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Role of Glutathione in Cardiovascular System Physiology

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ABSTRACT

Background: *The three-amino acid compound glutathione contains cysteine and is a tripeptide of cysteine, glutamate, and glycine and is the major antioxidant defense mechanism within eukaryotic cells. Participating in the removal of reactive oxygen species, it contributes in maintaining redox equilibrium and cellular homeostasis and is of particular importance in cardiovascular system.* ***Purpose****: This review aims at reviewing the literature on the biosynthesis and metabolism of glutathione and the ways that its actions are regulated for purposes of understanding its roles in cardiovascular physiology. The most critical aspect of the glutathione actions contributes to the reduction of oxidative stress, which is vital for maintaining the endothelium and vessel walls. That will help to eliminate toxic metabolites, that are involved in mitochondrial processes, and improve the cardiovascular system's resistance to ischemia/reperfusion damage. As shown by various researches and studies, heart failure, hypertension, and other cardiovascular diseases are associated with low glutathione levels or disruption of glutathione homeostasis, which only establishes the significance of maintaining adequate glutathione levels. This review makes a plea for the utilization of glutathione to reduce and combat oxidative stress, enhance endothelium stability, and protect the myocardium. Thus, the understanding of the pathways involved in the regulation of the cardiovascular system by glutathione can provide the basis for the design of new and effective preventive and therapeutic interventions for CVDs with a focus on aging and oxidative stress-related diseases. Additional studies are needed to collectively examine the potential treatments of glutathione which seems to improve cardiovascular functioning and hence heart health.*

Keywords: Glutathione, Cardiovascular Physiology, Antioxidant Defense, Endothelial Function, Redox Homeostasis.

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INTRODUCTION

One of the most important thiol-containing peptides used in eukaryotic cells is glutathione which is responsible for the protection of cells against damage caused by oxidation and other cellular regulation. By doing so, it plays the role of a very important antioxidant defense and helps to purge reactive oxygen species and maintain an redox status of the cell (Bajic *et al*., 2019). More to the point, it is crucial and sensitive to metabolic functioning and oxidative stress in general, as well as cardiovascular disease in particular, to view the ratio of the reduced form of glutathione (GSH) to the oxidized form (GSSG) as constantly in flux (Strutynska *et al.*, 2023).

Cardiovascular diseases often develop with aging attributed to disturbance in the increased oxidative and antioxidant systems, Further, mitochondrial abnormalities, among other causes (Izzo *et al*. 2021). It has been reported that exogenous GSH can improve the mitochondrial redox state and the cardiovascular function in elderly rats by

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increasing the levels of H2S, reducing the levels of oxidative stress markers, preventing the mPTP open, and improving the resistance to ischemia/reperfusion (Scammahorn *et al*. 2021). Furthermore, after treatment with glutathione the endothelium-dependent vasorelaxation responses have been restored, suggesting the therapeutic benefits of the molecule in cardiovascular health (Camargo *et al*. 2023).It has been reported in the literature that alteration of glutathione levels is consequential to a number of diseases which comprise cardiovascular diseases. Both changes in the absolute levels of GSH and in its oxidation status correlate with the development and further course of cardiometabolic diseases including heart failure. Awareness of glutathione in managing redox balance helps in canvassing its consequences on cardiovascular function and disorder (Raut & Khullar 2022). The review wanted To conclude, therefore, to identify and discuss the potential of glutathione in the regulation of the cardiovascular system based on its effects on redox equilibrium and endothelium.

2. Glutathione Biosynthesis and Metabolism

2.1. Glutathione synthesis pathways

Glutathione is a sulfur-containing, water-soluble tripeptide, being synthesized from cysteine, glutamate, and glycine; it exists in both the reduced (GSH) and oxidized (GSSG) forms and plays a vital role in sustaining redox homeostasis in cardiomyocytes and preventing oxidative stress in the cardiovascular system. According to (Rybka *et al*., 2011) glutathione is an important thiol-disulfide redox buffer in cells and plays a crucial role in a number of physiological processes. The regulation of synthesis of glutathione depends on -glutamyl cysteine synthetase and GSH synthetase, whereas the production of -GCS depends on such factors as GSH deficiency, inflammatory cytokines, and oxidative stress (Luo *et al*. 2023).

