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Dietary Antioxidants in Human Physiology and Pathogenesis: Molecular Pathways, Therapeutic Applications, and Clinical Translational Challenges in Redox-Based Interventions for Chronic Disease Management

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Abstract

The "antioxidant" buzzword has infested public health literature, more often than not with huff and hyperbole. This review surpasses broad-brush claims to present a critical appraisal of the fine chemical mechanisms underlying the activity of key dietary antioxidants: vitamins C and E, the glutathione system, and polyphenols. We begin by outlining their targets and the reactive oxygen species (ROS) they assail, emphasizing their unique redox chemistry, including hydrogen atom transfer (HAT) and single electron transfer (SET) activity. The review then evaluates the multifaceted roles these compounds play in combating oxidative stress within the pathophysiological context of atherosclerosis and liver disease, two diseases wherein oxidative damage is a major driving force. We synthesize 2020-2024 new in vitro, animal, and human evidence, emphasizing conditions under which antioxidant interventions work and where they have failed. Close examination reveals that the biological effectiveness of antioxidants is not solely a function of concentration but is increasingly modulated by their bioavailability, the cell redox state, and by their complex interaction with cellular signaling. The conclusion stresses that a comprehensive, mechanism-centered comprehension is needed to tailor effective nutritional and therapeutic interventions, moving beyond the reductionist notion of antioxidants as an overall panacea and towards their targeted application in precision nutrition and medicine.

Keywords: Antioxidants, Oxidative Stress, Redox Chemistry, Vitamin C, Vitamin E, Glutathione, Polyphenols, Atherosclerosis, Liver Disease.

1. Introduction

Oxidative stress, as an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses, is a key factor in the pathogenesis of a wide variety of diseases, including cancer, neurodegenerative diseases, cardiovascular disease, and metabolic disease (Sies, 2020). ROS such as superoxide anion ($O_2^{\bullet -}$), hydrogen peroxide (H_2O_2), and the very reactive hydroxyl radical ($^{\bullet}OH$) are unavoidable byproducts of aerobic metabolism but are also generated as a response to exogenous insults (Drejza et al., 2022). At low or moderate levels, ROS serve as crucial signaling molecules in redox biology phenomena; however, at elevated levels, they inflict damage on lipids, proteins, and DNA, leading to cell death and malfunction (Forman & Zhang, 2021).

The human organism has developed a very sophisticated, multi-layered system of antioxidant protection in order to maintain redox homeostasis. This system consists of endogenous enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase, as well as an enormous range of exogenous, diet-derived compounds known collectively as dietary antioxidants (Pizzino et al., 2017). It is to this latter category—vitamins C and E, the tripeptide glutathione (and its precursors), and the vast polyphenol family of plant compounds—that the public has attached itself and driven a vast nutraceutical industry (Turcov et al., 2023). However, the narrative regarding these compounds is often oversimplified into a panacea for aging and disease. This review seeks to debunk this hype by providing a critical, chemistry-based appraisal.

The primary aim of this review is to detail the specific chemical mode of action of important dietary antioxidants beyond their general classification and into their specific redox processes, kinetics, and interactions. We will in particular focus on vitamins C and E, the glutathione pathway, and dietary polyphenols, tracing out their common dietary sources and their individual roles within the antioxidant panel. This mechanistic foundation will then be employed to discuss at length their involvement in two relevant oxidative stress-related pathologies: atherosclerosis and liver disease. By synthesizing the most current evidence between 2020 and 2024, the review will critically examine the conditions under which antioxidant supplementation is effective clinically, and most crucially, where it has not worked, reporting a balanced view that is critical to advancing both scientific understanding and public health guidance.

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The Chemical Foundations of Antioxidant Activity

To be able to appreciate the biological role of antioxidants, one must first grasp their chemistry. Antioxidants basically function to donate electrons to neutralize and stabilize ROS without becoming radicals themselves or through the cleavage of reactive species. The primary mechanisms are Hydrogen Atom Transfer (HAT), Single Electron Transfer (SET), and metal chelation (Liang & Kitts, 2015; Singh et al., 2023).

Defining Antioxidant Mechanisms: HAT, SET, and Metal Chelation

HAT is the direct transfer of a hydrogen atom from an antioxidant (ArOH) to a radical (R•), which quenches it: ArOH + R• → ArO• + RH. The ability of an antioxidant to donate a hydrogen atom is quantified by its Bond Dissociation Enthalpy (BDE); the lower the BDE, the better the HAT antioxidant. This mechanism is particularly relevant in lipid media, where antioxidants like vitamin E form complexes with lipid peroxyl radicals (LOO•), effectively stopping the continuation of lipid peroxidation (Shahidi et al., 2023; Christodoulou et al., 2022).

