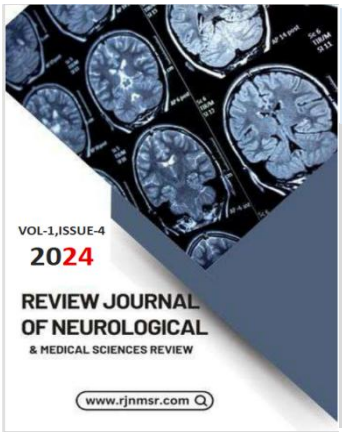


Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

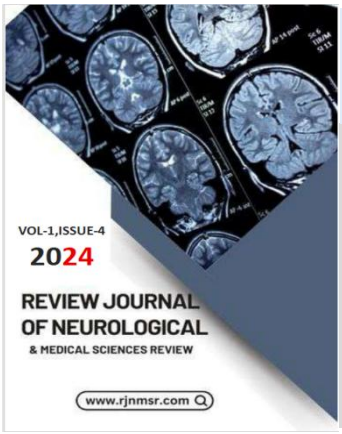
E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

The Role of Oxidative Stress and Antioxidants in Human Disease

Azeem Sarwar[1]
University Institute of Medical Laboratory Technology, University of Lahore Pakistan. Email: azeem.sarwar@mlt.uol.edu.pk
Bibi Amina[2]
Regional Blood Centre Dera Ismail Khan, Khyber Pakhtunkhwa Pakistan. Email: Muhammad18318@gmail.com
Mufakkir Aziz[3*]
Department of Medical Laboratory Technology, Faculty of Allied Health Sciences, The University of Agriculture, Dera Ismail Khan, Khyber Pakhtunkhwa Pakistan.
Corresponding Author Email: mufakkiraziz125@gmail.com
Muhammad Nadeem[4]
Institute of Microbiology Gomal University, Dera Ismail Khan. Email: nadeemmasood0008@gmail.com
Tehseen Ullah[5]
Department of Medical Laboratory Technology, Sarhad University of Science and Information Technology, Peshawar.
Email: mlstahsin2611@gmail.com
Salwa Mohamed Ahmed Dahesh[6]
Research Institute of Medical Entomology, General Organization for Teaching Hospitals and Institutes, Giza, Egypt. Email : Salwamohamed970@gmail.com

Abstract

Oxidative stress, defined as an imbalance between the formation of reactive oxygen species (ROS) and the body's antioxidant defenses, is a key factor in the pathophysiology of many human diseases. This review investigates the molecular mechanisms underpinning oxidative stress, focusing on its sources and the physiological harm it causes. The role of oxidative stress in the genesis and progression of neurodegenerative disorders, cardiovascular diseases, cancer, and metabolic disorders is extensively examined, with a focus on its impact on cellular function and overall health. Furthermore, the article investigates the body's natural antioxidant systems, dietary antioxidants, and new antioxidant therapies



Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

aimed at reducing oxidative damage. While antioxidants' medicinal potential is intriguing, issues such as appropriate dose, bioavailability, and potential side effects persist. Future research should concentrate on determining targeted antioxidant strategies based on specific disease pathways. This review highlights the dual character of oxidative stress as both a physiological need and a pathological driver, with the goal of inspiring future research in this dynamic subject.

Keywords: Stress, Antioxidants, Disease.

Introduction

Oxidative stress is defined as a metabolic imbalance between the creation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) and the body's ability to neutralize these reactive molecules using antioxidant defenses. ROS, including superoxide anion (O_2^- •), hydroxyl radicals (•OH), and hydrogen peroxide (H_2O_2), are byproducts of normal cellular metabolism, especially mitochondrial oxidative phosphorylation. A balance is maintained under healthy settings, allowing ROS to participate in signaling cascades and cellular stability. However, high ROS levels or low antioxidant defenses can cause oxidative stress, causing lipid, protein, and DNA damage and disrupting cellular function (1).

Antioxidants play an important role in reducing oxidative stress by neutralizing ROS and limiting their detrimental effects. Endogenous antioxidants include superoxide dismutase (SOD), catalase, and glutathione, while exogenous antioxidants include vitamins C and E, carotenoids, and polyphenols received through diet (2). These mechanisms work together to maintain cellular redox equilibrium and prevent oxidative damage.

It is impossible to overestimate the importance of oxidative stress in human health and illness. Numerous diseases, including neurological disorders like Alzheimer's and Parkinson's, cardiovascular ailments like atherosclerosis and hypertension, and metabolic disorders like diabetes mellitus, have been linked to elevated oxidative stress in their genesis and progression. Furthermore, because ROS can cause genetic abnormalities and encourage chronic inflammation, they can play a role in the aging process and the development of cancer (3).

Therapeutic improvements could be greatly aided by addressing oxidative stress and utilizing antioxidants' protective properties. Research in this area is crucial because it may lead to new treatments and preventative measures for a variety of illnesses if the processes of oxidative stress and the function of antioxidants are better understood.

The Oxidative Stress Mechanisms

Two extremely reactive chemicals that are essential to oxidative stress are reactive oxygen species (ROS) and reactive nitrogen species (RNS). When

Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

their levels are not appropriately controlled, these species—which are mostly produced as byproducts of cellular metabolism—can seriously harm cellular structures and result in a number of disease processes. Clarifying the fundamental mechanisms of oxidative stress requires an understanding of the production of ROS and RNS, their sources, and the mechanisms that keep them in balance.