In normal diet conditions, the synthesis of cysteine tends to limit the synthesis of GSH. According to (Matuz-Mares *et al*., 2021), the levels of intracellular reduced glutathione are determined by its use in conjugation reactions with xenobiotics or reactive oxygen species (ROS). It can also be oxidatively used up in detoxication pathways, yet it can be recycled from GSSG with aid from NADPH-dependent glutathione reductase (Georgiou-Siafis & Tsiftsoglou 2023). Furthermore, as reported by (Strutynska *et al*., 2023), the redox stability of glutathione influences cellular stability and affects the subcellular structures. Low levels of GSH lead to ferroptosis whereby the resultant cell death can be prevented by the chelation of iron. Besides its antioxidant effects, glutathione protects mitochondria from the damaging effects brought about by hydrogen peroxide and lipid hydroperoxides through enzymes such as GPx1 and GPx4 (Li *et al*. 2020). It could be asserted that the anabolism of glutathione is equally well controlled to provide for the right concentrations that would be of benefit to cardiovascular health. Owing to its antioxidant properties, it has a vital stand in the maintenances of cell redox status and with this, it shields one from oxidative stress and serves the capacity of a cardiovascular health booster, a property that is indicated to be actively present in 2024 as stated by Pinilla-González.

Table 1: Enzymes That Regulate Protein S-Glutathionylation. (Pimentel *et al*., 2012).

Enzyme Category	Enzymes
Glutathione-S-transferases	GSTp, GSTm
Flavoprotein sulfhydryl oxidase	QSOX, ERV1
Glutaredoxins	Glrx 1: cytosolic, Glrx 2: mitochondrial
Sulfiredoxin (SRx)	-

Mechanisms that control intracellular concentrations of glutathione. Green arrows depict either synthesis or regeneration of glutathione through other pathways. The enzymes that are well involved are -glutamylcysteine synthetase, glutathione synthetase, and glutathione reductase. The red arrows show how glutathione is applied to cleave and excrete drugs or toxic metabolites to the body, threatened by oxidative stress with alcoholism and smoking. Intracellular glutathione also reduces as it is translocated from the tissues producing it in large quantities to other tissues by the need for more antioxidant activity in the tissues (Matuz-Mares *et al*., 2021), (Figure 1).

