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Review Article

Therapeutic Repurposing Strategies for Cardiovascular Disease Management

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ABSTRACT

Background: Antioxidants are vital in maintaining cellular homeostasis by neutralizing Reactive Oxygen Species (ROS) and mitigating oxidative stress. This review aims to explore their role in disease modulation, with a particular focus on cardiovascular disorders, including myocardial infarction and atherosclerosis. **Materials and Methods:** A comprehensive review of peer-reviewed literature was conducted to assess the biochemical mechanisms, efficacy, and clinical relevance of both natural and synthetic antioxidants. Antioxidants were found to significantly minimize damage from oxidative stress to lipids, proteins, and DNA. These effects contribute to decreased inflammatory responses, inhibition of LDL oxidation, and improvement in endothelial function, key factors in preventing atherosclerosis and myocardial damage. However, therapeutic outcomes vary depending on the type of anti-oxidant, dosage, and bioavailability. **Results:** Evidence demonstrates that antioxidants reduce oxidative damage, thereby inhibiting LDL oxidation and enhancing endothelial function. While preclinical data support their role in mitigating inflammatory responses, clinical efficacy remains inconsistent due to variations in dosage and bioavailability. **Conclusion:** The anti-oxidant's advantages in preventing disease and treatment are well-supported, with several key challenges remaining. Furthermore, clinical and translational research is scarce, with most findings derived from preclinical or observational studies. This review highlights these critical gaps by offering mechanistic insights and identifying future research directions.

Keywords: Antioxidants, Reactive Oxygen Species, Oxidative Stress, Biomarkers, Cardiovascular Diseases.

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INTRODUCTION

Aerobic living processes transform approximately 5% of inhaled oxygen into Reactive Oxygen Species (ROS), which are unstable chemical species characterized by unpaired electrons. This process causes extensive damage to cellular proteins, lipids, and carbohydrates, contributing to diverse medical conditions including diabetes, cancer, neurological disorders, and aging. In the cardiovascular system, excessive ROS production is a primary driver of atherosclerosis and myocardial infarction.[1] During the development of atherosclerosis, ROS generated by enzymes like NADPH oxidase trigger endothelial dysfunction and the oxidation of Low-Density Lipoprotein (LDL) into its pathogenic form, ox-LDL. This leads to the recruitment of macrophages which transform into "foam cells," the foundational component of arterial plaques. Chronic oxidative stress eventually weakens the plaque's fibrous cap, leading to rupture and life-threatening thrombosis. In both atherosclerosis and Myocardial Infarction (MI), ROS production drives vascular and tissue damage. In atherosclerosis, hypertension and high LDL activate NADPH Oxidase (NOX) and cause mitochondrial dysfunction, leading to NOS uncoupling; this generates superoxide that oxidizes LDL to form plaque-building foam cells. In MI, a massive ROS surge occurs during reperfusion, where the sudden return of oxygen triggers acute oxidative stress that causes cardiomyocyte death and impairs contractile function. Antioxidants are critical chemical substances that mitigate these damaging effects by donating electrons to neutralize free radicals.[2] Beyond simple oxidative damage, CVD is driven by redox derangement a systemic failure of redox homeostasis where excessive ROS from NADPH Oxidase (NOX) and dysfunctional mitochondria "re-wire" cellular signalling. In atherosclerosis, this imbalance fuels endothelial dysfunction and foam cell formation, while in myocardial infarction, it triggers acute reperfusion injury. This shift creates a persistent pro-inflammatory and pro-thrombotic vascular environment that acts as the primary driver of disease progression. This shift creates a persistent pro-inflammatory and pro-thrombotic vascular environment that acts as the primary driver of disease progression. This oxidation promotes the

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recruitment of macrophages, which ingest the lipids to become "foam cells," forming the core of atherosclerotic plaques. As the disease progresses, chronic oxidative stress weakens the plaque's fibrous cap by activating matrix metalloproteinases, leading to plaque rupture and subsequent thrombosis.[3]

Databases used

Common databases for a high-impact review on drug repurposing in cardiovascular disease include: PubMed, ScienceDirect, Wiley Online Library, Google Scholar, Scopus, Cochrane Library.

