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Antioxidant Protection Mechanisms in the Cardiovascular System

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

The cardiovascular system, consisting of the heart and blood vessels, plays a critical role in maintaining the consistency of blood flow to supply oxygen throughout the body. Changes in the dynamics of blood flow can occur with the progression of disease exposure. Reactive oxygen species (ROS) are a major trigger for cardiomyocyte and endothelial dysfunction. Therefore, an antioxidant defense system is essential for prevention. This review aims to provide insights into the primary mechanisms of antioxidants in their role as cardioprotective agents. The human body has at least five defense mechanisms against ROS. Understanding these mechanisms will offer readers a strong perspective on the importance of sufficient antioxidants in the body to maintain cardiovascular function.

Keywords: Antioxidants; cardiovascular mechanisms.

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1. INTRODUCTION

The cardiovascular system is vital in maintaining blood flow to all body tissues, transporting nutrients, and facilitating the exchange of oxidants, carbon dioxide, and various other gases. A healthy heart and blood vessels are essential for ensuring these processes function correctly. However, as body dynamics change due to illness, blood flow may become problematic, obstructed, or even blocked due to internal structural changes in the blood vessels, leading to progressive hypoxia and peripheral tissue damage due to oxygen deprivation. Many factors can cause damage to blood vessels. Specifically, oxidative stress plays a significant role in the development of several cardiovascular diseases, including coronary artery disease, hypertension, and heart failure [1–3]. This oxidative damage can lead to chronic inflammation and endothelial dysfunction, exacerbating these conditions.

Oxidants represent a formidable challenge in the cardiovascular system, primarily due to the damaging effects of reactive oxygen species (ROS). These highly reactive molecules can aggressively attack cellular structures, proteins, and DNA within the vascular system, leading to a cascade of detrimental effects. Key manifestations of ROS exposure include mitochondrial dysfunction, which impairs cellular energy production; cardiomyocyte hypertrophy, which disrupts the normal function and structure of heart muscle cells; and endothelial dysfunction, which compromises the integrity of blood vessels and impairs vascular function [4]. The pervasive influence of oxidative stress extends to accelerating the progression of various cardiovascular diseases such as atherosclerosis, heart failure, and hypertension. It is intricately linked with poorer prognoses, significantly impacting patient survival rates and quality of life. Moreover, oxidative stress can reduce the effectiveness of pharmacological treatments, making it a critical factor in the management and outcome of cardiovascular conditions [5,6]. To counteract these profound impacts, a strategic emphasis on enhancing the body's antioxidant defenses is crucial. This includes dietary and pharmacological strategies to boost the levels of endogenous antioxidants and the supplementation of exogenous antioxidants, which collectively help neutralize ROS and mitigate its harmful effects. Ensuring an adequate supply of antioxidants thus plays a pivotal role not only in the prevention of initial cardiovascular injury but also in the management and therapeutic intervention in established cardiovascular diseases.

By definition, antioxidants are substances capable of neutralizing oxidant effects by donating electrons. This mechanism prevents a chain reaction from ROS exposure. However, failure to neutralize these effects can trigger oxidative stress [7].

The importance of antioxidants in maintaining vascular health highlights the integral knowledge of their mechanisms of action.

2. SOURCES AND TYPES OF OXIDANTS

Oxidants can originate internally or externally. Externally, humans are continuously exposed to free radicals from environmental sources such as pollution, cigarette smoke, industrial chemicals, and ultraviolet radiation. Throughout life, humans are continuously exposed to free radicals from external environments [8]. Internal sources are byproducts of various metabolic processes. Commonly known oxidants include ROS. Free radicals are atoms or molecules with an unpaired single electron, such as nitric oxide (•NO), superoxide ($O2^{•–}$), hydroxyl radicals (•OH), and lipid peroxyl radicals (LOO•) [9]. These radical molecules are highly reactive and can alter the character of a molecule. These external factors are significant contributors to oxidative stress, accelerating the accumulation of free radicals that can lead to vascular endothelial damage and play a role in the pathogenesis of cardiovascular diseases [10,11].

