Plant-Derived Antioxidants as a Protective Strategy against Oxidative Stress

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Abstract
Free radicals are unstable molecules produced during normal cell metabolism lead to harm DNA, various enzymes, and membranes, which can result in a number of human disorders including cancer., and neurodegenerative illnesses. Free radicals in the body can be increased by environmental variables such as prolonged contact with UV light, exposure smoking, and other toxins. This process takes place when the levels of antioxidant defences and free radicals are out of equilibrium. In the body, antioxidants protect the body from oxidative stress by scavenging free radicals and repairing damaged cells, and therefore increasing the ingesting of fruits and vegetables comprising high antioxidant content is suggested to prevent oxidative stress from occurring. The biological effects of natural products such as anti-aging effects, anti-inflammatory properties, anticancer effects or anti-atherosclerosis effects have also been demonstrated. Hence, the objective of this article is to investigate the impact of natural healing antioxidants in mitigating oxidative stress associated with various diseases.

Keywords: Drosophila, Antioxidants, Reactive Oxygen Species

1. Introduction
Oxidative stress ensues when unwarranted surplus of reactive oxygen species (ROS) manifests, surpassing the body's ability to eliminate, scavenge, or repair them through the available antioxidant mechanisms, leading to biological imbalance [1].
Cells generate reactive oxygen species (ROS) as natural by products of their internal metabolic processes, such as glycolysis, citric acid cycle, oxidative phosphorylation, etc., or produce them in response to external stressors such as radiation, environmental pollutants, and various toxins. These chemicals are highly reactive and intensely tend to react with other molecules [2, 3].
Three of the most prevalent kinds of reactive oxygen species (ROS) include hydroxyl radicals (OH⁻), hydrogen peroxide (H₂O₂), and superoxide anion (O₂⁻). The hydroxyl radical (OH⁻) is recognised as the most reactive among the reactive oxygen species (ROS) primarily due to the presence of an unpaired electron in its atomic structure [4].
ROS can act as signals for normal cell processes (i.e. apoptosis, immune cell activation, etc.) in small amounts. Still, excessive and uncontrolled production can cause cell damage, dysfunction, DNA mutations, cell death, and a variety of medical conditions and disorders, such as neurodegenerative diseases, cancer, cardiovascular illnesses, and ageing [5].
In order to protect themselves from harmful substances and free radicals, cells rely on an antioxidant defence system which is composed of enzymatic components such as glutathione peroxidase (GPx), catalase (CAT), superoxide dismutase (SOD) and heme oxygenase (HO-1), and other enzymes to safeguard themselves against ROS-induced cellular damage. [6.7].

2. Sources of Reactive Oxygen Species (ROS) Production

Both endogenous and exogenous sources can generate ROS. Physiological processes and conditions contribute to endogenous generation, while environmental factors, such as pollutants, radiation, etc., contribute to the exogenous generation of free radicals [8].

Both Enzymatic and non-enzymatic reactions can generate Reactive Oxygen Species (ROS) [9]. NADPH oxidase, xanthine oxidase, mitochondrial enzymes, etc., generate the Superoxide radical. It participates in various reactions that generate ROS and RNS, such as Hydrogen peroxide (Dismutation reaction), Hydroxyl radical (Fenton Reaction), Peroxynitrite (Superoxide + Nitric oxide = Peroxynitrite), etc. [10].

Hydrogen peroxide, a non-radical molecule, is mainly generated by a dismutation reaction. This reaction involves enzyme superoxide dismutase catalyses the reaction that converts superoxide into hydrogen peroxide. In addition, several enzymes, such as xanthine oxidase, monoamine oxidase, etc., are responsible for hydrogen peroxide generation.[11,12]

Hydroxyl radical (OH⁻) the most reactive ROS, is generated through the Fenton reaction. In this reaction, hydrogen peroxide (H₂O₂) reacts with ferrous ions (Fe²⁺) in the presence of an acidic environment to produce the Hydroxyl radical (OH⁻), along with water (H₂O) and ferric ions (Fe³⁺) [13].

Non-enzymatic reactions generate ROS through the reaction of metal ions with hydrogen peroxide or molecular oxygen. ROS are also produced as a result of exposure to environmental elements such as radiation, toxins, and contaminants. The electron transport chain in mitochondria is a primary source of ROS, generating ROS through both enzymatic and non-enzymatic reactions [14, 15].

3. Detrimental impacts of Oxidative Stress on Human Health

As previously mentioned, oxidative stress can occur when the body has too many free radicals. Numerous biological constituents, including proteins, lipids, and DNA, are adversely impacted by this destructive process. It has been implicated as a critical player in developing various chronic diseases, from cardiovascular disease, cancer, and neurodegenerative disorders, diabetes, autoimmune conditions, chronic obstructive pulmonary disease, kidney disease, and eye diseases [16-18].