Overview of free radicals and oxidative stress

Radicals without Chains

Electrons without pairing function as electron acceptors, stealing electrons from other molecules and altering the chemical reactivity of an atom or molecule, often making it more reactive than identical nonradicals. Oxidation is the term for this loss of electrons. Because free radicals tend to cause other molecules to give up their electrons, they are also known as oxidizing agents. These sources continually expose us.[4,5] The instability of unpaired electrons frequently enhances the reactivity of the free radical. Lipid peroxide radicals (LO_2•), superoxide (O_2•), alkoxyl (OR•), peroxyl (RO_2•), and hydroxyl (OH•) radicals are examples of ROS. RNS consists of a combination of nitrogen dioxide (NO_2•) and nitric oxide (NO•). Free radicals devoid of oxygen and nitrogen can quickly transform into other reactive species that are not radicals but still pose a health risk. Despite being categorized as oxidants rather than free radicals, these compounds easily trigger free radical actions in living organisms.[6] ROS comprises both radical and nonradical species. Under specific physiological and pathological conditions, humans and animals increase the quantity of these reactive species produced.[6,7]

Oxidative Stress

The concept of "oxidative stress" provides a more comprehensive understanding of the connection between molecular damage and free radicals. We refer to the detrimental effects of free radicals, which may result in biological damage through nitrosative and oxidative stress.[8] Oxidative stress is a dangerous condition resulting from excess ROS formation and a reduction in the level of antioxidants. Molecular oxygen, an essential element of aerobic life, creates hazards in specific situations, highlighting the oxygen paradox. The oxygen paradox involves the fact that, although a necessary component of aerobic life, molecular oxygen can be hazardous in certain situations.[9] Membrane peroxidation of lipids, oxidation of proteins, destruction of DNA, and disruption of the cell's reducing equivalents, which result in cell death and abnormal signaling pathways, are four critical oxidative stress mechanisms contributing to many illnesses. A lot of ailments, including diabetes, neurological problems, and ageing, have been caused by oxidative stress. Numerous mechanisms are involved in the pathophysiology of these diseases, including "inflammatory oxidative conditions, which include pro-oxidants that alter the thiol/disulphide redox state and impair glucose tolerance, along with enhanced activity of xanthine oxidase or NADPH oxidase-induced ROS production, or both.[10-12] Lipid peroxidation, DNA damage, and protein oxidation by free radical activity are the major causes of ageing. Damaged cell molecules can potentially disrupt the cell's normal functioning or even cause cell death, which can result in pathological conditions.[13]

The Figure 1 shows how endothelial dysfunction, inflammation, and vascular damage are all facilitated by oxidative stress, which in turn leads to CVD.

Oxidative damage in cardiovascular disease

The main cause of atherosclerosis is oxidative alteration of circulating lipoproteins, particularly Low-Density Lipoproteins (LDL) by free radicals. Smaller, denser LDL particles, which are recognized as a cardiovascular disease risk factor, may encourage atherogenesis for several reasons. These altered LDL particles, due to their difficulty in attaching to the endogenous LDL receptor, remain in the bloodstream, contributing to the disease process.[14,15] The lower anti-oxidant content of these molecules makes them more susceptible to rapid oxidation, and macrophage scavenger receptors actively absorb them, speeding up the formation of foam cells.[16]

Oxidative Stress Biomarkers in Individuals with Cardiovascular Risk Factors

Cardiovascular Disease (CVD), which ranks as the world's leading cause of death and morbidity, is fueled by atherosclerosis. In particular, before an acute event like Ischemic Heart Disease (IHD), stroke, atherosclerosis, a chronic inflammation of the arteries, may go years without presenting any clinical symptoms.[17] While unmodifiable risk features are very appropriate for risk stratification, modifiable factors have the benefit of serving as a target for pharmaceutical intervention aimed at reducing cardiovascular risks.[18,19] Clinical human studies have confirmed the relationship between oxidative stress and cardiovascular events, and various molecular biomarker types offer a potent method for identifying cardiovascular risk factors, which has implications for clinical research, epidemiology, and the prevention, diagnosis, and treatment of cardiovascular disease.[20] Figure 2 Schematic illustrates the mechanistic basis of oxidative stress. It depicts that oxidative stress originates from endogenous processes such as cellular metabolism, as well as exogenous stimuli and age-associated pathologies.[21]

Types of Antioxidants

Antioxidants can stop or reduce the harm that the unstable molecules produced by the body in response to external stimuli cause to cells. It takes antioxidants to keep all living things alive. Fruits and vegetables are excellent providers of antioxidants.[22-24] The therapeutic impact of these compounds is further governed

by their bioavailability, which describes the portion of the anti-oxidant that successfully enters systemic circulation. This is often limited by the food matrix where certain cooking methods can either enhance or hinder nutrient release and the low oral solubility of many potent phytochemicals, which often undergo rapid metabolism before they can exert their full protective effects on cellular health. Optimal anti-oxidant dosage follows a hermetic curve, where low to moderate concentrations provide protection, but excessively high doses can shift the redox balance into a harmful pro-oxidative state. As Table 1 examines the mechanisms of natural and synthetic antioxidants in managing myocardial infarction and atherosclerosis using animal models. While dietary intake from whole foods is safe, pharmacological mega dosing may disrupt essential cellular signalling and exceed the Upper Tolerable Intake Level (UL). The clinical challenge remains achieving therapeutic systemic concentrations without triggering the oxidative damage these compounds are intended to prevent.