Alternatively, the SET process involves one electron transfer from the antioxidant to the oxidant: ArOH → $ArOH^{\bullet+}$ + e^- followed by $ArOH^{\bullet+}$ + R• → ArO• + RH. Its tendency is governed by the antioxidant's ionization potential. The majority of antioxidants, especially polyphenols, under water-like environments, operate via SET (Liang & Kitts, 2015; Wang et al., 2022). Interestingly, the relative contribution of HAT to SET with regard to each other depends on the antioxidant structure and the surrounding environment (pH, solvent).

A third critical mechanism independent of radical quenching is metal chelation. Transition metals like iron (Fe^{2+}) and copper (Cu^+) can catalyze the formation of the highly reactive •OH radical from H_2O_2 via the Fenton reaction. The majority of polyphenols, for instance, within green tea and curcumin, contain functional groups (e.g., catechol or β-diketone moieties) capable of chelating these metal ions and rendering them redox-inert, thus preventing •OH generation (Munteanu & Apetrei, 2021). Figure 1 illustrates the three core antioxidant mechanisms.

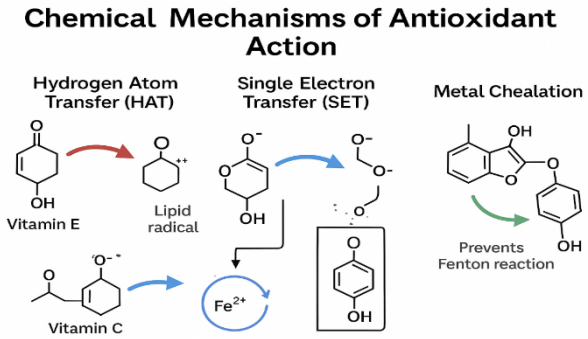

Figure 1: Chemical Mechanisms of Antioxidant Action (HAT, SET, and Metal Chelation)

The Antioxidant Network and Regeneration

A second concept greatly underappreciated in the world of popular science is that antioxidants don't work alone but as a network. A nice example is the synergism between vitamin E and vitamin C. Vitamin E, the lipid-soluble antioxidant found within cell membranes, annihilates a lipid peroxyl radical and is transformed into a tocopheryl radical in the process. This tocopheryl radical is then recycled back to active vitamin E by vitamin C (ascorbate) within the aqueous phase at the membrane interface. The formed ascorbyl radical is quite stable and is recyclable back to ascorbate by enzymes with glutathione (GSH) or NADPH utilized as a reductant (Traber & Stevens, 2011). Such a cascade shows how a network of antioxidants with different solubilities and positions provides comprehensive cellular protection. Failure of this regeneration system can lead to a pro-oxidant effect, where the antioxidant radical itself is the cause of oxidative damage.

Principal Dietary Antioxidants: Sources and Mode of Action

The efficacy of dietary antioxidants is largely regulated by their chemical makeup, as this dictates their solubility, reactivity, and mechanism of action. An understanding of these nuances is necessary to appreciate fully their distinct functions in the antioxidant system of the body.

Vitamin C (Ascorbic Acid)

Vitamin C or ascorbic acid is a typical water-soluble antioxidant with high content in citrus fruits (oranges, lemons), berries (strawberries, acerola), kiwi, bell peppers, broccoli, and tomatoes. Its main chemical mechanism is Single Electron Transfer (SET) by which it donates a single electron to neutralize a wide variety of reactive oxygen and nitrogen species, including the hydroxyl radical (•OH), superoxide anion ($O_2^{\bullet-}$), and peroxynitrite ($ONOO^-$). This one-electron oxidation yields the ascorbyl radical ($Asc^{\bullet-}$), a very stable and low-reactivity species that terminates radical chain reactions very efficiently (Carr & Lykkesfeldt, 2023). In addition to its direct scavenging activity, vitamin C's huge reducing capacity also allows it to be a prominent regenerator of other antioxidants. It is particularly significant in its ability to reduce the tocopheryl radical to active vitamin E at the lipid-water interface, which is a necessary synergistic interaction. Further, ascorbate is an essential cofactor for metalloenzymes involved in routine physiological activities, such as the formation of collagen and the production of neurotransmitters.