This high reactivity enables free radicals to interact aggressively with cellular components, potentially altering DNA, proteins, and cell membranes [12,13]. Such interactions can lead to cellular dysfunction and contribute to the aging process and the development of various diseases, including cardiovascular diseases. Furthermore, oxidative stress is intricately linked with chronic inflammation. Persistent inflammation can exacerbate the effects of oxidative stress, leading to a vicious cycle where each condition intensifies the other. This interplay significantly impacts cardiovascular health, as chronic inflammation can lead to further endothelial damage, atherosclerosis, and ultimately heart failure [14–16]. Managing these oxidants is crucial for maintaining cellular integrity and overall health, highlighting the importance of both understanding their origins and implementing strategies to mitigate their impact effectively.

3. SOURCES AND TYPES OF ANTIOXIDANTS

Antioxidants are available from external sources outside the body through fruits and vegetables and from within the body in the form of enzymes. Plant-derived polyphenols are known to have beneficial effects as cardioprotective agents [17]. These external sources are rich in essential vitamins and other bioactive compounds that help in neutralizing free radicals and reducing oxidative stress, thereby protecting against endothelial dysfunction [1]. Foods such as blueberries, spinach, and nuts are particularly high in antioxidants and are recommended for maintaining good cardiovascular health [18,19].

In addition to external sources, the body inherently produces several powerful antioxidant enzymes that play a crucial role in combating oxidative damage [20]. These enzymes include superoxide dismutase (SOD), catalase, and glutathione peroxidase, which are synthesized in various tissues and help mitigate the accumulation of reactive oxygen species (ROS) [21]. The balanced activity of these enzymes is vital for maintaining cellular health and preventing oxidative stress, which is often a precursor to chronic diseases including cardiovascular disorders. This intrinsic defense system complements dietary antioxidants and is essential for holistic cardiovascular protection.

These enzymatic antioxidants form a primary defense line against oxidative stress by mitigating the accumulation of ROS and thereby reducing their ability to inflict cellular damage. This intrinsic defense system is vital for maintaining cellular integrity and health, particularly in the cardiovascular system where oxidative stress can lead to serious chronic conditions [14]. By working in concert with dietary antioxidants, endogenous enzymes ensure a comprehensive shield against oxidative damage, thus playing an indispensable role in preventing the onset and progression of cardiovascular disorders.

This intrinsic defense system, complemented by dietary antioxidants, is crucial for comprehensive cardiovascular protection. Emerging compounds like coenzyme Q10, resveratrol, and astaxanthin are gaining attention for their potential cardiovascular benefits [22–25]. Coenzyme Q10 helps improve cardiac efficiency and prevent mitochondrial dysfunction, resveratrol enhances endothelial function and arterial health, and astaxanthin protects against lipid peroxidation and improves lipid profiles. Integrating these antioxidants into a balanced diet, enhanced by targeted supplementation, can significantly fortify the body's defense against oxidative stress and boost cardiovascular health.

4. ANTIOXIDANT MECHANISMS IN THE CARDIOVASCULAR SYSTEM

The body's antioxidant system operates effectively through a series of complex, interconnected, and supportive mechanisms. These mechanisms establish several antioxidants also known as cardioprotective. Important antioxidants include:

- **Superoxide Dismutases (SODs)** play a crucial role in converting superoxide anions into hydrogen peroxide [26], thus preventing peroxynitrite formation [27].

- **Catalase** helps neutralize the negative effects of hydrogen peroxide by converting it into water, predominantly found in the liver and kidneys [28].

- **Glutathione Peroxidase (Gpx)** functions similarly to catalase, converting hydrogen peroxide into water and is found in cytoplasmic (Fig.1), mitochondrial, and nuclear compartments [21,29].

- **Peroxiredoxin (Prx)** can reduce peroxides from various molecules [30], including hydrogen peroxide and peroxynitrite, with six distinguishable isoforms found in different subcellular locations [4].

- **Glutathione** serves multiple antioxidant roles: as a co-factor for Gpx, a chelator of transition metals, and a regenerator of vitamins C and E. It can also interact with hydroxyl radicals or function as a peroxide [28].

Fundamental to the orchestration of antioxidant enzyme activity are transcription factors, notably NF-E2-related factor 2 (Nrf2) and forkhead box O (FOXO) proteins [31–33]. These factors critically bolster cellular defenses against oxidative stress by upregulating the expression of key antioxidant enzymes, thereby sustaining redox balance and enabling effective neutralization of reactive oxygen species (ROS). Such regulatory mechanisms are essential for averting excessive oxidative damage that could otherwise compromise cellular integrity.