Challenges in Clinical Translation: The Bioavailability Barrier

The effectiveness of antioxidant therapy is highly contingent upon the compound's chemical nature, the administered dose, and its pharmacokinetic profile. Natural antioxidants often suffer from poor bioavailability and rapid systemic clearance, preventing them from reaching critical concentrations within the vascular intima or the mitochondrial matrix. Furthermore, the dosage is a double-edged sword; while optimal levels can neutralize harmful radicals, excessive dosing can lead to "anti-oxidant stress," inadvertently disrupting essential redox signalling and contributing to drug failure in clinical settings.[39] The success of anti-oxidant therapy depends on the precision of targeted synthetic mimetics versus non-specific natural scavengers, as natural compounds often fail to reach critical subcellular sites. Efficacy is further constrained by a "U-shaped" dosage curve, where excessive levels trigger harmful pro-oxidant effects. Consequently, repurposing efforts must prioritize bioavailability and plaque-specific penetration to ensure agents survive first-pass metabolism and neutralize ROS at the pathological source.[40]

Epidemiology of Antioxidants

Epidemiological studies are the primary source of evidence in unveiling the possibilities of these agents in prevention and treatment. Epidemiological studies suggest that among many ethnic groups, there is a clear difference in the incidence of diseases, given the various lifestyles and variants of environmental exposure they have been subjected to.[39,40] The French paradox refers to the observation of low cardiovascular mortality, despite a high fat intake among the French population, attributed to the anti-oxidative properties of the red wine they consume. The Spanish Mediterranean diet meets these same antioxidants and thus provides the benefit of cardiovascular protection. Many of the observed benefits were attributed to the synergistic effect of natural antioxidants with more commonly known vitamin antioxidants.[41]

Natural Sources of Antioxidants

The following beverages have the highest concentration of antioxidants: green juice, beetroot juice, pomegranate juice, acai juice, coconut water, herbal tea and coffee. According to scientific research, synthetic antioxidants such as propyl gallate, Butylated Hydroxyanisole (BHA), Butylated Hydroxytoluene (BHT), and Tertiary Butyl Hydroquinone (TBHQ) have several negative consequences.[42] They are, therefore, harmful to use around humans. Gallic acid can be a suitable candidate due to its antioxidative properties, anti-hypertensive action, and other health benefits. Gallic acid shows cardioprotective activity through its antihyperglycemic, anti-lipid peroxidative, and anti-oxidant effects.[43,44]

The role of antioxidants in human health to prevent cardiovascular diseases is discussed as follows

Cardiovascular Diseases

Cardiovascular diseases can arise from a variety of circumstances, including smoking, inadequate eating habits, stress, inactivity, elevated blood pressure, elevated cholesterol levels, diabetes, and poor nutrition.[45] The Pathogenic stimuli linked to cardiovascular diseases include oxidized Low-Density Lipoprotein (LDL), hyperglycemia, activated macrophages, and even angiotensin II.[46-49] These stimuli primarily cause harm by increasing the local synthesis of reactive oxygen species. These active metabolites can alter the usual balance between apoptosis, proliferation, and extracellular matrix formation in the walls of the heart and arteries.[50] They also cause severe endothelial dysfunction. Figure 3 illustrates that oxidative stress in cardiovascular disease and heart failure is primarily driven by the overactivation of the RAAS and SNS. This increases angiotensin II, which stimulates NOX enzymes to generate excess ROS. The resulting oxidative stress causes mitochondrial damage, hypertrophy, and cell death, leading to heart failure. This process is worsened by ageing, risk factors, and environmental stress.[51-53]

According to the literature survey, numerous herbal medicines possess anti-oxidant properties. Antioxidants actively treat ROS-mediated cardiovascular disorders. They have the power to scavenge free radicals, inhibit lipid peroxidation, reduce platelet aggregations, inhibit vascular inflammation, inhibit the oxidation of LDL and reduce ROS generation.[54,55] Natural sources of polyphenols possess anti-oxidant properties and help promote good health.[56,57] Cardiovascular disease can be actively treated with antioxidative drugs derived from natural sources. Resveratrol, for example, is a naturally occurring polyphenolic molecule that helps prevent oxidative damage in cardiovascular disease. The use of anti-oxidant drugs can actively benefit

the prevention and management of hypertension.[58-60] Drug combinations are not a new phenomenon in the pharmaceutical industry. Combining antioxidants with cardiovascular medications amplifies the effects of the medications by enhancing their enzymatic action, scavenging internally produced free radicals, and creating a synergistic impact that leads to better therapy against cardiovascular diseases.[61,62]

Benefits of Antioxidant Treatment

Pharmacologically active anti-oxidants include lycopene, ellagic acid, quercetin, epigallocatechin 3-O-gallate, genistein, SOD

Table 1: Explores the mechanisms by which natural and synthetic antioxidants exert cardioprotective effects in the management of myocardial infarction and atherosclerosis, with evidence derived from various experimental animal models.

