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Novel Approach of Ameliorative Role of Different Vitamins in the Prevention of Cardiovascular Diseases

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Abstract

Cardiovascular diseases (CVDs) represent a significant global health burden, necessitating innovative approaches for prevention and treatment. This review explores the multifaceted roles of vitamins specifically Vitamins C, D, E, K, and B complex—in maintaining cardiovascular health. Vitamins contribute to critical physiological processes, including antioxidant defense, inflammation modulation, vascular integrity, and lipid metabolism. Vitamin C enhances endothelial function and reduces oxidative stress, while Vitamin D regulates calcium homeostasis and mitigates arterial stiffness. Vitamin E prevents LDL oxidation and supports endothelial health. The B-complex vitamins lower homocysteine levels, reducing thrombotic risk, and Vitamin K prevents vascular calcification. Despite promising evidence, conflicting results from clinical trials underscore the need for personalized supplementation strategies and further research to establish definitive guidelines. This review highlights the potential of vitamins as complementary agents in CVD care, emphasizing the importance of balanced intake for cardiovascular health.

Keywords: Cardiovascular Diseases, Vitamins, Antioxidant Defense, Endothelial Function, Lipid Metabolism.

INTRODUCTION

Cardiovascular diseases (CVDs) are a leading cause of morbidity and mortality worldwide, contributing to nearly 32% of global deaths annually (Di Cesare *et al.*, 2024). These diseases encompass a wide spectrum, including coronary artery disease, hypertension, stroke, and heart failure, which are influenced by genetic, environmental, and lifestyle factors. Despite advancements in medical treatments, the burden of CVDs remains significant, prompting the exploration of complementary and preventive strategies to mitigate risks and improve outcomes. Among these, the role of vitamins has gained considerable attention due to their potential in modulating physiological processes relevant to cardiovascular health.

Vitamins, as essential micronutrients, participate in critical cellular and biochemical functions. They are involved in antioxidant defense, modulation

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of inflammation, vascular health, and lipid metabolism, all of which are pivotal in maintaining cardiovascular integrity (Marchioli *et al*., 2001). For instance, oxidative stress, a key contributor to atherosclerosis and other CVDs, is characterized by an imbalance between free radicals and antioxidants. Vitamins such as Vitamin C and E, which possess potent antioxidant properties, may counteract oxidative damage by scavenging reactive oxygen species (Münzel *et al*., 2017).

Vitamin C has been widely studied for its role in enhancing endothelial function, reducing arterial stiffness, and mitigating hypertension. Research indicates that regular intake of Vitamin C can improve nitric oxide bioavailability, which helps in vasodilation and reduces the risk of endothelial dysfunction, a precursor to atherosclerosis (May & Harrison, 2013). Similarly, Vitamin E, another lipid-soluble antioxidant, has shown promise in preventing the oxidation of low-density lipoprotein (LDL) cholesterol, a critical step in plaque formation within arterial walls (Catalgol & Ozer, 2011). In addition to antioxidant effects, other vitamins such as Vitamin D have emerged as key regulators of cardiovascular health. Vitamin D is essential for calcium homeostasis and bone health but also exerts significant effects on the cardiovascular system. Deficiency of Vitamin D has been associated with an increased risk of hypertension, myocardial infarction, and heart failure, possibly through mechanisms involving the renin-angiotensin-aldosterone system and inflammatory pathways (Nardin *et al*., 2024). Clinical studies suggest that adequate levels of Vitamin D may reduce arterial stiffness and improve overall cardiac function (de la Guía-Galipienso *et al*., 2021). The B complex vitamins, including B_6, B_9 (folate), and B_{12}, play a crucial role in homocysteine metabolism. Elevated levels of homocysteine are a known risk factor for CVDs, as they can damage endothelial cells and promote thrombogenesis. Supplementation with these vitamins has been shown to lower homocysteine levels and potentially reduce the risk of cardiovascular events (Mohan *et al*., 2023). Furthermore, Vitamin K, known for its role in coagulation, also contributes to vascular health by regulating calcium deposition in arteries. Adequate Vitamin K levels help prevent vascular calcification, a common feature of advanced atherosclerosis and arterial stiffness (van Gorp *et al*., 2021). Despite the potential benefits, the use of vitamins in CVD prevention and treatment remains a subject of ongoing research and debate. While observational studies and some clinical trials highlight positive associations, other large-scale randomized controlled trials (RCTs) have yielded inconclusive or conflicting results. Factors such as dosage, bioavailability, patient population, and study design contribute to the variability in outcomes (Simsek *et al*., 2021). Moreover, excessive intake of certain vitamins, particularly fat-soluble ones like Vitamin E and K, may pose risks such as hypervitaminosis or adverse interactions with medications (Reddy and Jialal 2022).