Vitamin E (Tocopherols and Tocotrienols)

Vitamin E is not a single compound or eight distinct compounds but a complex of eight lipid-soluble compounds, such as tocopherols and tocotrienols, among which the most biologically active compound is α-tocopherol. Its principal dietary sources include vegetable oils (olive oil, sunflower, wheat germ), nuts (hazelnuts, almonds), seeds, and green vegetables. Because it is the preeminent chain-breaking antioxidant in lipid environments, vitamin E is positioned in cell membranes and

lipoproteins in a strategic manner. Its mechanism of action is primarily Hydrogen Atom Transfer (HAT), whereby it donates a phenolic hydrogen from its chromanol ring to a peroxyl radical lipid (LOO•), forming a more stable lipid hydroperoxide (LOOH) and a tocopheryl radical. The phytyl tail is responsible for anchoring the molecule within the lipid bilayer (Doudin & Al-Malaika, 2016). The generated tocopheryl radical is very unreactive but must be regenerated once more to active α-tocopherol in order to prevent it from sustaining additional oxidative damage. This reduction is carried out quite effectively by vitamin C (ascorbate) or other reductants, showing the dependency of the antioxidant system.

The Glutathione System

Glutathione (GSH; γ-glutamyl-cysteinyl-glycine) is the most prevalent non-enzymic antioxidant within cells. Because glutathione per se is poorly absorbed from the diet, attention is placed on the consumption of precursors that provide its constituent amino acids. Primary dietary sources include sulfur foods (garlic, onion, cruciferous vegetables like broccoli and Brussels sprouts), lean protein (which provides cysteine, glycine, and glutamate), and whey protein. The chemical reactivity of glutathione concerns the thiol (-SH) group of its cysteine residue. It might be a direct free radical scavenger by HAT, but its most critical activities are enzymic. The seleno-enzyme glutathione peroxidase (GPx) uses the co-substrate GSH to convert hydrogen peroxide (H_2O_2) and lipid hydroperoxides (LOOH) into water and harmless alcohols, respectively, generating oxidized glutathione (GSSG) in the process. GSSG is then recycled back to GSH with high efficiency by glutathione reductase (GR) enzyme, which is an NADPH-dependent electron donor (Forman & Zhang, 2021). The GSH/GSSG ratio is also the major biomarker of cellular redox balance. GSH is also required for the detoxification of electrophilic agents and xenobiotics via conjugation reactions catalyzed by glutathione S-transferases (GSTs).

Dietary Polyphenols

Dietary polyphenols represent a chemically extremely heterogeneous and large class of substances in an extremely wide range of plant foods, including fruits (berries, apples), vegetables (spinach, artichokes), tea (especially green tea), coffee, red wine (moderate intakes), dark chocolate, herbs (e.g., oregano, turmeric), and spices. Their chemical activity is extremely complex and structure-dependent. They may function directly as antioxidants through HAT or SET, depending on the number and the position of phenolic hydroxyl groups. Flavonoids having catechol-like quercetin are very good metal chelators and scavengers of radicals (Munteanu & Apetrei, 2021). But a significant paradigm shift in recent years has shown that the in vivo concentrations of most polyphenols are not sufficient to exert important direct antioxidant effects. Instead, their primary health contributions are now largely because they act as indirect antioxidants. They have the ability to initiate important cellular signaling pathways, most notably the Keap1-Nrf2 pathway.

Under oxidative stress, some polyphenols can induce the release of the transcription factor Nrf2 from its inhibitor Keap1, which allows Nrf2 to migrate into the nucleus and induce the transcription of a large number of cytoprotective genes. These genes code for critical endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), and glutathione S-transferases (GSTs) (Tebay et al., 2015). This "preconditioning" or hormetic effect strongly upregulates the native defense processes of the body, a highly advanced, long-term adaptive reaction to oxidative injury (Table 1). Figure 2 shows the antioxidant network and regeneration pathway.

Table 1: Summary of Key Antioxidants, Their Mechanisms, and Dietary Sources

Antioxidant	Solubility	Primary Mechanism(s)	Key Dietary Sources
Vitamin C	Water-soluble	Single Electron Transfer (SET), Regeneration of Vitamin E	Citrus fruits, berries, kiwi, bell peppers, broccoli
Vitamin E	Lipid-soluble	Hydrogen Atom Transfer (HAT) in lipid membranes	Vegetable oils, nuts, seeds, green leafy vegetables
Glutathione	Water-soluble	Enzyme cofactor (for GPx), Direct scavenging, Conjugation	Precursors in sulfur-rich veggies, lean protein, and whey
Polyphenols	Varied	HAT, SET, Metal Chelation, Indirect activation of Nrf2	Tea, coffee, berries, dark chocolate, herbs, spices