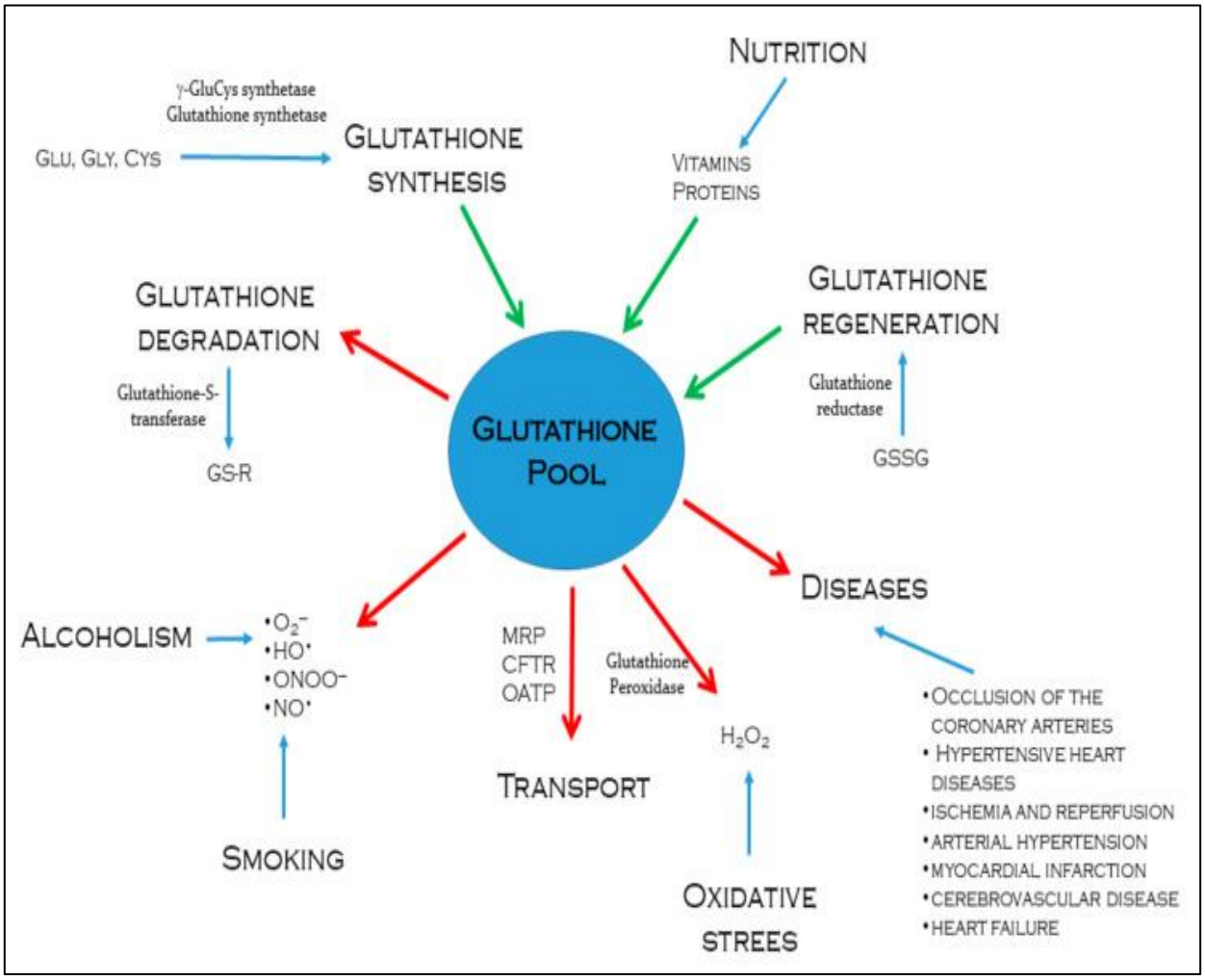

Figure 1: Regulation and Utilization of the Intracellular Glutathione Pool. (Matuz-Mares *et al*., 2021).

2.2. Regulation of glutathione levels

Intervention to ensure that glutathione is kept at the appropriate concentrations is fundamental for redox homeostasis and cardiovascular integrity. It is formed from the products of important enzymes, and it maintains the intracellular oxidative/reduction balance since it is capable of counteracting oxidative stress and other toxic compounds(Pisoschi *et al*. 2021). The irreversible damage also results when the cysteine residues in glutathione are depleted.

Glutathione reductase changes oxidized glutathione to its reduced form whereas amino acids such as cysteine are useful in the synthesis of glutathione (Averill-Bates, 2023). This study reveals that oxidative stress or GSH depletion, hypertension, and cardiovascular disease are linked. Low GSH levels in heart disease and diabetes patients mean that there is a solid rationale for healthy levels of GSH in the heart and diabetes patients particularly (Dubois-Deruy *et al*. 2020). Several animals stepped

endorsed the efficacy of GSH supplementation in offering protection against oxidative stress and lipid peroxidation-related cardiovascular pathologies (Wang & Kang, 2020). Knowledge about the control of glutathione is important for understanding redox balance and the development of practices and treatments for cardiovascular diseases associated with the disruption of the redox balance (Zullo *et al*. 2022).

3. Mechanisms of Action

3.1. Antioxidant properties of glutathione

A tripeptide comprising of L-glutamate, L-cysteine, and L-glycine is a vital molecule in the antioxidant defense system of cells (George *et al*. 2024). It is considered as one of the most accumulated Rp's within the cell and exists ultimately in the form of GSH, which plays a great role in cellular homeostasis and redox balance (Rachet, 2023). The total glutathione level measured in the cell varies between 1 and 15 mM thus underlining the importance of the antioxidant agent for the cellular function (Rai *et al*. 2021).