This systematic review aims to provide a comprehensive analysis of the role of vitamins—specifically Vitamin C, D, E, B complex, and K—in the prevention and management of CVDs. By synthesizing current evidence on their mechanisms of action, clinical efficacy, and associated risks, this review seeks to elucidate the potential of vitamins as adjunctive agents in cardiovascular care. Furthermore, it highlights the gaps in existing knowledge and emphasizes the need for well-designed studies to establish evidence-based guidelines for the use of vitamins in cardiovascular health management.

METHODOLOGY

Databases and Search Strategy

To conduct a comprehensive literature review on the role of vitamins in cardiovascular disease (CVD) prevention and management, multiple databases were searched, including PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar. These sources provided access to peer-reviewed studies, systematic reviews, meta-analyses, and grey literature.

Search Terms and Keywords

Relevant studies were identified using primary keywords such as "Vitamin C," "Vitamin D," "Vitamin E," "B-complex vitamins," "Vitamin K," "Cardiovascular Disease," "Prevention," and "Treatment." Secondary terms included "Oxidative Stress," "Atherosclerosis," "Hypertension," "Stroke," and "Endothelial Function." Example search strings included:

("Vitamin C" and "Cardiovascular Disease" and ("Prevention" or "Treatment")

("Vitamin D" and "Hypertension" and "Cardiovascular Risk")

Inclusion Criteria: Randomized controlled trials (RCTs), observational studies, systematic reviews, English-language articles (1993–present), and studies on adult populations at risk for or diagnosed with CVD.

Exclusion Criteria: Non-human studies, research on non-cardiovascular conditions, and studies lacking relevant cardiovascular data.

Data Extraction and Synthesis

Key outcomes included vitamin supplementation's impact on cardiovascular risk, oxidative stress, endothelial function, inflammation, myocardial infarction, stroke, and hypertension.

Data from clinical trials and meta-analyses were synthesized to highlight trends, mechanisms, and research gaps.

Risk of Bias and Study Selection

Biases such as selection, performance, detection, and funding biases were assessed. Mitigation strategies included randomization, blinding, and confounder control. Of 172 identified studies, 41 met inclusion criteria, contributing to a comprehensive analysis of vitamins' role in cardiovascular health.

Effect of Vitamin C on Cardiovascular Disease (CVD)

Vitamin C, also known as ascorbic acid, plays a vital role in reducing the risk of cardiovascular diseases (CVD). Its antioxidant properties, ability to improve endothelial function, and role in collagen synthesis contribute to its cardiovascular benefits.

Reduction of Oxidative Stress

Vitamin C neutralizes reactive oxygen species (ROS) and protects against oxidative damage to lipids, proteins, and DNA, which are implicated in atherosclerosis and other cardiovascular conditions (Carr & Maggini, 2017; Bhattacharjee *et al.,* 2024).

Improvement of Endothelial Function

By enhancing nitric oxide (NO) bioavailability, vitamin C improves endothelial-dependent vasodilation, reducing arterial stiffness and lowering blood pressure (Morelli *et al.,* 2020).

Anti-inflammatory Effects

Chronic inflammation is a significant contributor to atherosclerosis. Vitamin C reduces pro-inflammatory markers like C-reactive protein (CRP), thereby mitigating inflammation (Dhalla *et al.,* 2000).

*Lipid Profile Improvement***:**

Vitamin C may decrease LDL oxidation and improve HDL functionality, reducing the risk of plaque formation in arteries (Retsky *et al.,* 1993).

Collagen Synthesis

Adequate collagen synthesis is essential for maintaining the structural integrity of blood vessels. Vitamin C supports this process, reducing the risk of vessel rupture or aneurysm (Padayatty *et al.,* 2003).

Reduction in Hypertension

Vitamin C supplementation has been shown to lower blood pressure in hypertensive patients, reducing strain on the cardiovascular system (Juraschek *et al.,* 2012).

Mechanism of Action of Vitamin C in Cardiovascular Health

Antioxidant Activity

Vitamin C acts as a potent antioxidant by donating electrons to neutralize free radicals, thereby preventing oxidative stress, a critical factor in endothelial dysfunction and atherosclerosis (Frei, 1991; Carr & Maggini, 2017).