Anti-oxidant Type	Source/Drug Class	Cardiovascular Condition	Experimental Model	Mechanism of Action	Key Outcomes	Reference No.
Gallic acid (Natural polyphenol)	Plant phenolic acid	MI, Atherosclerosis	H9c2 cardiomyocytes, ISO-induced MI rats, ApoE -/- mice	Scavenges ROS; inhibits lipid peroxidation; suppresses NF-κB and MAPK signalling; improves endothelial NO bioavailability	Reduced infarct size; decreased LDL oxidation; improved cardiac anti-oxidant enzymes	25
Resveratrol (Natural stilbene)	Grapes, red wine	MI, Atherosclerosis	Ischemia–reperfusion (I/R) rat model; ApoE -/- mice	Activates SIRT1–AMPK pathway; inhibits NADPH oxidase; enhances e NOS activity	Cardio protection; reduced plaque formation improved vascular function	26
Quercetin (Natural flavonoid)	Fruits and vegetables	MI, Atherosclerosis	ISO-induced MI rats; endothelial cell lines	ROS scavenging; inhibits LOX-1 mediated ox-LDL uptake; anti-inflammatory	Reduced myocardial necrosis; decreased foam cell formation	27
Curcumin (Natural polyphenol)	Turmeric	MI, Atherosclerosis	I/R injury rats; high-fat diet mice	Inhibits NF-κB and NLRP3 inflammasome; reduces mitochondrial oxidative stress	Attenuated myocardial apoptosis; reduced atherosclerotic lesions	28
Catechins (EGCG) (Natural flavanol)	Green Tea	Atherosclerosis	ApoE -/- mice; macrophage models	Prevents LDL oxidation; downregulates scavenger receptors; anti-oxidant gene upregulation	Reduced plaque progression; improved lipid profile	29
Ascorbic acid (Vitamin C) (Natural anti-oxidant)	Dietary Vitamin	N-Acetylcysteine (Synthetic)	Clinical supplementation studies; animal MI models	Direct ROS neutralization; regenerates vitamin E; improves endothelial function	Reduced oxidative stress markers; improved vascular reactivity	30
α-Tocopherol (Vitamin E) (Natural anti-oxidant)	Fat-soluble vitamin	Atherosclerosis	LDL oxidation assays; clinical trials	Inhibits lipid peroxidation; stabilizes cell membranes	Reduced LDL oxidation; mixed clinical outcomes	31
N-Acetylcysteine (Synthetic)	Thiol Anti-oxidant	MI, Atherosclerosis	I/R injury rats; endothelial cells	Glutathione precursor; scavenges free radicals; reduces oxidative endothelial injury	Reduced myocardial damage; improved endothelial redox balance	32

Anti-oxidant Type	Source/Drug Class	Cardiovascular Condition	Experimental Model	Mechanism of Action	Key Outcomes	Reference No.
Coenzyme Q10 (Synthetic anti-oxidant)	Mitochondrial electron carrier	MI, Heart failure	I/R injury models; clinical trials	Improves mitochondrial function; inhibits ROS generation	Improved cardiac energy metabolism; reduced infarct damage	33
Probucol (Synthetic lipid-lowering anti-oxidant)	Phenolic drug	Atherosclerosis	Rabbit and mouse models	Inhibits LDL oxidation; reduces foam cell formation	Reduced plaque progression despite lowering HDL	34
Edaravone (Synthetic free-radical scavenger)	Neuroprotective agent	MI	I/R injury rat models	Scavenges hydroxyl radicals; reduces lipid peroxidation	Reduced infarct size; improved cardiac function	35
Tempol (Synthetic SOD mimetic)	Nitroxide radical	MI, Atherosclerosis	Hypertensive and I/R models	Mimics superoxide dismutase; reduces superoxide burden	Improved myocardial recovery; reduced vascular oxidative stress	36
MitoQ (Synthetic)	Synthetic Derivative of CoQ10	MI, Atherosclerosis	Aged mice, MI-reperfusion models.	Mitochondria-targeted ubiquinone; prevents mtDNA damage.	Reduces mitochondrial ROS-induced endothelial dysfunction.	37
Allopurinol (Synthetic)	Purine Analog	MI, Atherosclerosis	Balloon-injury models; Rabbit models.	Xanthine Oxidase (XO) inhibitor (Repurposed).	Reduces ROS-driven pathological ventricular remodelling.	38