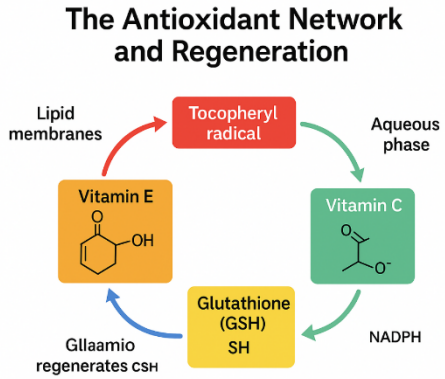

Figure 2: The Antioxidant Network and Regeneration Pathway.

Antioxidants in the Pathogenesis and Management of Chronic Disease

The role of oxidative stress in causing chronic disease is firmly entrenched, and the therapeutic potential of antioxidants has been extensively studied in this context. Their efficacy, however, is highly dependent on the specific pathology and involved mechanisms.

Atherosclerosis: Protection against Oxidation of Vasculature

Atherosclerosis, the chronic inflammatory atherogenesis that causes most cardiovascular disease, is heavily dependent upon oxidative stress in the arterial wall. One of the precipitating factors is the oxidation of low-density lipoprotein (LDL) (Zhuravlyova et al., 2021). Although native LDL is innocuous, when it becomes trapped in the subendothelial space, it becomes vulnerable to endothelial cell, smooth muscle cell, and macrophage-derived reactive oxygen species (ROS) modification. This ox-LDL is an active pro-inflammatory species that is internalized by macrophages via receptors like CD36, leading to the aberrant ingestion of cholesterol and formation of lipid-loaded foam cells—the feature of early atherosclerotic lesions (Poznyak et al., 2022). Ox-LDL also induces endothelial dysfunction by inhibiting the bioavailability of nitric oxide (NO•), a potent vasodilator (Nauryzbaevish et al., 2023).

The mechanistic argument for single antioxidants in preventing this process is compelling, but clinical outcomes have been variable. Vitamin E, the primary lipid-soluble antioxidant, was the obvious choice to try for inhibiting the oxidation of LDL itself. Preclinical studies all consistently indicated that supplementing LDL particles with α-tocopherol makes them more resistant to oxidation (Gamna & Spriano, 2021). Large-scale trials in humans like HOPE and GISSI, however, largely failed to show cardiovascular benefit. This divergence can be explained by the isolated administration of synthetic α-tocopherol that is able to displace other beneficial tocopherols like γ-tocopherol, and the inability to address patient subgroups with higher baseline oxidative stress (Huang et al., 2020).

Vitamin C has another but complementary role. Its contribution to atherosclerosis is not only due to its ability to recycle vitamin E but to its critical function in safeguarding endothelial NO•. By direct scavenging of superoxide radicals that otherwise suppress NO•, vitamin C preserves endothelium-dependent vasodilation (Lykkesfeldt & Tveden-Nyborg, 2019). While epidemiological data firmly associate high dietary vitamin C intakes with reduced cardiovascular risk, interventional trials have yielded inconsistent results, perhaps due to short supplementation periods or excellent baseline health status of the volunteers. Polyphenols, such as quercetin and epigallocatechin-3-gallate (EGCG) from green tea, exert multi-faceted anti-atherogenic activities. They not only prevent LDL oxidation but also dampen vascular inflammation by preventing the NF-κB signaling pathway and increasing endothelial function through PI3K/Akt activation, which indirectly stimulates endothelial nitric oxide synthase (eNOS) (Newcomer et al., 2012; Oliveira et al., 2020). The available evidence for polyphenols supports a food pattern over an individual supplement for optimal cardiovascular health.

Liver Disease: Combat Hepatic Oxidative Insult

The central metabolism organ, the liver, is particularly sensitive to oxidative damage, one of the predominant pathological mechanisms in Non-Alcoholic Fatty Liver Disease (NAFLD) and Alcoholic Liver Disease (ALD). In NAFLD, the initial accumulation of fat in the liver (steatosis) renders the organ vulnerable to oxidative damage. Mitochondrial and cytochrome P450 enzyme-catalyzed oxidation of fatty acids in excess yields reactive aldehydes like 4-hydroxynonenal (4-HNE) and malondialdehyde (MDA) (Arumugam et al., 2023). Toxin byproducts with proteins form adducts that increase hepatocyte injury, cause inflammation (resulting in steatohepatitis, or NASH), and activate hepatic stellate cells, thereby inducing fibrosis (Loureiro et al., 2023). In ALD, alcohol metabolism by mechanisms involving alcohol dehydrogenase and CYP2E1 produces acetaldehyde and ROS directly and simultaneously reduces hepatic glutathione (GSH), with resulting concurrent cascade of damage, inflammation, and fibrogenesis.