Discussed here are roles of glutathione in battling oxidative stress that results from reactive oxygen species (ROS) through several pathways and mechanisms (Griendling & Brown, 2015). Acting together with other antioxidant enzymes including SOD, catalase, and GPx, glutathione effectively participates in the process of reducing oxidants and avoiding the impact of oxidative stress on the cells (Demirci-Çekiç *et al*. 2022). Also, redox signaling regulation is done by glutathione, which activates transcription factors such as Nrf2 involved in signaling genes that play a vital role in the detoxification of cells (Adelusi *et al*. 2020). Concerning cardiovascular health, the antioxidant functionality of glutathione is of paramount significance. Scientific investigations show that aged rats administered with exogenous glutathione had a remarkable transient change in the levels of the reduced form of glutathione and a decreased density of oxidative stress markers in the heart mitochondria (Asejeje & Ogunro, 2024). These changes were accompanied by the improvement of mitochondrial activity and Ischemia/reperfusion injury, thus proving the cardioprotective role of glutathione (Strutynska *et al*., 2023). In addition, the restoration of endothelium-dependent, vasorelaxation responses also takes the beneficial effect of glutathione on vascular health in aging animals to a higher level (Valencia *et al*. 2022).

All in all, it has been evident from the foregoing discussion that antioxidant activity of glutathione is essential in the regulation of the cellular redox potential and protection from oxidative injury. Cats and dogs apply glutathione in cardiovascular physiology where they play a significant role in the protection of the heart and vascular tissues from oxidative stress, contributing immensely to the general cardiovascular health (Dwivedi *et al*. 2020). More studies on the beneficial effects of glutathione supplementation are needed to explore possible treatment strategies for CVDs and aging comorbidities (Scioli *et al*. 2020).

3.2. Detoxification role of glutathione

It actively participates in detoxifying the cardiovascular system. As emphasized in the information gathered in the study "Glutathione Homeostasis and Functions: Among the potential targets for medical interventions, "glutathione" is of fundamental role in the elimination of toxic byproducts formed during cellular metabolism. In particular, it helps to clear products of lipid peroxidation such as malondialdehyde and 4-hydroxy-2-nonenal ((Lushchak, 2012). Further, glutathione helps in the detoxification of formaldehyde through the reaction with formaldehyde dehydrogenase as a cosubstrate (Singh *et al*. 2022). In addition, glutathione is synthesized in the process of creating glutathione S-conjugates which are considered to be significant since they

play the role of detoxifying toxins in the human body. This process involves the conjugation of toxins with glutathione and the elimination of the cells; Potęga, 2022). However, this conjugation can also take place biotransformationally mediated or without being mediated by enzymes such as the glutathione transferases (GSTs) which have a large substrate specificity that allows them to compete for the reactive metabolites of both endogenous and exogenous compounds ((Pizzorno & Katzinger, 2012). This particular detoxification process allows for the elimination of one or many substances, especially toxic metals for example, mercury, arsenic, lead, substances such as acetaminophen and persistent organic pollutants (Jaiswal, Pandey & Agrawal 2021).

Also, the transport of GSH is important in hepatic cells since it sends glutathione into the bloodstream through the sinusoidal transporters on the basolateral membrane of hepatocytes (Basiglio *et al*. 2021). Another system which is also on the canalicular membrane transports Glutathione S-conjugates into bile and is very critical for drug and reactive species clearance in liver, This demonstrates complex transport machinery that explains the central role of glutathione for detoxification and regulation of intracellular redox that is pertinent in cardiovascular physiologic functions. The rapid evolution is discussed in the article Roy-Chowdhury, Wang & Roy-Chowdhury 2020.