(superoxide dismutase), coenzyme Q10, vitamin E, and vitamin C. Antioxidants serve as preventative and treatments for oxidative stress-related illnesses. Innovative medication delivery methods enhance the effectiveness of antioxidants. *In vitro* research reveals that lycopene, a fundamental chemical component of tomatoes, possesses potent anti-oxidant potential.[63-65] It helps shield humans from cardiovascular disease and prostate cancer. Foods high in polyphenolic substances may lower Cardio-Metabolic Syndrome Risk Factors (CMSRF) by enhancing vascular health, reducing insulin resistance, lowering cholesterol, controlling inflammation, and improving endothelial function.[66-70] An imbalance between ROS and anti-oxidant molecules may be the cause.[71]

Literature supporting data regarding Antioxidant benefits in CVDs

Pharmacologically active anti-oxidants include lycopene, ellagic acid, quercetin, epigallocatechin 3-O-gallate, genistein, SOD (superoxide dismutase), coenzyme Q10, vitamin E, and vitamin C. Antioxidants serve as preventative and treatments for oxidative stress-related illnesses. Innovative medication delivery methods enhance the effectiveness of antioxidants. *In-vitro* research reveals that lycopene, a fundamental chemical component of tomatoes, possesses potent anti-oxidant potential.[71] It helps to shield humans from cardiovascular. Lycopene's anti-oxidant properties are most likely responsible for this. Ellagic acid protects rat mitochondria against the myocardial damage caused by β-adrenergic agonists. Ellagic acid works by chelating metals and scavenging free radicals, as demonstrated by in vitro experiments.[72] Numerous *In vitro, In vivo*, and physical methods have conclusively demonstrated the anti-oxidant qualities of catechin.[73]

Role of Antioxidants in Cardiovascular Disease Management

Numerous scholarly works have proposed that eating foods high in antioxidants, particularly those with anti-oxidant properties, may reduce the risk of stroke and cardiovascular disease. Oxidative functions also favorably impact cell health by their involvement in energy metabolism, cellular signaling, detoxification, and biosynthesis. To preserve health, pro-oxidants and anti-oxidant defense mechanisms must be in balance. Recent reports warn that synthetic antioxidants pose a risk to human health, and therefore, researchers recommend employing antioxidants derived from natural sources for medical purposes.[74]