3.1 Cardiovascular disease:

The lining of blood arteries can be damaged by oxidative stress and lead to inflammation, which can result in atherosclerosis [19]. Plaque accumulates inside arteries as a result of atherosclerosis, reducing blood flow and possibly triggering cardiovascular illnesses. Oxidative stress promotes the oxidation of LDL cholesterol particles, which contribute to plaque formation. This plaque build-up can rupture and cause blood clots, leading to heart attacks and strokes. In addition, oxidative stress can also contribute to other cardiovascular diseases such as hypertension, heart failure, and arrhythmias [20, 21].
3.2 Cancer:
Oxidative Stress can damage DNA, leading to mutations in certain genes, such as tumour suppressor genes and oncogenes, which can disrupt normal cell growth and division, leading to uncontrolled cell proliferation and tumour formation. ROS can cause the transcription factor NF-B to become active, which regulates the expression of genes related to inflammation, cell growth, and survival [22]. The onset and spread of several cancer forms, including lung, breast, and prostate cancer, have been linked to dysregulated NF-B activation. ROS have the ability to activate the Akt/mTOR/PI3K pathway. This pathway is dysregulated in cancer. This pathway regulates cell growth, survival, and metabolism by promoting protein synthesis. Dysregulation of this pathway can lead to uncontrolled cell growth and resistance to apoptosis in cancer cells [23-25].

3.3 Neurodegenerative diseases:
A number of neurodegenerative diseases are linked to the presence of oxidative stress, including Alzheimer's disease, Parkinson's disease and multiple sclerosis [26]. In Alzheimer's illness, it can damage brain cells and promote beta-amyloid protein accumulation, a hallmark of the disease. In Parkinson's disease, oxidative stress can cause the loss of dopamine-producing neurons [27-28].

3.4 Diabetes: Oxidative stress can impair insulin secretion and signalling, leading to the development of insulin resistance. Insulin resistance causes glucose to accumulate in the bloodstream, leading to high blood sugar levels. Over time, this leads to the development of type 2 diabetes. Oxidative stress can also cause beta-cell dysfunction which harm pancreatic beta cells, which are in charge of making and releasing insulin. This can result in decreased insulin secretion and worsen blood sugar control. It also causes vascular complications which can damage blood vessels, contributing to the development of diabetic vascular problems such as diabetic retinopathy, nephropathy, and neuropathy [29].

4. *Drosophila* (fruit flies) as a model organism for investigating the effects of oxidative stress.
*Drosophila*, commonly known as fruit flies, is a popular model organism for research because it is small, easy to maintain, has a short life cycle, and has a well-annotated genome. It also shares many of its genes and biological processes with humans, making it a valuable tool for studying various diseases and physiological processes. These properties make it an excellent model for investigating the impact of oxidative stress and ROS. ROS play vital roles in the development, metabolism, and stress response of *Drosophila* [30-32].

Oxidative stress has adverse effects on various life parameters of *Drosophila* [33-36], such as
1. Reduction in lifespan
2. Reduced fecundity (ability to produce offspring),
3. Altered behaviour,
4. Delayed development
5. Neurodegeneration
6. Disruption of normal metabolic processes
7. Immune dysfunction
8. Disruption of tissue homeostasis

*Drosophila* has multiple genes that regulate the endogenous antioxidant system, enabling it to combat oxidative stress. These genes include superoxide dismutase (SOD), Catalase, Glutathione peroxidase, etc. The SOD genes encode enzymes that catalyse the conversion of superoxide radicals into less dangerous forms of oxygen and hydrogen peroxide. Conversely, glutathione peroxidase uses glutathione to reduce hydrogen peroxide and other organic peroxides, whereas catalase changes hydrogen peroxide into water and oxygen. The primary function of these genes is to scavenge reactive oxygen species (ROS), which helps maintain redox balance within the cell, which is crucial for cellular health [37-41].

5. Role of Exogenous Antioxidants in Combating Oxidative Stress

Apart from these endogenous antioxidants, Dietary intake and nutritional supplementation can introduce numerous exogenous antioxidant molecules of both plant and animal origin into the body, which has been shown to help reduce oxidative stress by lowering the levels of reactive oxygen species in the body [42]. Plant-based antioxidants have many health-promoting properties beyond their antioxidant effects, including anti-inflammatory, anti-cancer, and cardiovascular benefits [43].

