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Green tea and green coffee for cardiac fibrosis treatment: A review

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Abstract

Cardiac fibrosis, marked by excessive collagen accumulation and tissue remodelling, is a key factor in heart dysfunction across various cardiovascular conditions. With limited effective treatments currently available, there is growing interest in exploring natural therapies like green tea and green coffee for their potential antifibrotic properties. Both beverages contain bioactive compounds, such as catechins and caffeic acid, known for their antioxidant, anti-inflammatory, and cardioprotective effects. Green tea has been shown to reduce oxidative stress, lower fibrosis-related markers, and limit collagen deposition in heart tissue. Similarly, caffeic acid from coffee has demonstrated the ability to block fibrosis-driving pathways, such as TGF-β1 signalling, and support cardiac recovery following myocardial infarction. Moreover, the combined use of green tea and decaffeinated green coffee has been found to improve metabolic health by influencing cardiac insulin pathways, which could help mitigate fibrosis in metabolic syndrome models. This review consolidates recent evidence on the mechanisms and benefits of green tea and green coffee in addressing cardiac fibrosis. It highlights their potential as accessible, non-invasive treatment options and underscores the need for further studies to confirm their therapeutic applications in clinical settings.

Keywords: Green tea; Green coffee; Cardiac fibrosis; Metabolic; Cardioprotective

1. Introduction

Cardiovascular disease (CVD) encompasses a wide range of conditions that affect the heart and blood vessels, both of which are crucial for maintaining the flow of oxygen and nutrients throughout the body. These conditions can either be inherited at birth or develop later in life due to various factors such as poor diet, lack of exercise, smoking, or underlying health conditions like diabetes and high blood pressure. CVD doesn't just affect the heart and circulatory system, this disease also impacts lives in profound ways [1]. For more than 30 years, cardiovascular diseases (CVDs) have been the leading cause of death worldwide, responsible for about one-third of all global fatalities. In 2021 alone, 20.5 million lives were lost to CVD [2]. While death rates from CVD have declined in high-income countries, progress has been slower in low- and middle-income countries, where over 80% of these deaths now occur. Regions like Central Europe, Eastern Europe, and Central Asia continue to experience the highest rates of CVD-related mortality globally. Interestingly, while women generally have lower CVD death rates than men, there are notable exceptions. In nearly 30% of countries across North Africa, the Middle East, and parts of Sub-Saharan Africa (especially West Africa), women face higher mortality rates from CVD than men. These disparities highlight the urgent need for tailored healthcare solutions and prevention strategies to address the unique challenges faced by different populations [3].

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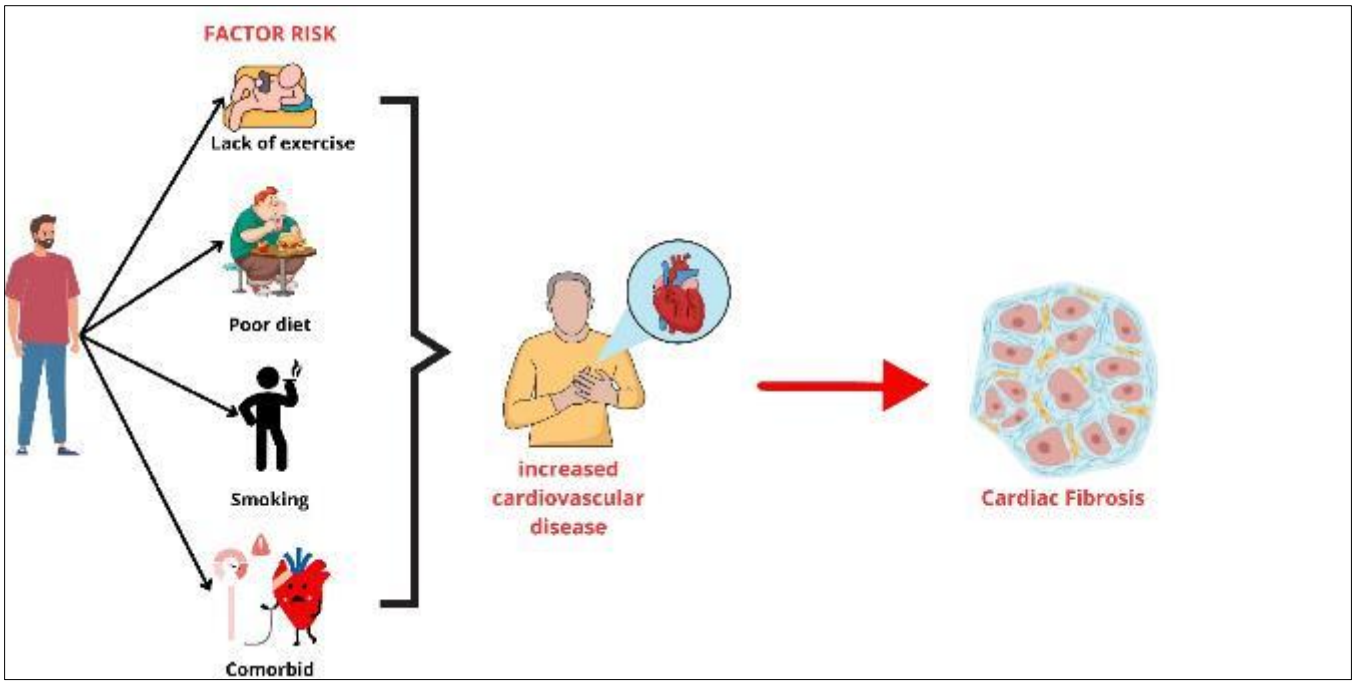

