

Antioxidants on Coronary Artery Disease

Md S Alieozaman, Megha Roy*

Department of Food and Nutrition, Swami Vivekananda
University, Barrackpore, W.B., India

*Corresponding E-mail: megha96.official@gmail.com

Antioxidants on Coronary Artery Disease – A Review

Md S Alieozaman, Megha Roy*

Department of Food and Nutrition, Swami Vivekananda
University, Barrackpore, West Bengal, 700121

*Corresponding author e-mail: megha96.official@gmail.com

Abstract

Coronary artery disease (CAD) is a leading cause of increasing worldwide mortality rates. CAD is generally caused by oxidative stress and inflammation that result in endothelial dysfunction and Atherosclerosis. Both endogenous and exogenous antioxidants are crucial in reducing oxidative damage by neutralizing the free radicals and reducing lipid oxidation. This review paper helps understand the antioxidants' mechanisms influencing CAD progression and management. This paper mainly focuses on dietary and pharmacological antioxidants, like vitamins C and E, polyphenols, and carotenoids. Also, it evaluates the research studies and clinical tests, to highlight the potential benefits and limitations of antioxidant therapy in CAD management. The effectiveness of antioxidants can vary, and some studies suggest that excessive intake of certain antioxidants, like beta-carotene, may have negative effects on the heart.

In summary, although antioxidants show potential in the prevention and treatment of CAD, their use should be sensible, and further research is necessary to identify the best dosages and combinations for maximum safety and effectiveness.

Keywords: *Coronary artery disease, Antioxidants, Vitamins, Polyphenols, Carotenoids.*

Introduction

I. Coronary Artery Disease (CAD)

Coronary Artery Disease (CAD), also known as ischemic heart disease, is a condition characterized by the narrowing or blockage of the coronary arteries, the blood vessels that supply oxygen-rich blood to the heart muscle (*Dhakal & Pokhrel et. al; 2024*). This narrowing is primarily due to the buildup of plaque, a combination of fat, cholesterol, and other substances, in the arterial walls; a process known as atherosclerosis (*Sevras et. al; 2024*). CAD is a leading cause of morbidity and mortality worldwide, contributing significantly to the global burden of cardiovascular diseases (*Kumar et. al; 2020*).

The development of CAD is influenced by a variety of risk factors, including hypertension, hyperlipidaemia, diabetes, smoking, obesity, and a sedentary lifestyle (*Malakar et. al; 2019*). The pathophysiology of CAD involves endothelial dysfunction, inflammation, oxidative stress, and the formation of atherosclerotic plaques, which can lead to myocardial infarction (heart attack), angina, heart failure, and sudden cardiac death (*Aashiq et. al; 2019*).

II. Antioxidants

Antioxidants are molecules that inhibit the oxidation of other molecules, thereby preventing the formation of free radicals and reactive oxygen species (ROS) that can cause cellular damage (*Alkadi, 2020*). Oxidation is a chemical reaction that can produce free radicals, leading to chain reactions that may damage cells. Antioxidants terminate these chain reactions by removing free radical intermediates and inhibiting other oxidation reactions (*Sanjay and Shukla; 2021*).

A. Types of Antioxidants

Antioxidants can be broadly classified into two categories: endogenous and exogenous.

1) Endogenous Antioxidants: These are produced naturally within the body and include enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, as well as non-enzymatic molecules like glutathione, coenzyme Q10, and uric acid (*Neha et.al; 2019*).

2) Exogenous Antioxidants: These are obtained from the diet or supplements and include vitamins (such as vitamin C, vitamin E, and beta-carotene), minerals (such as selenium and zinc), and phytochemicals (such as flavonoids, polyphenols, and carotenoids) (*Qi et. al; 2022*).

B. Sources of Antioxidants

Antioxidants are abundant in various foods, particularly fruits, vegetables, nuts, and whole grains (*Rahaman et. al; 2023*). Some of the richest sources of antioxidants include:

a) Vitamin C: Found in citrus fruits, strawberries, bell peppers, and broccoli (*Baek et. al; 2021*).

b) Vitamin E: Found in nuts, seeds, spinach, and vegetable oils (*Sinbad et. al; 2019*).

c) Beta-carotene: Found in carrots, sweet potatoes, and dark leafy greens (*Dewanjee et al; 2021*).

d) Selenium: Found in Brazil nuts, seafood, and whole grains (*Wan et.al; 2018*).

e) Flavonoids: Found in berries, tea, red wine, and dark chocolate (*Khan et. al; 2021*).

f) Polyphenols: Found in coffee, tea, olives, and extra virgin olive oil (*Ranjha et. al; 2022*).

• The action of Antioxidants in Coronary Artery Disease

The role of antioxidants in CAD is primarily linked to their ability to mitigate oxidative stress, a key contributor to the development and progression of atherosclerosis (*Pahimi et. al; 2019*). Oxidative stress occurs when there is an imbalance

between the production of ROS and the body's ability to detoxify these reactive intermediates or repair the resulting damage ((*Alkadi, 2020*).