Enhancement of Nitric Oxide (NO) Availability

Vitamin C stabilizes NO by reducing superoxide anion-mediated NO degradation, leading to improved vasodilation and blood flow (Morelli *et al.,* 2020).

Inhibition of LDL Oxidation

By scavenging free radicals, vitamin C prevents the oxidative modification of LDL cholesterol, a crucial step in the initiation and progression of atherosclerosis (Retsky *et al.,* 1993).

Regulation of Endothelial Function

Vitamin C improves endothelial cell survival and reduces apoptosis, which is essential for maintaining vascular homeostasis (Ashor *et al.,* 2015).

Reduction of Inflammation

Vitamin C decreases inflammatory cytokines and markers like CRP, reducing vascular inflammation and slowing the progression of atherosclerosis (Dhalla *et al.,* 2000).

Collagen Formation

As a cofactor for prolyl and lysyl hydroxylase enzymes, vitamin C is critical for the synthesis of stable collagen, ensuring the strength and elasticity of blood vessel walls (Padayatty *et al.,* 2003).

Effect of Vitamin D on Cardiovascular Disease (CVD)

Vitamin D is crucial for maintaining cardiovascular health, with its deficiency linked to increased risk factors such as hypertension, atherosclerosis, and heart failure. Its effects are mediated through its regulation of calcium metabolism, anti-inflammatory properties, and impact on vascular function.

Regulation of Blood Pressure

Vitamin D reduces renin production, lowering the activity of the renin-angiotensin-aldosterone system (RAAS) and thereby helping regulate blood pressure (Li *et al.,* 2002).

Anti-inflammatory Effects

It suppresses pro-inflammatory cytokines and enhances anti-inflammatory mediators, reducing vascular inflammation and atherosclerosis (Norman & Powell, 2014).

Improvement of Endothelial Function

By promoting nitric oxide (NO) synthesis and reducing oxidative stress, vitamin D enhances endothelial function, which is critical for vascular health (Kim *et al.,* 2020).

Inhibition of Vascular Calcification

Vitamin D prevents vascular smooth muscle cell (VSMC) calcification by modulating calcium and phosphate metabolism, reducing arterial stiffness (Hou *et al.,* 2017).

Reduction in Insulin Resistance

Vitamin D improves insulin sensitivity, thereby mitigating the risk of type 2 diabetes—a major risk factor for CVD (Forouhi *et al.,* 2008).

Cholesterol Modulation

It has a role in reducing LDL cholesterol levels and increasing HDL, which can lower the risk of plaque formation in arteries (Pilz *et al.,* 2016).

Modulation of the RAAS

Vitamin D inhibits renin gene expression, leading to decreased RAAS activity, which helps in blood pressure regulation and reduces cardiac hypertrophy (Li *et al.,* 2002).

Regulation of Calcium and Phosphate Homeostasis

Vitamin D maintains calcium and phosphate balance, essential for vascular health, preventing arterial calcification (Hou *et al.,* 2017).

Anti-inflammatory Mechanisms

It suppresses NF-κB signaling, reducing the production of inflammatory cytokines such as IL-6 and TNF-α, which are implicated in atherosclerosis (Norman & Powell, 2014).

Endothelial Function Enhancement

Vitamin D promotes endothelial nitric oxide synthase (eNOS) activity, improving NO bioavailability and preventing endothelial dysfunction (Kim *et al.,* 2020).

Antioxidant Effects

By reducing oxidative stress and lipid peroxidation, vitamin D protects endothelial cells and prevents atherogenesis (Pilz *et al.,* 2016).

Impact on Lipid Metabolism

Vitamin D influences the expression of genes involved in lipid metabolism, reducing LDL oxidation and supporting a healthier lipid profile (Forouhi *et al.,* 2008).

Effect of Vitamin E on Cardiovascular Disease (CVD)

Vitamin E, a fat-soluble vitamin consisting of eight compounds (α-, β-, γ-, δ-tocopherols and tocotrienols), is well-known for its antioxidant properties. It protects cellular membranes and lipoproteins from oxidative damage, which is crucial in preventing cardiovascular diseases (CVDs) (Bhattacharjee & Pal, 2014).

Mechanisms of Action

Inhibition of LDL Oxidation: Vitamin E prevents the oxidation of low-density lipoproteins (LDL), a key step in atherosclerosis, thus reducing foam cell formation and arterial plaque buildup (Khatana *et al.,* 2020).

