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ANTIOXIDANTS: A COMPREHENSIVE REVIEW OF MECHANISMS, HEALTH BENEFITS, AND THERAPEUTIC APPLICATIONS

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ABSTRACT

Antioxidants play a crucial role in mitigating oxidative stress-related diseases by acting as the body's natural defense system against "free radicals"—unstable molecules that damage cells. This review discusses major types of antioxidants, such as Vitamin C (found in citrus fruits), Vitamin E (found in nuts and seeds), and Polyphenols (found in green tea and berries). We examine how they work, from directly neutralizing harmful molecules to "locking up" dangerous metals in the body through a process called chelation. A key focus is the synergistic effect, where different antioxidants work better as a team in food than they do as single supplements. Therapeutic applications in cancer treatment, neurodegenerative diseases, and wound healing are also explored. Beyond diet, this review looks at how these compounds are used as medicine to help the body heal wounds faster and protect the brain from aging.

KEYWORDS: Antioxidants, Oxidative Stress, Free Radicals, Health Benefits, Supplement Safety

INTRODUCTION

Every day, our bodies use oxygen to create energy, but this process also produces unstable molecules called free radicals. Think of these as "electron-hungry" particles that can damage cell walls, DNA, and proteins if they aren't controlled. When these unstable molecules outnumber our natural defenses, we experience oxidative stress, a state that has been linked to over 100 conditions, including heart disease, cancer, and memory loss. Antioxidants are the body's natural defense force that neutralises these harmful molecules. They come from two main places: those our body makes itself (like enzymes) and those we get from our diet, such as Vitamin C from citrus fruits, Vitamin E from nuts, and polyphenols from berries and tea. In medicine, these compounds are being studied for their ability to protect the brain and speed up wound healing. However, recent research suggests a "paradox": while antioxidants in food are highly beneficial, taking high-dose pills (supplements) often doesn't provide the same protection and can sometimes even be harmful. This may happen because our bodies need a small amount of "stress" to stay healthy, and high doses of single vitamins can disrupt this balance. Furthermore, many natural antioxidants have poor bioavailability, meaning our bodies have a hard time absorbing them effectively. This review summarizes current evidence on antioxidant mechanisms, health benefits, and therapeutic applications, providing insights into their potential use in preventing and treating various diseases.

MATERIALS AND METHODS

A comprehensive literature review was conducted using PubMed, ScienceDirect, and Google Scholar, focusing on antioxidant mechanisms, health benefits, and therapeutic uses.

ANTIOXIDANT TYPES AND MECHANISMS

Antioxidants are typically categorized into **vitamins, carotenoids,** and **polyphenols** (which include flavonoids and phenolic acids). Antioxidants often work more effectively in their natural food matrix than as isolated supplements.

Table 1: Dietary Antioxidants and Their Natural Sources

Antioxidant Category	Specific Antioxidant	Primary Food Sources
Vitamins	Vitamin C (Ascorbic Acid)	Citrus fruits (oranges, lemons), bell peppers, strawberries, broccoli, kiwi
	Vitamin E (Tocopherols)	Vegetable oils (wheat germ, sunflower), almonds, sunflower seeds, avocados, spinach
	Vitamin A / β-Carotene	Carrots, sweet potatoes, pumpkin, spinach, mangoes
Carotenoids	Lycopene	Tomatoes (especially cooked/processed), watermelon, pink grapefruit, guava
	Lutein & Zeaxanthin	Kale, spinach, corn, egg yolks, collard greens
	Astaxanthin	Salmon, trout, krill, shrimp, microalgae
Polyphenols	Anthocyanins	Blueberries, blackberries, raspberries, red cabbage, eggplant
	Flavonoids (Quercetin, etc.)	Onions, apples, tea (green and black), red wine, dark chocolate
	Catechins (EGCG)	Green tea, white tea, cocoa, berries
	Resveratrol	Red wine, skin of dark grapes, peanuts, berries
Phenolic Acids	Chlorogenic Acid	Coffee, blueberries, tomatoes, apples
	Ferulic Acid	Whole grains (wheat, brown rice, oats), seeds
	Curcumin	Turmeric root
Minerals (Cofactors)	Selenium	Brazil nuts, seafood, organ meats, whole grains
	Zinc	Oysters, beef, pumpkin seeds, chickpeas

MECHANISM OF ANTIOXIDANTS

1. Free Radical Scavenging

- AH + R• → A• + RH (Antioxidant donates a hydrogen atom to a free radical)
- Example: Vitamin C (ascorbic acid) + OH• → Ascorbyl radical + H2O

2. Metal Chelation:

- M^n+ + AH → M^(n-1)+ + A• (Antioxidant chelates metal ions, reducing their reactivity)
- Example: EDTA + Fe^3+ → Fe-EDTA complex

3. Singlet Oxygen Quenching:

- ^1O2 + A → ^3O2 + A (Antioxidant quenches singlet oxygen, preventing oxidative damage)
- Example: Carotenoids + ^1O2 → Carotenoid triplet state + ^3O2

4. Enzymatic Modulation

Enhancing the activity of endogenous enzymes like **superoxide dismutase (SOD), catalase (CAT),** and **glutathione peroxidase (GPx),** which serve as the body's primary defense against ROS.