Figure 1 Proposed mechanism of cardiac fibrosis

Cardiovascular disease is one of the most pressing health issues in Indonesia, with the country ranking among the highest globally for related fatalities. In 2019 alone, over 375,000 lives were lost due to this condition, reflecting its widespread impact. Beyond the loss of life, cardiovascular disease also leads to a significant decline in overall quality of life, contributing to a substantial portion of health-related challenges in the country. Its burden extends beyond physical health, affecting communities and straining healthcare systems, making it a critical area for prevention and intervention efforts [4–7]. Cardiac fibrosis is a serious condition associated with cardiovascular disease and contributes significantly to mortality. It occurs when excessive extracellular matrix proteins accumulate in the heart, leading to tissue thickening and stiffness. This process can impair heart function, increase the risk of arrhythmias, and is commonly observed in patients with heart failure [8].

Cardiac fibrosis happens when the heart is under increased pressure, such as from high blood pressure or aortic stenosis, forcing it to work harder and undergo significant changes. Over time, this strain causes fibrous tissue to build up, making the heart stiffer and less able to relax and fill properly. Initially, this leads to diastolic dysfunction, but if the pressure persists, the heart can enlarge and weaken, eventually resulting in a dangerous combination of diastolic and systolic heart failure [9]. Myocardial fibrosis can be classified into three types based on how fibrous tissue is deposited in the heart. The first type, replacement or reparative fibrosis, occurs when heart muscle cells are lost and replaced by collagen fibers, as seen in scar tissue after a heart attack. The second type, interstitial fibrosis, involves fibrous tissue forming around bundles of heart muscle (perimysium) and individual heart cells (endomysium). The third type, perivascular fibrosis, happens when fibrous tissue builds up around blood vessels in the heart. Each type reflects a unique pattern of damage and repair within the heart. Significant fibrosis is commonly seen in patients in heart failure with reduced ejection fraction (HFrEF) or heart failure with preserved ejection fraction (HFpEF). This fibrosis is linked to the key underlying conditions that lead to heart failure, such as chronic ischemia, inherited cardiomyopathies, excessive pressure or volume in the heart, and metabolic disorders [10]. Research shows that about 41 percent of patients with dilated cardiomyopathy (DCM) develop myocardial fibrosis, which is linked to worse clinical outcomes, including a higher risk of death and complications related to heart failure [11]. While the need to address cardiac fibrosis is well understood, effective treatments that specifically target fibrosis remain out of reach. Current medical approaches focus on managing underlying conditions like hypertension and diabetes but fall short of directly reversing the fibrotic changes in the heart [12].

Tea and coffee have long been linked to a variety of health benefits, particularly for heart health. The active compounds found in these beverages, such as catechins in green tea and caffeine and chlorogenic acid in coffee, are known for their antioxidant and anti-inflammatory properties [13,14]. Research suggests that regularly drinking green tea may help lower blood pressure and reduce the risk of atherosclerosis [15]. Similarly, coffee has been associated with a lower risk

of hypertension, thanks to its ability to protect blood vessels and reduce oxidative stress [16]. The bioactive compounds in tea and coffee, such as epigallocatechin gallate (EGCG) in green tea, have been found to inhibit the activation of fibroblasts and reduce the expression of TGF-β1, a key protein driving fibrosis [17]. Coffee's caffeine content can also influence inflammation and fibrosis by affecting adenosine pathways.

However, research on the specific effects of tea and coffee on cardiac fibrosis remains limited. Most studies have focused on their general cardiovascular benefits. Thus, further investigations are needed to clarify their mechanisms and therapeutic potential for this specific condition. In this review, we'll take a closer look at how green tea and green coffee might offer new hope in treating cardiac fibrosis, highlighting the exciting possibilities these everyday drinks could have in improving heart health.