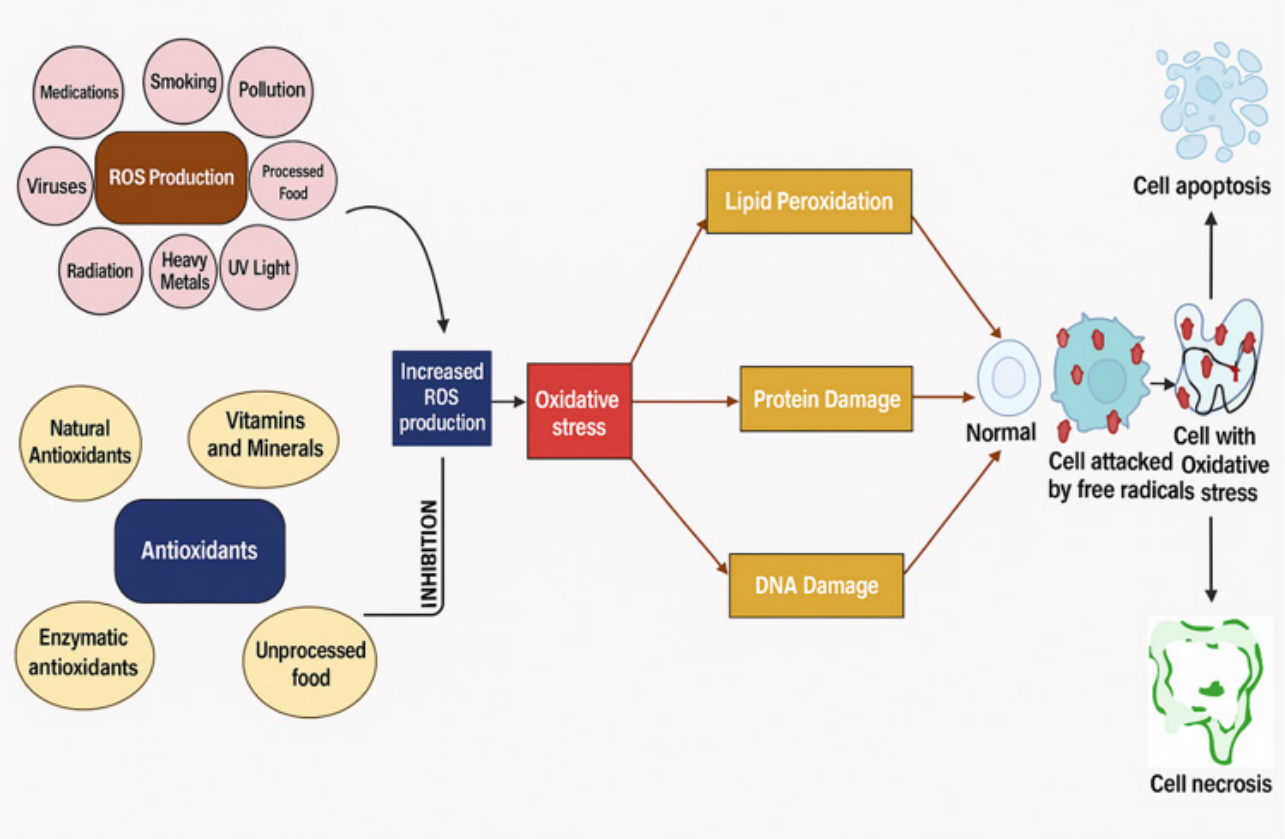

Figure 1: Role of ROS and Antioxidants in Oxidative Stress-Mediated Cellular Damage. Shows that oxidative stress promotes CVD via endothelial dysfunction, inflammation, and vascular injury, while antioxidants counteract these effects by scavenging ROS and restoring redox balance.

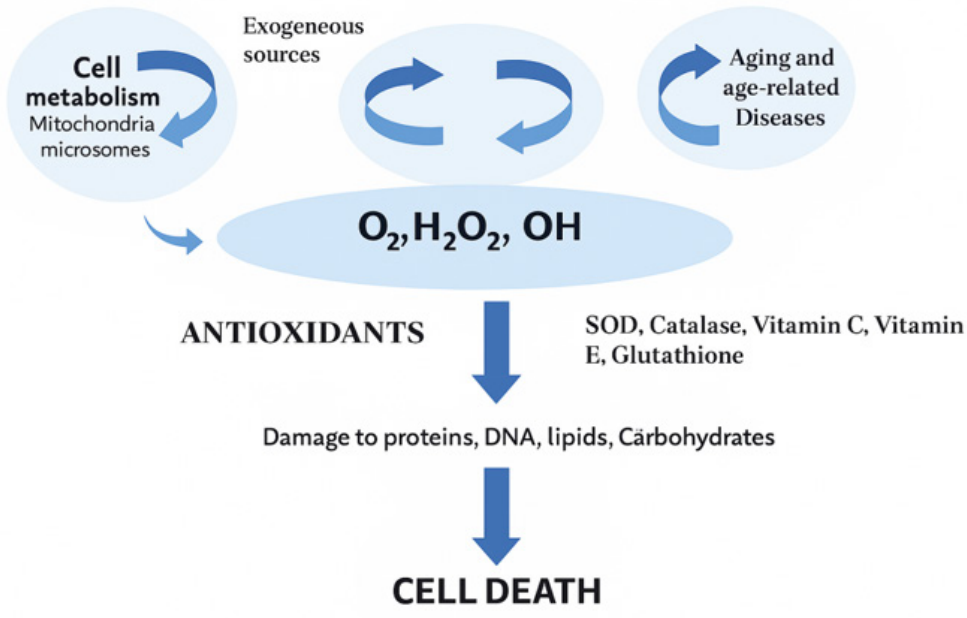

Figure 2: The Mechanism of Oxidative Stress and Cellular Damage. The figure depicts oxidative stress resulting from metabolic, environmental, and aging-related sources that generate ROS, which are neutralized by enzymatic and non-enzymatic antioxidants.

In vivo Antioxidants Model in Treatment of Cardiovascular Diseases

More than twelve investigations on antioxidants and atherosclerosis in animals have been carried out, with the majority reporting favorable outcomes. Probucol is a lipid-lowering drug with vigorous anti-oxidant activity; eight studies utilizing different animal models have shown reduced formation of atherosclerotic lesions.[75] Nevertheless, until recently, it was impossible to determine whether the effects of probucol were due to its anti-oxidant activity, lipid-lowering effects, or a combination of the two. The lipid-lowering effect of probucol was investigated in a recent study using hyperlipidemic rabbits, which also evaluated lovastatin, a lipid-lowering medication with no known anti-oxidant activity. The percentage of the aorta's surface area occupied by early atherosclerotic lesions in each therapy group served as the trial's endpoint. Lipid-lowering in the lovastatin and probucol groups of this experiment was comparable.[61] The data show that the probucol group's anti-oxidant properties actively prevented atherosclerosis, as evidenced by the significantly higher decrease in aortic atherosclerotic lesions compared to the untreated group and the lovastatin group, which received equal lipid-lowering treatment. Aortic atherosclerotic lesions were 25% less common in hypercholesterolemic mongrel rabbits.[76]