THERAPEUTIC APPLICATIONS

Antioxidant systems function as a sophisticated, multi-layered defense network essential for maintaining **redox homeostasis** and protecting cells from oxidative damage (Sies, H.,2015). These defenses categorized into three primary lines: enzymatic systems (such as **Superoxide Dismutase** and **Catalase**), non-enzymatic scavengers (including **Vitamins C and E, carotenoids**, and **polyphenols**), and specialized repair enzymes that fix damaged DNA and proteins. These compounds operate through precise chemical mechanisms, such as **Hydrogen Atom Transfer (HAT)** and **Metal Chelation**, to neutralize reactive oxygen species (ROS) before they can trigger chronic conditions like cardiovascular disease or neurodegeneration. In therapeutic settings, antioxidants are increasingly explored for their role in **neuroprotection** and accelerated **wound healing** (Sies,H., 2015, Khalil, *et al.* 2019). However, researchers frequently highlight the **"Antioxidant Paradox,"** noting that while dietary intake is protective, high-dose isolated supplements can disrupt natural signaling pathways and may not provide the same clinical benefits (Halliwell, B. 2012).

Table 2: Overview of Antioxidant Systems, Mechanisms, and Therapeutic Applications

Category	Antioxidant Examples	Primary Mechanisms	Therapeutic Targets
Exogenous (Dietary)	Vitamin C, Vitamin E, Polyphenols, Carotenoids	Direct Free Radical Scavenging; Hydrogen Atom Transfer	Cancer Prevention, Cardiovascular Health, Immune Support
Endogenous (Enzymatic)	Superoxide Dismutase (SOD), Catalase, Glutathione Peroxidase	Enzymatic decomposition of ROS (O_2^- and H_2O_2)	Cellular Redox Homeostasis, Aging Mitigation
Molecular Signaling	Nrf2/ARE Pathway activation	Upregulation of Phase II detoxifying enzymes	Metabolic Syndrome, Chronic Inflammation
Secondary Mechanisms	Flavonoids, Phenolic acids	Metal Chelation (Fe^{2+}, Cu^{2+}); Inhibition of pro-oxidant enzymes	Neuroprotection (Alzheimer's, Parkinson's)
Advanced Delivery	Nanocarriers, Liposomes, Micelles	Improving Bioavailability and metabolic stability	Targeted Drug Delivery, Chronic Wound Healing
Mitochondria-Targeted	MitoQ, SkQ1, Astaxanthin	Neutralizing ROS at the primary site of production	Mitochondrial Dysfunction, Neurodegenerative Diseases

Recommended Dietary Allowances (RDA)

For individual antioxidants, the WHO and associated bodies like the Indian Council of Medical Research (ICMR, 2000) and NIH (2010) provide specific daily targets:

Antioxidant	Daily Recommended Amount (RDA)	WHO-Aligned Food Sources
Vitamin C	40 mg (ICMR) to 75–90 mg (NIH/Global)	Citrus fruits, amla, guava, tomatoes
Vitamin E	7.5 mg (ICMR) to 15 mg (Global)	Vegetable oils, nuts, seeds, dark leafy greens
Vitamin A	600–900 µg (as Retinol/ Carotenoids)	Carrots, spinach, papaya, orange-fleshed fruits

DISCUSSION

Antioxidants' ability to reduce oxidative stress underlies their health benefits. Polyphenols and vitamins C and E show promise in preventing chronic diseases (Aruoma, 2018; Chen *et al.*, 2018; Lee *et al.*, 2018). Their mechanisms of action involve scavenging free radicals, chelating metal ions, and modulating signaling pathways, which contribute to their therapeutic effects (Sies *et al.*, 2017; Zhang et al., 2018; Valko *et al.*, 2016).

Further research is needed to understand the bioavailability and therapeutic dosing of antioxidants (Halliwell, 2018; Pham-Huy *et al.*, 2018; Tiwari *et al.*, 2015). Additionally, personalized antioxidant strategies may be necessary for specific health conditions (Lobo et al., 2018; Singh *et al.*, 2018; Gupta *et al.*, 2014). The potential synergistic effects of antioxidants with other nutrients or pharmaceuticals also warrant investigation (Kumar et al., 2018; Sharma *et al.*, 2018; Khan *et al.,* 2015). Moreover, the development of antioxidant-based therapies could provide new avenues for treating diseases. For instance, antioxidant supplementation has shown promise in reducing oxidative stress in patients with neurodegenerative diseases (Rajasekaran *et al.,* 2018; Khan *et al.*, 2018; Uttara *et al.*, 2012). However, more studies are needed to confirm these findings and establish optimal dosing regimens (Patel *et al.*, 2018; Wang *et al.*, 2018; Kumar *et al.*, 2012). The role of antioxidants in preventing chronic diseases is complex and multifaceted. While antioxidants have shown promise in reducing oxidative stress, their effects on disease outcomes are not always clear-cut. Further research is needed to understand the relationships between antioxidant intake, oxidative stress, and disease prevention (Aruoma, 2018; Sies *et al*., 2017; Valko *et al*., 2016).

CONCLUSION

Antioxidants are essential for maintaining cellular homeostasis by mitigating oxidative stress through a combination of endogenous enzymes and exogenous dietary sources. While therapeutic applications show promise for managing chronic conditions, future research must address bioavailability challenges and utilize targeted delivery systems to optimize health outcomes.

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