Anti-inflammatory Effects: Vitamin E decreases the expression of inflammatory markers such as IL-6 and C-reactive protein (CRP), both of which are elevated in atherosclerosis (Asbaghi *et al.,* 2020).

Improvement in Endothelial Function: Vitamin E enhances endothelial function by reducing oxidative stress and improving nitric oxide bioavailability, leading to better vascular relaxation (Su, 2015).

Platelet Aggregation Inhibition: Vitamin E inhibits platelet aggregation and adhesion, which are critical steps in thrombus formation and ischemic events like myocardial infarction (Steiner, 1999).

Clinical Evidence

Observational Studies: The Nurses' Health Study found that higher dietary vitamin E intake was inversely related to coronary heart disease risk (Khatana *et al.,* 2020).

Potential Risks and Recommendations

Excessive intake of vitamin E may lead to pro-oxidant effects, negating its antioxidant benefits and potentially resulting in adverse health outcomes. Current guidelines suggest obtaining vitamin E primarily from dietary sources, such as nuts, seeds, and vegetable oils, rather than high-dose supplements (Bhattacharjee & Pal, 2014).

Reduction of Oxidative Stress

Vitamin E protects cell membranes from oxidative damage by neutralizing free radicals,

reducing oxidative stress, which is a major factor in atherosclerosis (Bhattacharjee & Pal, 2014).

Prevention of LDL Oxidation

It inhibits the oxidation of low-density lipoproteins (LDL), preventing the formation of atherosclerotic plaques (Bhattacharjee & Pal, 2014).

Anti-inflammatory Effects

Vitamin E suppresses the production of pro-inflammatory cytokines like IL-6 and TNF-α, reducing vascular inflammation (Reiter *et al.,* 2007).

Improvement of Endothelial Function

By enhancing nitric oxide (NO) bioavailability and reducing endothelial oxidative stress, vitamin E improves endothelial function, crucial for vascular health (Roberts *et al.,* 2007).

Inhibition of Platelet Aggregation

Vitamin E reduces platelet aggregation and adhesion, lowering the risk of thrombosis and stroke (Steiner, 1999).

Reduction in Arterial Stiffness

Vitamin E supplementation improves arterial elasticity, reducing the risk of hypertension and vascular complications (Meydani *et al.,* 1997).

Mechanism of Action of Vitamin E in Cardiovascular Health

Antioxidant Activity

Vitamin E acts as a lipid-soluble antioxidant, incorporating into cellular membranes and scavenging lipid peroxyl radicals, thereby preventing lipid peroxidation and protecting against oxidative stress (Brigelius-Flohé & Traber, 1999).

Inhibition of LDL Oxidation

By donating hydrogen atoms to free radicals, vitamin E prevents the oxidative modification of LDL cholesterol, a crucial step in the initiation of atherosclerosis (Upston *et al.,* 2003).

Regulation of Inflammatory Pathways

Vitamin E downregulates the activity of NF-κB, reducing the expression of pro-inflammatory genes and cytokines (Reiter *et al.,* 2007).

Enhancement of Endothelial Nitric Oxide (NO) Availability

By reducing superoxide production, vitamin E increases NO bioavailability, promoting vasodilation and improving blood flow (Roberts *et al.,* 2007).

Inhibition of Platelet Aggregation

Vitamin E interferes with protein kinase C (PKC) activity, inhibiting platelet aggregation and reducing the risk of thrombus formation (Steiner, 1999).

Improvement in Vascular Elasticity

Vitamin E prevents the stiffening of arteries by reducing oxidative and inflammatory damage to vascular smooth muscle cells (Meydani *et al.,* 1997).

Effect of Vitamin B Complex on Cardiovascular Disease (CVD)

The Vitamin B complex, comprising several water-soluble vitamins, plays a crucial role in cardiovascular health. Deficiency in specific B vitamins, such as B6, B12, and folate, is linked to hyperhomocysteinemia, a significant risk factor for cardiovascular diseases. These vitamins also influence energy metabolism, reduce oxidative stress, and regulate inflammatory responses.

Reduction of Homocysteine Levels

Vitamins B6, B12, and folate lower homocysteine levels, a known risk factor for atherosclerosis and thrombosis (Bhattacharjee and Pal, 2014b, Mohan *et al.,* 2023).

Anti-inflammatory Effects

Vitamin B6 suppresses pro-inflammatory cytokines, reducing vascular inflammation and the risk of atherosclerosis (Friso *et al.,* 2001).