DISCUSSION

Based on the literature, we found that certain antioxidants have a significant impact on the treatment of cardiovascular disease. They significantly lower the likelihood of cardiovascular danger. They are effective against various ROS-mediated illnesses in addition to cardiovascular disease. A critical analysis of past clinical failures reveals that the lack of efficacy was rarely due to the anti-oxidant's chemistry, but rather to Pharmacokinetic (PK) and targeting limitations. "Old" antioxidants, such as generic Vitamin E or Beta-carotene, were often administered without regard for their poor bioavailability or their inability to accumulate at specific sites of ROS generation. Precision Targeting: Unlike untargeted supplements, repurposed molecules like MitoQ utilize lipophilic cations to concentrate specifically within the mitochondrial matrix, neutralizing ROS at the source during reperfusion. Overcoming PK Barriers: Repurposed drugs like Allopurinol or N-acetylcysteine benefit from well-documented pharmacokinetic profiles, allowing clinicians to optimize dosing for vascular delivery. Systemic Redox Reset: Modern strategies move beyond "scavenging" and instead use repurposed drugs to inhibit upstream enzymes (e.g., SGLT2 inhibitors dampening NOX activity). This "resetting" of the redox state is more effective than attempting to mop up ROS after the damage has already been initiated.

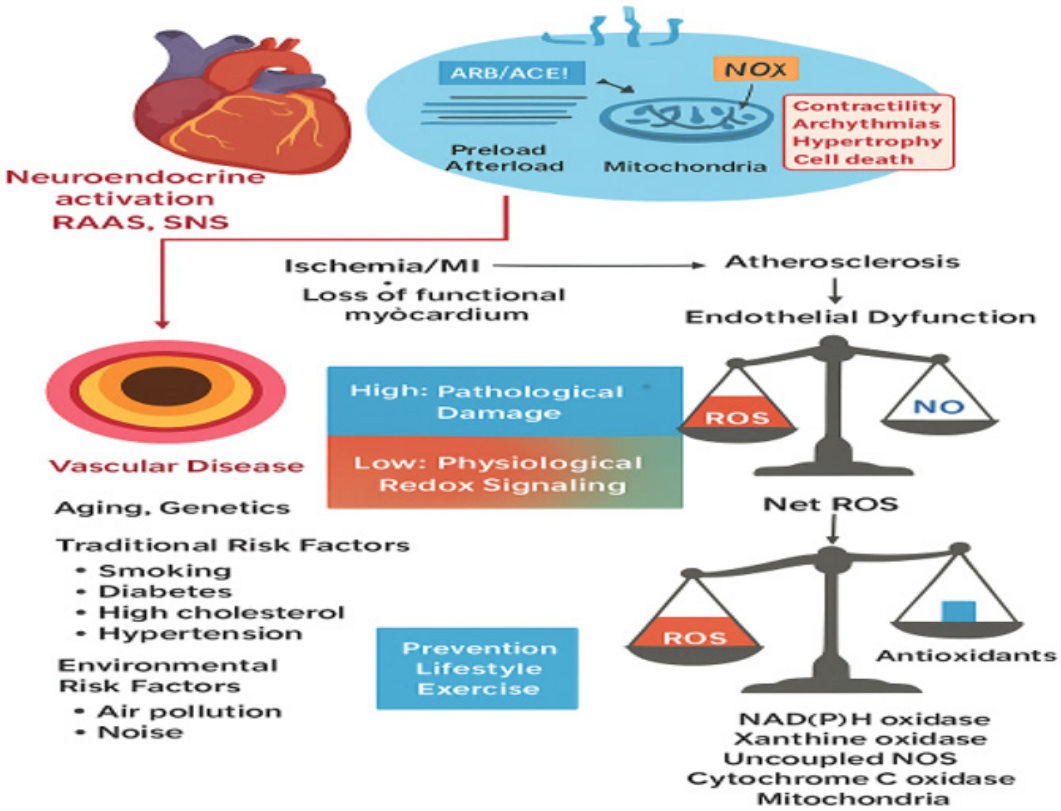

Figure 3: Oxidative Stress in Cardiovascular Pathophysiology. The figure illustrates how oxidative stress drives CVDs and heart failure via RAAS/SNS overactivation, angiotensin II–mediated ROS generation, mitochondrial damage, and vascular dysfunction, ultimately leading to cardiac hypertrophy and cell death.