Table 2: Antioxidant Actions in Specific Disease Pathologies

Disease	Key Oxidative Event	Antioxidant	Proposed Mechanism of Action	Clinical Evidence Summary
Atherosclerosis	LDL Oxidation, Endothelial Dysfunction	**Vitamin E**	Incorporation into LDL prevents lipid peroxidation	Large trials largely negative; potential benefit in high-risk subgroups.
		Vitamin C	Regenerates Vitamin E, protects NO• bioavailability	Epidemiological support is strong; interventional trials are mixed.
		Polyphenols (e.g., Quercetin)	Reduces LDL oxidation, anti-inflammatory, and improves endothelial function	Strong preclinical data: human evidence supports food consumption over supplements.
Liver Disease (NAFLD/NASH)	Lipid Peroxidation, GSH Depletion	**Vitamin E**	Chain-breaking antioxidant in hepatic lipids reduces inflammation	PIVENS trial: Effective for non-diabetic NASH. A recommended therapy.
		Glutathione (NAC)	Replenishes hepatic GSH, detoxifies reactive aldehydes	Effective for acetaminophen toxicity; evidence for NAFLD/ALD is promising but less definitive.
		Polyphenols (e.g., Silymarin)	Nrf2 activation, anti-fibrotic, anti-inflammatory	Preclinical data are strong; clinical studies show modest improvements in liver enzymes.

Antioxidants have proven targeted efficacy for the treatment of these liver disorders. Hepatic detoxification is based on the glutathione system. Hepatic GSH depletion defines both ALD and NASH. While N-acetylcysteine (NAC), a GSH precursor, is a standard treatment for acetaminophen poisoning, its application in ALD and NASH has been encouraging in preclinical and some clinical trials by inhibiting lipid peroxidation and preserving mitochondrial function (Cichoz-Lach & Michalak, 2014; Michalak et al., 2021). Vitamin E has defined clinical efficacy in a specific patient group. The landmark PIVENS trial demonstrated that high-dose α-tocopherol (800 IU/day) significantly improves steatohepatitis in non-diabetic patients with NASH, making it one of the very few pharmacologically indicated therapies for this group (Sanyal et al., 2023). They are believed to act by direct inhibition of liver lipid peroxidation chains and thereby reduce oxidative stress-dependent inflammation and fibrogenesis. Polyphenols also hold enormous promise. Silymarin, which is a milk thistle flavonoid complex, has long been employed in the treatment of liver disease due to its antifibrotic, anti-inflammatory, and antioxidant action, partly mediated through the Nrf2 pathway (Dallio et al., 2021). Curcumin, which is an active component of turmeric, and EGCG, which is an active component of green tea, were also effective in models of NAFLD as they reduced hepatic fat, oxidative stress, and inflammation (Cossiga et al., 2022). One of the most significant barriers in bridging these promising preclinical results for polyphenols to reproducible clinical advantages is their poor overall bioavailability (Table 2).

Critical Appraisal and the "Antioxidant Paradox"

The initial enthusiasm for high-dose antioxidant supplementation, founded on compelling mechanistic biology and encouraging epidemiologic correlations, has been considerably tempered by a sequence of large, randomized controlled trials that have consistently reported null or even adverse health outcomes (Buentzel et al., 2022). This profound disparity between preclinical evidence and clinical efficacy is often referred to as the "antioxidant paradox." One such traditional example is the Selenium and Vitamin E Cancer Prevention Trial (SELECT), which reported a statistically significant risk increase in prostate cancer among healthy men taking vitamin E and selenium supplements, in the opposite direction of the hypothesized protective effect (Klein et al., 2011). This paradox demands a careful re-evaluation of the reductionist "the more, the better" approach to antioxidant intervention and highlights the multifaceted nature of redox biology in vivo.