Moreover, antioxidants are pivotal in modulating inflammatory responses and improving endothelial function [34,35]. They attenuate the production of pro-inflammatory cytokines and enhance the bioavailability of nitric oxide, thus preserving endothelial cell integrity and function. This modulation of inflammatory pathways and maintenance of endothelial health are crucial for thwarting the progression of cardiovascular pathologies and fostering comprehensive cardiovascular protection.

Reactive oxygen species (ROS), a group of highly reactive molecules derived primarily from oxygen, play a pivotal role in triggering dysfunction in cardiomyocytes and endothelial cells, the fundamental components of the cardiovascular system. These reactive molecules, when present in excess, can initiate a cascade of oxidative stress that leads to cellular damage. This oxidative stress affects the structural integrity and function of cardiomyocytes, the muscle cells responsible for heart contractions, and endothelial cells, which line the blood vessels. Such damage compromises the heart's ability to pump blood and the vessels' capacity to regulate blood flow and pressure, ultimately impairing cardiovascular health [3,36,37]. Recognizing the impact of ROS is crucial for understanding the molecular mechanisms underlying cardiovascular diseases and for developing strategies to mitigate these harmful effects.

Significant advancements are being made in the field of antioxidant-based therapies for cardiovascular diseases, reflecting a proactive approach towards therapeutic interventions targeting oxidative stress. Research is increasingly focusing on the development of drugs that efficiently mitigate oxidative stress, thereby addressing its deleterious effects on the cardiovascular system. For instance, innovations in enhancing the bioavailability and efficacy of conventional antioxidants are currently under investigation, with emerging evidence suggesting their potential to significantly improve cardiovascular outcomes [38]. Moreover, lifestyle modifications, including dietary changes to increase natural antioxidant intake and structured exercise programs, are being evaluated for their complementary effects in reducing oxidative stress. Notably, the integration of dietary supplements such as vitamin E has shown promise in modulating oxidative stress markers, although clinical outcomes remain mixed [39–41]. These evolving strategies emphasize the integration of pharmacologic and lifestyle interventions, underscoring a comprehensive approach to managing cardiovascular health and potentially reshaping future therapeutic landscapes.

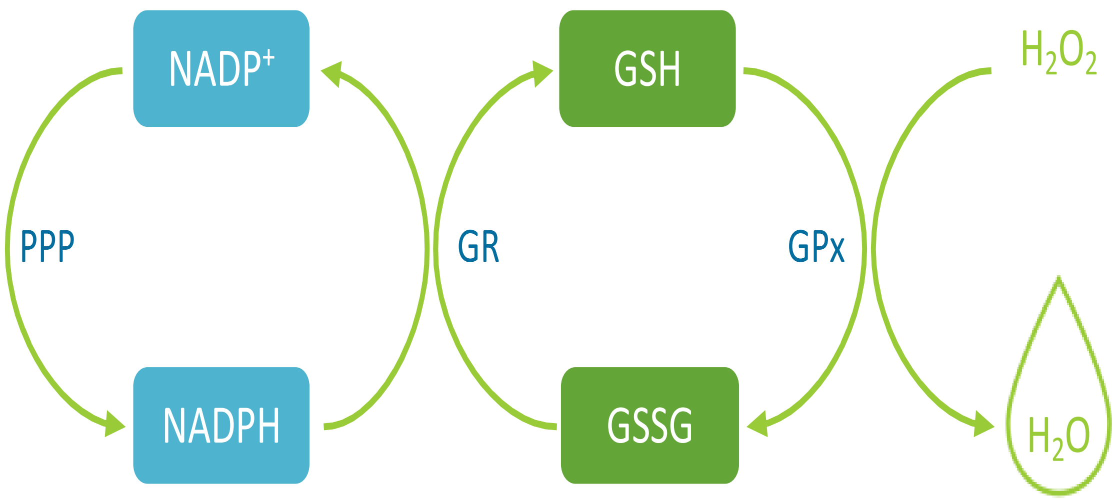

Fig. 1 The Role of glutathione as an antioxidant

5. CONCLUSION

The cardiovascular system is vulnerable to ROS attacks, leading to further manifestations including vascular and cardiac cell dysfunction. However, the body possesses antioxidant defense mechanisms involving enzymes and vitamins from externally sourced that can prevent oxidative stress.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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