2. Review of Literature

We conducted a published literature study both *in vitro* and *in vivo* on the use of green tea and green coffee for cardiac fibrosis therapy. The literature study was conducted using Publish and Perish ver.8 software with the keywords "Green tea and cardiac fibrosis" and "green coffee and cardiac fibrosis".

The study conducted by Akter et al. [18] which used Swiss-albino mice as a model of myocardial damage induced with isoproterenol. In the study, heart-specific markers were tested, including Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and Alkaline Phosphatase (ALP). Isoproterenol treatment increased these markers, indicating oxidative stress. However, green tea treatment in this study significantly reduced their levels, suggesting its protective effect. Further tests focus on Creatinine Kinase Muscle Brain (CKMB), creatinine, and uric acid. Isoproterenol-induced oxidative stress increased these markers, leading to heart damage. Green tea treatment effectively reduced their concentration in this study. For histological analysis, green tea has been shown to reduce collagen deposition in heart tissue, effectively mitigating the fibrosis caused by isoproterenol-induced damage. This suggests its potential in preventing or reducing collagen buildup in various tissues.

Research conducted by Lukitasari et al. [19] using green tea and green coffee extracts that have been decaffeinated in rat models of metabolic syndrome showed an increase and improvement in inflammatory genes and genes that cause cardiac fibrosis such as angiotensin-2 serum levels, NF-κB, TNF-α, IL-6, Tgf-β1, Rac-1, and α-sma. The combination of green tea and decaffeinated light roasted green coffee extract in this study also helped reduce the metabolic issues in a rat model of metabolic syndrome. Another study conducted by Chomsy et al. [20] using metabolic syndrome model mice showed that the use of green tea and green coffee extracts improved systolic blood pressure and increased tail blood flow when combined with metformin. This study also measured the expression of several genes related to fibrosis such as Angiotensinogen Receptor 1 (ATR1), Transforming Growth Factor β (TGFβ), and Collagen Type 1 (COL1A1). The results of the therapy showed that the use of green coffee tea as a single therapy or in combination with metformin successfully reduced the expression of genes related to cardiac fibrosis.

Research conducted by Guo et al. [21] using epicatechin compound from green tea showed that epicatechin administration can activate SIRT1/AKT/GSK3β pathway where SIRT1 is a gene responsible for inhibiting myofibroblast transformation. Administration of epicatechin in this study could improve heart function and reduce cardiac fibrosis in hearts of fibrosis mice model and inhibit AngII-induced α-SMA and COLI/III expression. In addition to *in vivo*, *in vitro* studies to investigate the function of green tea to treat cardiac fibrosis have also been conducted several times. Cai et al. [22] research showed that EGCG in green tea was proven to be able to reduce the proliferation of mouse fibroblast cells and extracellular matrix deposition. This study also succeeded in showing that EGCG can reduce the expression of the Connective tissue growth factor (CTGF) gene which plays an important role in the development of fibrosis in tissues induced by AngII. EGCG is also able to block NF-κB activation and transcriptional activity induced by Ang II.

On the other hand, caffeic acid from green coffee in the research of Jiang et al. [23] showed promising effects in improving cardiac function and reducing myocardial fibrosis following a myocardial infarction in mice. It works by inhibiting the TGF-β1-induced proliferation of cardiac fibroblasts and collagen deposition. As a targeted inhibitor of TGFBR1, it suppresses the activation of the TGFBR1-Smad2/3 signaling pathway. These findings suggest that caffeic acid could serve as a potential therapeutic agent for treating myocardial fibrosis after a heart attack. In a study by Chomsy et al. [24] combining green tea with decaffeinated green coffee was found to improve risk factors associated with metabolic syndrome by enhancing the cardiac insulin gene-related pathway. This improvement could help reduce cardiac fibrosis in mice with metabolic syndrome, as impaired glucose metabolism and increased pressure on the heart are known to trigger the activation and expression of profibrotic molecules, ultimately leading to fibrosis.

3. Conclusion

Green tea and coffee, especially their active compounds like catechins and caffeic acid, show great potential in supporting heart health and addressing cardiac fibrosis. Green tea has been found to reduce oxidative stress, improve heart-specific markers, and limit collagen buildup in heart tissue, making it a promising tool for preventing fibrosis. Likewise, coffee compounds, such as caffeic acid, have been shown to block fibrosis-related pathways like TGF-β1 signaling and improve heart function after a heart attack. The combination of green tea and decaffeinated green coffee has also been shown to enhance metabolic health by influencing cardiac insulin pathways, which may help reduce fibrosis in conditions like metabolic syndrome. These findings highlight the potential of these natural remedies in treating cardiac fibrosis and improving cardiovascular health. However, more research is needed to fully understand their effects and develop them into effective treatments.

Compliance with ethical standards

Disclosure of Conflict of interest

The author(s) declare there is no conflict of interest.

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