4. Glutathione in Endothelial Function

4.1. Impact on endothelial cell health

The oxidation and the health of endothelial cells is therefore inevitably linked to glutathione, particularly in relation to vasorelaxation (Handy & Loscalzo 2022). Various studies have shown that pre-treatment of the endothelium with exogenous glutathione greatly improved the contractile effect of ACh on the aortic rings of aged rats (Tracy *et al*. 2021). This improvement happens through the activation of the NO signaling pathway which is known to decline with aging, Response to acetylcholine-induced relaxation of the aortic rings was significantly higher in aged rats treated with glutathione than that of the control aged rats suggesting that NO is particularly depended on for the vasodilatory activity (Simonet *et al*. 2021). Also, glutamine has proven efficiency in protection from oxidative stress and endothelial damage due to increased synthesis of glutathione ((Ruiz-Ramirez *et al*., 2014). Supplementation of the levels of glutathione in the vascular tissue reduces the generation of superoxide anion radicals and the levels of protein carbonyls and lipid peroxidation; it improves the relaxation response to acetylcholine in aortic rings in sucrose-fed rats (Sharapov *et al*. 2021). Also, low levels of cellular glutathione peroxidase are a risk factor for endothelial dysfunction and defective vasodilators ((Forgione *et al*. 2002). Many studies have pointed out that a lack of GPx-1 leads to increased vascular oxidant stress and impaired endothelium-dependent vasodilation because of a decrease in bioavailable NO (Valaei *et al*. 2021). This dysfunctional response can be prevented by increasing intracellular thiols levels, as it underlined by the important contribution of GPx- 1 and glutathione to vascular homeostasis (Forgione *et al*., 2002).

4.2. Regulation of nitric oxide production

The synthesis of nitric oxide is a critical regulatory element in the cardiovascular system concerning the functioning of endothelial cells and the health of blood vessels. Nitric oxide (NO) is an essential molecule having properties that can bring about vasodilation to help regulate the vascular tone and thereby correct vascular imbalance (Gluvic *et al*. 2024). When there is a distorted shift in the ratio of NO and ROS, then one gets a condition known as ED, which results from a decreased availability of NO and irregularity in the regulation of

vasoconstriction (Salvagno *et al*. 2024). This state of imbalance may be attributed to factors like increased ROS levels, and the fact that eNOS is uncoupled and hence yields less of the beneficial NO and increased formation of ROS, or a reduction in the activity, or any of the antioxidant defense systems like glutathione mentioned by tan and colleagues in 2023.

Studies have disclosed a link between glutathione deficiency and heart disease and hypertension effecting the synthesis of the nitric oxide ((Fang *et al*., 2022). A study showed that subjects with a history of heart disease had significantly lower plasma value of glutathione implying that there exists the lowest plasma value of glutathione in subjects with poor cardiovascular health (Kotur-Stevuljević et al. 2023). In addition, the current treatment with external glutathione has shown the stimulation of the free radical production of the nitric oxide synthase active in mitochondria (mtNOS) in aged rats and augmentation of NO a level potentially improving endothelial function ((Strutynska *et al*., 2023).

Apart from the role of a free radical scavenger, glutathione plays a role in the control of signaling gases like NO and hydrogen sulfide (H2S) which are important in cardiovascular health (Kolluru *et al*. 2022). It has been demonstrated that treatment with glutathione enhances NO synthesis which is beneficial in the pathogenesis of cardiac mitochondria dysfunction and decrease of oxidative stress (Tan *et al*. 2023). Furthermore, the promotion of glutathione synthesis has been shown to improve the contractile force of the heart and the endothelium-dependent relaxation in diabetic animal models, underlining the clinical appeal of rationalizing on pathways involving glutathione in cardiology (Janaszak-Jasiecka *et al*. 2012). Most importantly, the ability to modulate the production of nitric oxide via these antioxidant systems, such as glutathione has major outcomes on cardiovascular physiologic processes. It seems necessary to keep the levels of NO and ROS appropriate, to optimize the functioning of antioxidant systems, and to pay attention to the metabolism that involves glutathione to achieve the improvement of endothelial function, vascular health and cardiovascular outcomes. More studies on mechanisms of glutathione in modulation of nitric oxide may prove useful for developing therapeutic approaches to cardiovascular illnesses (Woo *et al*. 2021).

5. Glutathione and Vascular Health

5.1. Role in maintaining vascular tone

It is pivotal to appreciate the role of glutathioneer in having control over vascular tone because it is vital for efficient cardiovascular performance. As cited by (Forgione *et al*., 2002), the deficiency in cellular glutathione peroxidase (GPx- 1) has been associated with poor endothelium-dependent vasodilation, increased vascular oxidative stress, and dysfunction of the endothelium. This dysfunction takes the form of pathophysiologic alterations of pro-inflammatory and pro-thrombotic features in endothelial cells which affecting vascular tone and balance (Li *et al*., 2023). In addition, according to (Strutynska *et al*., 2023) administration of exogenous glutathione in the rats increases the level of reduced glutathione form to enhance the redox status and decrease the oxidative stress biomolecules in the heart mitochondria (Kalamkar *et al*. 2022). This restoration of mitochondrial redox status returned mouse hearts to improved resistance to ischemia-reperfusion injury and better reactions to endothelium-dependent vasorelaxation (Kalamkar *et al*. 2022).