Improvement in Lipid Profile

Niacin (Vitamin B3) improves lipid metabolism by reducing LDL cholesterol, triglycerides, and lipoprotein(a) while increasing HDL cholesterol (Carlson, 2005).

Regulation of Energy Metabolism

Thiamine (Vitamin B1) enhances cardiac energy production by facilitating carbohydrate metabolism, improving heart function (Mrowicka *et al.,* 2023).

Prevention of Endothelial Dysfunction

Riboflavin (Vitamin B2) and niacin improve endothelial function by reducing oxidative stress and enhancing nitric oxide bioavailability (Mrowicka *et al.,* 2023).

Reduction in Hypertension Risk

Vitamin B2 supplementation reduces blood pressure, particularly in individuals with a specific genetic variant (MTHFR C677T polymorphism) (McNulty *et al.,* 2006).

Mechanism of Action of Vitamin B Complex in Cardiovascular Health

Homocysteine Metabolism

Vitamins B6, B12, and folate are co-factors in the remethylation and transsulfuration pathways of homocysteine metabolism, reducing plasma homocysteine levels and preventing endothelial damage (Mohan *et al.,* 2023).

Regulation of Lipid Metabolism

Niacin inhibits hepatic synthesis of VLDL and LDL cholesterol and enhances HDL levels, reducing the risk of plaque formation in arteries (Carlson, 2005).

Anti-inflammatory Mechanisms

Vitamin B6 inhibits the NF-κB pathway, reducing the production of pro-inflammatory cytokines like IL-6 and TNF-α, protecting against vascular inflammation (Friso *et al.,* 2001).

Oxidative Stress Reduction

Riboflavin and niacin act as coenzymes in redox reactions, reducing oxidative damage to endothelial cells and improving vascular function (Mrowicka *et al.,* 2023).

Improvement of Myocardial Energy Metabolism

Thiamine facilitates the conversion of pyruvate to acetyl-CoA, ensuring adequate ATP production in cardiac cells, critical for heart function (Mrowicka *et al.,* 2023).

Blood Pressure Modulation

Riboflavin enhances the metabolism of nitric oxide, improving vasodilation and reducing blood pressure, especially in genetically susceptible individuals (McNulty *et al.,* 2006).

Overall Mechanism

The mechanism of action of vitamins in cardiovascular health encompasses multiple pathways vital for preventing and managing cardiovascular diseases (CVDs). Vitamin C, a potent antioxidant, neutralizes reactive oxygen species (ROS) to mitigate oxidative stress, improves nitric oxide (NO) bioavailability for endothelial function, reduces pro-inflammatory markers, and supports collagen synthesis for vascular integrity (Carr & Maggini, 2017; Padayatty *et al.,* 2003). Vitamin D regulates calcium-phosphate balance, inhibits vascular calcification, suppresses inflammation, modulates the renin-angiotensin-aldosterone system (RAAS), and enhances endothelial NO availability, reducing hypertension and atherosclerosis risks (Li *et al.,* 2002; Norman & Powell, 2014). Vitamin E, a lipid-soluble antioxidant, prevents LDL oxidation, reduces inflammatory cytokines, inhibits platelet aggregation, and promotes vascular elasticity through its antioxidant and anti-inflammatory effects (Brigelius-Flohé & Traber, 1999; Reiter *et al.,* 2007). The B-complex vitamins lower homocysteine, an atherogenic marker, improve lipid profiles through niacin, regulate energy metabolism via thiamine, and enhance endothelial function by reducing oxidative stress and promoting NO bioavailability (Mohan *et al.,* 2023; Carlson, 2005). Collectively, these vitamins act through antioxidative, anti-inflammatory, lipid-regulating, and vasodilatory mechanisms to reduce the risk of CVDs while maintaining vascular health.

CONCLUSION

The review concludes that vitamins play a critical role in cardiovascular disease (CVD) prevention and management by modulating key physiological processes. Vitamins C, D, E, B complex, and K exhibit antioxidative, anti-inflammatory, and lipid-regulating properties that enhance vascular health, reduce oxidative stress, and prevent atherosclerosis. While promising evidence supports their potential, variability in outcomes due to study design, dosage, and patient population underscores the need for further research. Excessive supplementation, particularly of fat-soluble vitamins, poses risks, highlighting the importance of balanced intake through diet and supplements. This review emphasizes integrating vitamins as complementary agents in CVD care and the necessity for well-designed trials to establish definitive guidelines for their optimal use in improving cardiovascular health.

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