<table>
<thead>
<tr>
<th>Plant Based Antioxidants</th>
<th>Other Properties</th>
</tr>
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<tbody>
<tr>
<td>Flavonoids (e.g. quercetin, catechins)</td>
<td>Anti-inflammatory, anti-cancer, cardiovascular benefits, neuroprotective [44]</td>
</tr>
<tr>
<td>Carotenoids (e.g. beta-carotene, lycopene, lutein)</td>
<td>Eye health, anti-cancer, cardiovascular benefits, anti-inflammatory [45]</td>
</tr>
<tr>
<td>Phenolic acids (e.g. caffeic acid, ferulic acid)</td>
<td>Anti-inflammatory, anti-cancer, neuroprotective, cardiovascular benefits[46]</td>
</tr>
<tr>
<td>Resveratrol</td>
<td>Anti-cancer, cardiovascular benefits, anti-inflammatory[47]</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Anti-inflammatory, anti-cancer, neuroprotective, cardiovascular benefits [48]</td>
</tr>
<tr>
<td>Anthocyanins (e.g. cyanidin, delphinidin)</td>
<td>Anti-inflammatory, anti-cancer, cardiovascular benefits, eye health [49]</td>
</tr>
<tr>
<td>Glutathione</td>
<td>Immune system support, liver health, anti-ageing[50]</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>Anti-inflammatory, anti-cancer, cardiovascular benefits, neuroprotective [51]</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Immune system support, collagen production, wound healing[52]</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Cardiovascular benefits, anti-inflammatory[53]</td>
</tr>
<tr>
<td>Selenium</td>
<td>Immune system support, anti-cancer[54]</td>
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</tbody>
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6. Effects of Plant-Based Antioxidants on Oxidative Stress in *Drosophila*

Plant-based antioxidants have been found to possess strong antioxidant properties. These compounds can scavenge ROS and neutralise them. They have been found to activate endogenous antioxidant defence systems by increasing the upregulation of enzymes such as SOD, catalase, etc. [55]. Various Studies have demonstrated that plant-based antioxidants possess the remarkable ability to ameliorate the activation of genetic elements associated with the cellular fortification against oxidative stress. Transcription factors such as CncC (cap 'n' collar isoform C), AP-1 (activating protein-1), FOXO proteins (Forkhead Box O), Dmp 53, etc., are crucial in cellular defence against oxidative stress. When activated, they enhance the transcriptional upregulation of genes intricately involved in bolstering the antioxidant defense machinery. [56-58].

According to various researchers, oxidative stress has been related various neurological illnesses [59]. A study looked into the effect of fullerenols in a PD model in *Drosophila*. The result demonstrated that fullerenols exerted neuroprotective effects by reducing oxidative stress and improving locomotor activity in *Drosophila* [60]. Another study demonstrated that green tea catechins possess antioxidant, anti-inflammatory, and anti-amyloid properties, which are all relevant factors in neurodegenerative diseases. They help to protect neurons and mitigate the risk of neurodegeneration [61, 62]. Solanum vegetables, which include tomatoes, potatoes, eggplants, etc have been demonstrated to improve redox imbalance and have neuroprotective effects [63].

Oxidative stress has been closely associated with diabetes [64]. Various studies have demonstrated that plant-based antioxidants are beneficial in managing diabetes by reducing oxidative stress and inflammation, improving insulin sensitivity, and supporting overall metabolic health [65-66]. A study investigated the effects of dietary supplementation with almond, a rich source of antioxidants, on lifespan and metabolic health in *Drosophila*. The results showed that almond supplementation extended the lifespan of fruit flies and improved glucose tolerance, suggesting potential benefits in managing metabolic disorders like diabetes [67].

Another study suggest that plant based antioxidants have cardio protective effects. The study examined the effects of *Terminalia arjuna* extract on cardiac function and oxidative stress in *Drosophila*. The results indicated that *Terminalia arjuna* extract improved cardiac function, reduced oxidative stress markers, and exhibited cardioprotective effects [68].

Another study suggest that plant based antioxidants can help in tackling cancer. Curcumin, a compound derived from turmeric reduced tumour growth and altered the cell cycle progression of cancer cells, suggesting potential anti-cancer effects [69].

7. Conclusion

Free radicals and oxidative stress have long been considered as harmful aspects in an organism's health. Extensive research has continuously shown that free radicals play an important role in the initiation and progression of a variety of diseases, ranging from cardiovascular disease to cancer. After considering the diverse effects of antioxidant compounds in preventing and managing, it becomes evident that dietary antioxidants have proven beneficial.

We can conclude that oxidative stress remains a significant threat to an organism's wellness and health. This realization underscores the importance of continued research and innovative advancements to harness the potential therapeutic applications of oxidative stress.
References