Furthermore, the intracellular constraint of the endothelium's glutathione levels has been linked to increased levels of ROS and decreased bioavailability of nitric oxide, which in turn makes the endothelial dysfunctional (Fisher & Ekpo, 2020). This goes to show how beneficial and essential glutathione is in protecting the

endothelium and preventing vascular disease. Furthermore, altering antioxidant pathways, especially glutathione, has been indeed implicating in reducing endothelial dysfunction, and this may be a potential approach in PIN and CKD-associated cardiovascular risk factors (An *et al*., 2023). In other words, the fact that glutathione is responsible for the regulation of vascular tone makes this function vital for cardiovascular health. Through its position in protecting against oxidative stress, furthering redox state homeostasis, and regulating endothelial function, glutathione fills a significant responsibility in preserving vascular steadiness and avoiding vascular diseases such as atherosclerosis ((Li and Forster, 2023). The strategy of administering glutathione or modifying glutathione signaling can be therapeutic offered by the cardiovascular benefit and the decreased risk of cardiovascular diseases resulting from aging and oxidative stress (Zalachoras et al. 2020).

5.2. Effects on blood pressure regulation

It is reciprocally concerned with the regulation of blood pressure within the cardiovascular circuitry. In line with what has been presented by Kolluru et al., (2023), it is through its antioxidant ability that it plays a role in maintaining the vascular integrity as well as functioning of the endothelial cells as noted by Wang et al. 2024). One of the most critical processes that underlie hypertension and other cardiovascular diseases, It is endothelial dysfunction, which, conversely, is associated with decreased levels of glutathione in patients with hypertension; This is discussed in (Pacinella, Ciaccio & Tuttolomondo 2022). Also, glutathione backgrounds were supported by the fact that its deficiency contributes to the development of atherosclerosis – the basis for hypertension and other cardiovascular diseases. Scientific findings have shown that increasing the concentration of glutathione can reduce oxidative stress and improve the blood vessels' condition, which was proved on animals with the atherosclerosis disease receiving liposomal-coated glutathione (Biswas *et al*. 2005).

Other function of glutathione includes the maintenance of vascular tone Glutathione is thus a potent antioxidant. Vascular tone is an important component of blood pressure control and there have been positive findings regarding glutathione. Glutathione is involved in the protection of the cardiac tissue from oxidative stress and maintaining the health of endothelial lining; besides, it helps to avoid the development of other related disorders in conditions of high blood pressure (Tain & Hsu, 2022).

In all, the influence of glutathione in blood pressure control reinforces understanding of its role in cardiovascular functioning(Amponsah-Offeh et al. 2023). Placed in the perspective of oxidation and endothelial function, glutathione takes on an antioxidant function and a reserve of vascular tone that essentially is involved in the maintenance of cardiovascular health and the prevention of hypertension and associated diseases(Aragão *et al*. 2024). In the form of target treatments and modifiers, researchers might continue the investigation of glutathione signaling pathways for the improvement of cardiovascular data (Forman & Zhang 2021).

6. Glutathione and Myocardial Function

6.1. Influence on cardiac muscle contraction

The function of glutathione in the contraction of cardiac muscles has a great impact on the probability of the involvement of the substance in cardiovascular systems (D'Oria et al. 2020). Glutathione is well-known to protect cells for oxidation, and it is a crucial role in safeguarding cells, especially from aging impacts (Labarrere & Kassab 2022). Through boosting of mitochondrial redox status by raising the levels of reduced glutathione it helps in the functioning of cardiovascular system by improving the contraction of cardiac muscles (Bachhawat et al.

2020). In old rats, injected with GSH there was an increase in UCP3 in hearts, this helps to reverse some deleterious effects caused by aging, as well as improving the overall cardiac output of the older animals (Čater & Bombek 2022).