Several good explanations have emerged to resolve this paradox. The first is the biphasic hormetic effects theory. Many antioxidants, particularly polyphenols, are not linear. They are weak stressors at low, dietarily significant doses, causing adaptive health-promoting responses, e.g., the activation of endogenous antioxidant enzymes by the Nrf2 pathway. However, at supraphysiological doses often used in supplements, this hormetic effect is abolished, and the substances become pro-oxidant or inhibit the very signal cascades they otherwise stimulate (Calabrese et al., 2012; Haque et al., 2023). Second, and most significant, is interference with redox signaling at its most basic level. Reactive oxygen species are not merely toxic breakdown products; they are significant second messengers within numerous cellular processes, including immune defense, cell growth, and autophagy.

Non-specific, high-dose scavenging of ROS by exogenous antioxidants can silence these significant cascades of signals. For instance, it can undermine the body's ability to remove precancerous cells via apoptosis, restrict immune cell action, and disrupt the adaptive defensive reactions to physical training and thereby negate one of the most significant benefits of good living (Forman & Zhang, 2021). Third, issues of bioavailability and metabolism are commonly overlooked. The human body possesses strict regulatory control over micronutrient absorption and distribution. Isolated, high-dose antioxidant supplements also often fail to replicate the complex pharmacokinetics and synergistic effects of when the foods containing these substances are consumed as part of a whole food matrix, which provides numerous complementary phytochemicals and cofactors that control their action. Finally, improper population targeting in most clinical trials has also probably been a factor in the null findings. Adding to a healthy, well-nourished population with excellent baseline antioxidant status is not likely to be very helpful and potentially could only reveal risks.

The therapeutic benefit of antioxidants is far more likely in specific subgroups with pre-existing states of deficiency, heightened biomarkers of oxidative stress, or with specific genetic polymorphisms affecting redox homeostasis. This comprehensive critical analysis underscores a fundamental principle in nutritional science: "more is not always better." The future of antioxidant therapy, therefore, needs to move away from the pharmaceutical paradigm of bulk supplementation with purified agents toward a more evolved, food-based strategy centered on diversified antioxidant consumption, perhaps reserved for strategic use in individuals who have a demonstrated clinical need.

Conclusion and Future Directions

This intimate critical analysis attests that nutritional antioxidants are strong and pivotal controllers of human disease and health, but are intensely multifaceted and carefully context-dependent in their action. Their unique chemical processes, like Hydrogen Atom Transfer (HAT), Single Electron Transfer (SET), metal chelation, and indirect activation of cytoprotective mechanisms like Nrf2, dictate their differing and interrelated roles within the sophisticated system of cellular redox protection. In some disease states, e.g., atherosclerosis and liver disease, certain antioxidants have clear-cut therapeutic potential, as in the success of high-dose vitamin E in NASH with biopsied-proven disease and the life-saving, underpinning function of glutathione repletion in acetaminophen overdose. However, consistent and sobering failure of high-dose, single-antioxidant supplementation in mass primary prevention trials is a stern warning against reductionism and discountenance of the complexity of biological processes.

Future studies should definitively leave behind the dated and simplistic "antioxidant = good" dogma. Moving forward needs to be more intricate and personalized. Firstly, high priority should be given to Personalized Nutrition. This involves the discovery of strong genetic, metabolic, and oxidative stress biomarkers capable of identifying reliably what individuals or patient subgroups are most likely to benefit or be harmed by specific antioxidant interventions. Second, the development of Synergistic Formulations is crucial. Instead of turning towards isolated molecules, next-generation drugs should learn from nature by putting multiple antioxidants together with necessary cofactors in order to enhance efficacy and prevent potential pro-oxidant drifts, which will occur if a single molecule becomes overburdened.

Third, overcoming the key challenge of Bioavailability through Advanced Delivery Systems is crucial for many promising compounds, particularly polyphenols. Employing nanotechnology, phospholipid complexes, or other new carriers

may guarantee that these molecules find their way to target tissues at therapeutically relevant concentrations, thus closing the gap between promise on the preclinical horizon and reality in the clinic. Lastly, the new field of the Chronobiology of Antioxidants deserves investigation. Experiments would need to investigate how the temporal coordination of antioxidant intake—e.g., with meals or exercise periods—can be varied so as to optimize their protective effects without undesirable interference with mandatory, ROS-dependent signaling processes that are essential for metabolic integrity and physiological adaptation.

In short, dietary antioxidants are no magic bullet but integral components of a health-promoting diet. Their shrewd and evidence-based application, grounded in a deep and respectful knowledge of their fundamental chemistry and elaborate biology, is really promising to prevent disease and treat chronic disease. Deserving of this promise, however, is an unmistakable shift from a simple frame of mind to one that broadly welcomes and investigates the sheer complexity of redox biology and its contribution to human health.

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