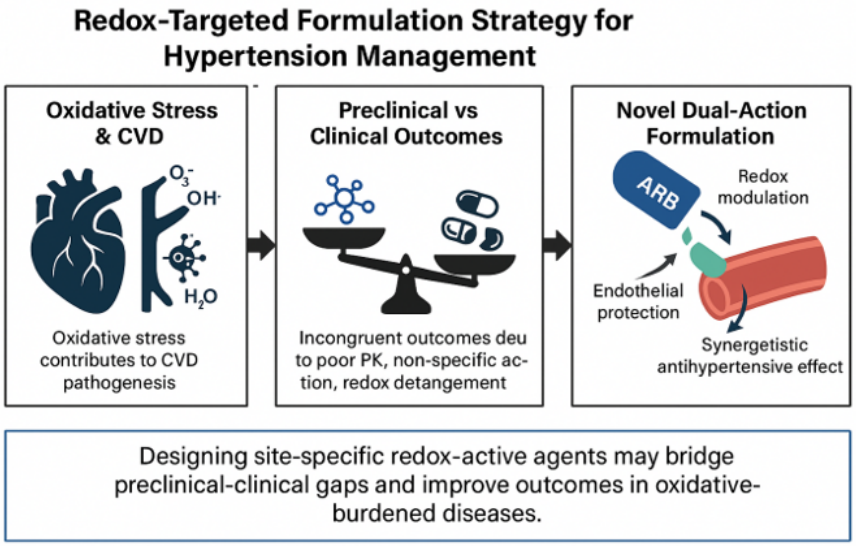

Figure 4: Redox-targeted formulation strategy for the management of hypertension. It helps to design site-specific redox-active agents that may help to bridge preclinical and clinical trial gaps for future research through this wide topic.

CONCLUSION

Studies have shown that antioxidative medications have antihypertensive properties; however, scientists have yet to develop an effective formulation. Numerous antihypertensive medications have been created and recommended by medical professionals. Reactive Oxygen Species (ROS), generated during excessive oxidative stress, are responsible for the pathophysiology of various cardiovascular disorders, including atherosclerosis, cardiac hypertrophy, cardiomyopathy, heart failure, ventricular remodeling, ischemia/reperfusion injury and myocardial infarction. Numerous antioxidants have demonstrated preventive and therapeutic benefits in various forms of cardiovascular disease, including CoQ10, beta-carotene, lycopene, quercetin, vitamin C, and vitamin E. Nevertheless, several antioxidants have weak biological qualities and inconsistent pharmacokinetics, restricting their application as medicinal agents. Therefore, the current situation requires the administration of stable anti-oxidants at the site of action (Figure 4). Numerous cutting-edge carrier-based strategies have demonstrated significant advantages for the systemic and site-specific administration of antioxidants in treating and preventing various cardiovascular diseases. Investigators have examined the effects of multiple dietary and naturally occurring bioactive antioxidants, including polyphenols, ubiquinol-10 proteins, β-carotene, carotenoids, uric acid, bilirubin, and vitamin C, in animal models, cell culture, and clinical trials, and have elucidated their mechanistic role in CVD prevention and treatment.

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ABBREVIATIONS

ROS: Reactive Oxygen Species; **DNA:** Deoxyribonucleic Acid; **LDL:** Low-Density Lipoprotein; **ATP:** Adenosine Triphosphate; **RNS:** Reactive Nitrogen Species; **NADPH:** Nicotinamide Adenine Dinucleotide Phosphate Hydrogen; **CVD:** Cardiovascular Disease; **IHD:** Ischemic Heart Disease; **SOD:** Superoxide Dismutase; **BHA:** Butylated Hydroxyanisole; **BHT:** Butylated Hydroxytoluene; **TBHQ:** Tertiary Butyl Hydroquinone; **RAAS:** Renin Angiotensin Aldosterone System; **SNS:** Sympathetic Nervous System; **CMSRF:** Cardio Metabolic Syndrome Risk Factors; **AT1 Receptor:** Angiotensin II Type 1 Receptor.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUMMARY

The growing body of evidence connecting oxidative stress to the etiology and development of Cardiovascular Disease (CVD) was the driving force behind this review. Clinically, outcomes have often been incongruous or indeterminate, despite clear anti-oxidant activity demonstrated in many preclinical models. This discrepancy highlights the need to investigate the functions of antioxidants as modulators of redox-sensitive signaling pathways, endothelial function, and vascular remodeling, rather than confining them to the simplistic concept of removing free radicals. The review highlights the importance of pharmacokinetic limitations, poor targeting, and redox derangement in contributing to drug failures. Future planning should focus on the connection between oxidative stress and several heart conditions. Lastly, it will concentrate on how oxidative stress affects cardiovascular disorders clinically. This rationale aligns with my current research, which aims to develop a new formulation combining an anti-oxidant and an angiotensin II receptor blocker. The aim is to enhance therapeutic outcomes by using both antihypertensive and antioxidative mechanisms. We have also prepared the docking of receptor proteins with various antioxidants.

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