Moreover, the oral administration of glutathione to elderly rats caused a reduction in oxygen consumption and the oxygen cost of the heart that was similar to that of adult rats (Pagan et al. 2022). This means that external glutathione can enhance oxygen use in aged myocardium, that might affect mitochondria function and energy metabolism (Bou-Teen et al. 2021). In addition, the lack of a reduction in the contractile force or coronary flow but improvements of oxygen consumption and cost effectiveness of the heart was observed from intraperitoneal administration of glutathione (Schlichte, 2021). The positive effect of glutathione on cardiac muscle contraction may be explained by the ability of agent to reverse redox changes in mitochondria and to reduce concentrations of oxidative stress indicators (Brancaccio et al. 2020).

6.2. Protection against oxidative stress in the heart

Antioxidant, anti-inflammatory, and detoxifying roles of glutathione are vital in protecting the heart from oxidative stress in patients with aging and cardiovascular diseases (Marí *et al*. 2020). Supplementation of glutathione has been proven to act on the cardiac mitochondria to rectify the imbalance in redox state, decrease severity of oxidant stress, increase the activity of mtNOS, and augment H2S (Belenichev et al. 2024). They lead to prevention of the opening of mPTP and generally improved cardiovascular function (Lozano et al. 2020). The decrease in the ratio between the reduced glutathione (GSH) and the oxidized glutathione (GSSG) can provoke mitochondrial disfunction, and there is an association between cardiovascular disorders and aging (Iskusnykh et al., 2022).

RNS has an essential role in the formation of CVD, in particular, in myocardial injury and dysfunction (Shaito et al. 2022). Being produced under pathological conditions, especially in mitochondria, ROS are dangerous to cells and can cause the damage of cellular structures, leading to cell death. The glutathione system that includes GSH and other associated enzymes can protect cardiomyocytes from the ravages of oxidative stress as shown by Tan et al., 2023. High levels of iron within cardiomyocytes can cause non-apoptotic cell death process called ferroptosis which is based on lipid peroxidation. Nevertheless, recent studies have shown that it is possible to avoid cardiomyopathy by modulating the glutathione-dependent antioxidant system in animal models and decreasing the levels of oxidative stress (Li et al. 2021). Moreover, cogent literature evidences show that oxidative stress plays a part in the transition from compensatory hypertrophy to CHF. Excessive ROS generation from various enzyme systems, and increased XO and NOX activity is also shown to impair the function of the heart in heart failure. The antioxidant enzymes such as glutathione peroxidase are known to be important in the prevention of cardiovascular diseases through a reduction in oxidative stress (Zhang et al., 2019).

7. Glutathione in Aging and Cardiovascular Diseases

7.1. Relationship between glutathione levels and aging

Investigate the role of free radicals, oxidants, and particularly glutathione on aging and heart disease. Imbalances between the GSH/GSSG ratio mention aging symptoms and various cardiovascular diseases (Sekhar 2021). As people age, oxidative and nitrosative stress increase in the heart in mitochondrial dysfunction and atherosclerosis diseases such as

Sekhar, *et al*. (2011) and Fujii and Homma (2015).

Also, various investigations have pointed out that supplementation with the precursors of glutathione will enhance the GSH store and have the potential to offer a cardio-protective effect. For Instance, N-acetyl-L-cysteine has already displayed a lowering effect on hypertension and a replenishing effect for GSH during myocardial infarction and heart failure (Adamy *et al*., 2007). It is thus important that sufficient glutathione be preserved within the body to ensure heart function is not impaired, more especially to the aged.

In addition, as shown in aspects discussed by Matuz-Mares et al. (2021), studying oxidative stress, which is a high production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), in the development of cardiovascular diseases, which increase with age, is important. It is clearly understood that glutathione plays a vital role as an antioxidant to neutralize ROS and RNS and to attenuate the oxidative damage that is related to heart ailments.

Also, according to the study conducted by (Rybka *et al*., 2011), hypertensive elderly patients on treatment had better glutathione-associated antioxidant status than the normal population. These results indicate the usefulness of the glutathione system to modulate blood pressure and increase antioxidant defenses through elevated GSH levels and increased activities of enzymes such as GST and GR. (Figure 2). Thus, all of these findings underscore the significance of homeostasis of glutathione in relation to prosages for healthy aging non-hazardous to the cardiovascular system. Thus, knowing how glutathione affects the oxidative stress pathways, it will be possible to identify effective therapeutic interventions that protect the heart in elderly people.

