplementation in colorectal cancer patients, including recurrence rates, overall survival, and quality of life. This includes evaluating the impact of vitamin supplementation on colorectal cancer recurrence, treatment-related side effects, and comorbidities in long-term survivorship.

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None

Authors contribution

The two authors are fully accountable for expertly executing and crafting every aspect and component of this work.

Declaration of interest

The authors declare no conflict of interest.

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