Mechanisms of Action

a) Reduction of Oxidative Stress: Antioxidants neutralize ROS, reducing oxidative damage to lipids, proteins, and DNA. This helps maintain endothelial function and prevents the initiation and progression of atherosclerosis (*Alkadi, 2020*).

b) Inhibition of LDL Oxidation: Oxidized low-density lipoprotein (LDL) is a critical factor in the formation of atherosclerotic plaques. Antioxidants, particularly vitamin E and beta-carotene, inhibit the oxidation of LDL, thereby reducing plaque formation (*Donia and Khamis; 2021*).

c) Anti-inflammatory Effects: Antioxidants can modulate inflammatory pathways by reducing the expression of pro-inflammatory cytokines and adhesion molecules. This helps to attenuate the inflammatory response associated with atherosclerosis (*Kabir et.al; 2022*).

d) Improvement of Endothelial Function: Antioxidants enhance the bioavailability of nitric oxide (NO), a molecule that promotes vasodilation and maintains vascular homeostasis. By preserving NO levels, antioxidants improve endothelial function and reduce the risk of CAD (*Murray et. al; 2023*).

e) Stabilization of Atherosclerotic Plaques: Antioxidants can stabilize vulnerable plaques by reducing oxidative stress and inflammation, thereby decreasing the likelihood of plaque rupture and subsequent thrombotic events (*Wang et.al; 2025*).

- **Positive Impact of Antioxidants on CAD**

- a) Epidemiological Evidence**

Numerous epidemiological studies have demonstrated an inverse association between dietary intake of antioxidants and the risk of CAD. For example, the Nurses' Health Study and the Health Professionals Follow-Up Study found that higher

intakes of vitamin E and vitamin C were associated with a reduced risk of coronary heart disease (*Keramat et. al;2022*).

b) Clinical Trials

Several clinical trials have investigated the effects of antioxidant supplementation on CAD outcomes. The Cambridge Heart Antioxidant Study (CHAOS) reported that vitamin E supplementation significantly reduced the risk of non-fatal myocardial infarction in patients with CAD (*Rychter et. al; 2022*). Similarly, the Lyon Diet Heart Study found that a Mediterranean diet rich in antioxidants reduced the risk of recurrent coronary events (*Martinez- Gonzalez et. al; 2024*).

c) Mechanistic Insights

Animal studies and in vitro experiments have provided mechanistic insights into the protective effects of antioxidants in CAD (*Falco et.al; 2023*). For instance, studies in apolipoprotein E-deficient mice have shown that antioxidant treatment reduces atherosclerotic lesion formation and improves endothelial function (*Cheng et.al; 2023*).

d) Polyphenols and Flavonoids:

Found in tea, wine, and cocoa, these compounds exhibit strong cardioprotective effects (*Ranjha et. al; 2022*).

e) Vitamin C and E:

These vitamins help prevent lipid peroxidation and endothelial dysfunction (*Sinbad et. al; 2019*).

f) Carotenoids:

Lutein and beta-carotene improve cardiovascular health by reducing inflammation and oxidative stress (*Dewanjee et al; 2021*).

• Negative Impact of Antioxidants on CAD

a) Inconsistent Clinical Trial Results

Despite the promising epidemiological and mechanistic evidence, some large-scale clinical trials have failed to demonstrate a clear benefit of antioxidant supplementation in CAD (*Petrucchi et. al; 2022*). The Heart Outcomes Prevention

Evaluation (HOPE) trial and the Women's Health Study (WHS) found no significant reduction in cardiovascular events with vitamin E supplementation (*Aday et. al; 2021*).

b) Potential Pro-oxidant Effects

In certain conditions, antioxidants can exhibit pro-oxidant effects, particularly at high doses. For example, beta-carotene supplementation has been associated with an increased risk of lung cancer in smokers, possibly due to the formation of harmful oxidation products (*Tian et.al; 2022*).

c) Interaction with Medications

Antioxidants may interact with certain medications, potentially reducing their efficacy (*Forman and Zhang; 2021*). For instance, vitamin E can interfere with the anticoagulant effects of warfarin, increasing the risk of bleeding (*Elango et.al; 2021*).

d) Lack of Synergistic Effects

The complex interplay between different antioxidants and other nutrients may not always result in synergistic effects (*Mitra et.al; 2023*). Some studies suggest that isolated antioxidant supplements may not provide the same benefits as a diet rich in a variety of antioxidants (*Rahaman and Hossain; 2023*).

Conclusion

The role of antioxidants in the prevention and management of coronary artery disease (CAD) is a topic of significant interest and ongoing research. While there is substantial evidence supporting the beneficial effects of antioxidants in reducing oxidative stress, inflammation, and atherosclerosis, the results from clinical trials have been mixed. The discrepancies between epidemiological studies and clinical trials may be attributed to differences in study design, population characteristics, dosage, and the form of antioxidants used.

It is important to recognize that antioxidants are not a panacea for CAD. A balanced diet rich in a variety of antioxidants, along with other lifestyle modifications such as regular physical activity, smoking cessation, and weight

management, is essential for cardiovascular health. Future research should focus on identifying the optimal combination and dosage of antioxidants, as well as understanding the underlying mechanisms that govern their effects in different populations.

In conclusion, while antioxidants hold promise in the fight against CAD, their use should be approached with caution, and further research is needed to fully elucidate their role in cardiovascular disease prevention and treatment.

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