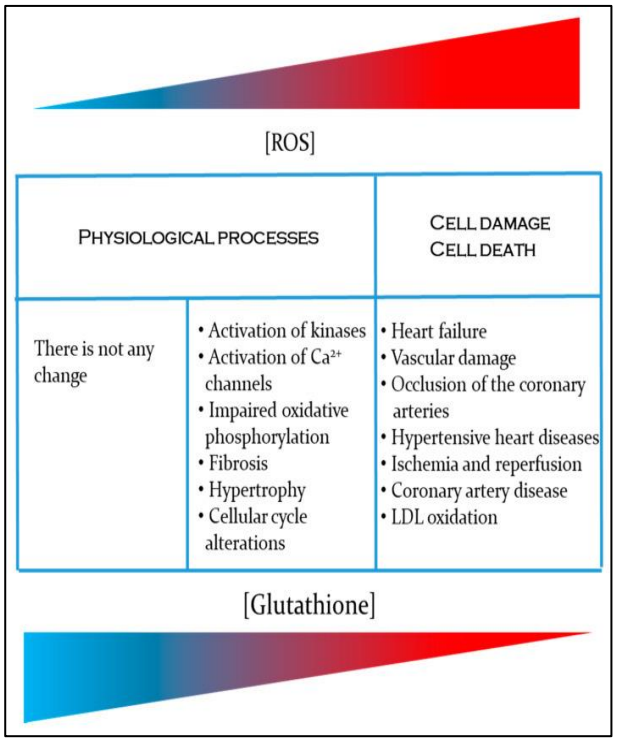

Figure 2: Role of Glutathione (GSH) in Preventing Cardiovascular Diseases Linked to Increased Production of Reactive Oxygen and Nitrogen Species (ROS and RNS). (Matuz-Mares *et al*., 2021).

7.2. Link to cardiovascular diseases such as atherosclerosis

Glutathione is an antioxidant of specific importance, which is involved in the etiology and promotion of heart diseases particularly atherosclerosis (Batty, Bennett & Yu 2022). Atherosclerosis is when there is a deposit of plaque in arteries leading to lower blood flow an raised heart-related cases (Dhakal & Pokharel 2024). oxidative stress has now been established as one of the fundamental causes of atherosclerosis Different studies have revealed that older people have a shortage of glutathione as they fail to produce it as they used to this has been associated with oxidation stress and the age-related damage to heart diseases (Egea, Jiménez-Altayó & Campuzano 2020). However, vascular aging which refers to a change in the structure and function of blood vessels is also responsible for factors such as atherosclerosis((Guo *et al*., 2022). Endothelial dysfunction owing to the production of formed

products such as nitric oxide and endothelin-1 promotes inflammation within the blood vessels and a narrowing that contributes to vascular aging and atherosclerosis development (Naderi-Meshkin & Setyaningsih 2024). Conversely, Nrf2 disruption by oxidative stress could be triggered by aging endothelial cells, which greatly enhances oxidative stress levels and accelerates other age-related changes (Leyane, Jere & Houreld, 2022). Also, there are imbalances in glutathione associated with diseases apart from cardiovascular that come with aging ((Pizzorno & Katzinger, 2012). For example, it has been linked to metabolic disturbances characteristic of diabetes mellitus, obesity, insulin resistance, the metabolic syndrome for which adequate concentrations of GSH therefore play a role in human health and disease. (Bizerea-Moga *et al*. 2024)

CONCLUSION

Therefore, this research has shown that glutathione is highly effective in the health of the cardiovascular system due to its antioxidant properties, detoxification mechanism, and control of endothelium. This review is aimed at the use of glutathione supplementation in the treatment of oxidative stress and decrease in cardiovascular risk. Understanding the roles of glutathione and the roles it plays in cardiovascular diseases gives new opportunities for the prevention and treatment of cardiovascular diseases, especially the ones that are associated with aging and oxidative stress.

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