Formation of Reactive Nitrogen and Oxygen Species: When oxygen is partially reduced, reactive oxygen species (ROS) are created, including hydrogen peroxide (H_2O_2), hydroxyl radical (•OH), and superoxide anion (O_2^- •). Numerous biological mechanisms, such as the electron transport chain (ETC) in mitochondria, can produce these species. Superoxide is a byproduct of electrons leaking from the ETC interacting with oxygen. In the presence of transition metals like iron and copper, this superoxide can subsequently be transformed into hydrogen peroxide, which can then decompose further to create the extremely reactive hydroxyl radical (1). However, nitric oxide synthase (NOS) converts L-arginine into nitric oxide (NO•), which is the source of RNS. Peroxynitrite ($ONOO^-$), a strong oxidant that may nitrate tyrosine residues and cause damage to proteins, lipids, and DNA, is created when nitric oxide and superoxide react (4).

ROS and RNS Sources

Both endogenous and external sources can produce ROS and RNS.

Internal Sources

Mitochondria: The electron transport chain, which is essential for ATP generation, is the main generator of ROS in eukaryotic cells. Superoxide may arise as a result of electron leakage during this phase and thereafter be transformed into additional ROS (5).

NADPH Oxidase (NOX) Enzymes: When active, these enzymes contribute to the formation of ROS and are involved in a number of cellular processes, such as signaling and immunological response (6).

Endoplasmic Reticulum (ER): The ER contributes to oxidative conditions in the cell by generating ROS during protein folding and stress responses (7).

Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

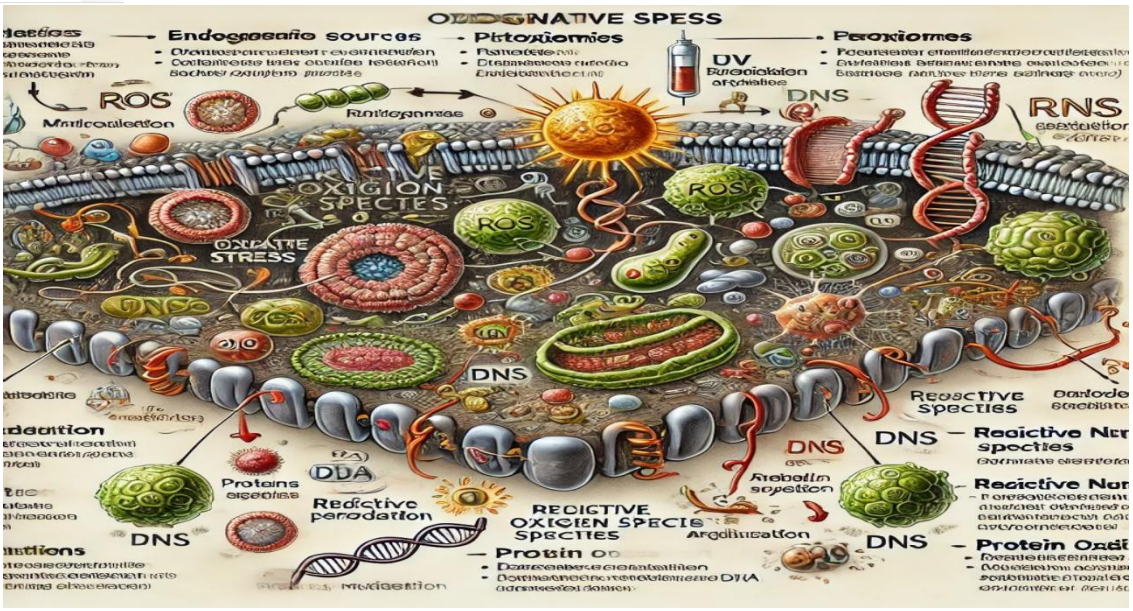


Figure: 1 The mechanisms of oxidative stress in human cells. The picture depicts endogenous sources like mitochondria, peroxisomes, and enzymatic activity, as well as foreign sources like pollution, UV radiation, and poisons. It demonstrates how reactive oxygen species (ROS) and reactive nitrogen species (RNS) interact with biological components, resulting in lipid peroxidation, protein oxidation, and DNA damage. Antioxidants are essential for neutralizing reactive species and preserving cellular homeostasis.

External Sources

Environmental Pollution: The respiratory system and other tissues may produce more reactive oxygen species (ROS) as a result of exposure to pollutants including ozone and particulate matter (8).

Radiation: Ionizing radiation, such as X-rays and ultraviolet (UV) light, can cause hydroxyl radicals to develop by disturbing cellular water (9).

Diet and Lifestyle: By causing inflammation and mitochondrial dysfunction, high-fat and high-sugar diets, as well as behaviors like smoking and drinking alcohol, can exacerbate oxidative stress (3).

Antioxidant Defenses and ROS Production in Balance

To preserve homeostasis and stop oxidative damage, the generation of ROS and antioxidant defenses must be balanced within the cell. Low to moderate ROS levels are necessary for metabolic processes and cellular communication under typical physiological settings. Oxidative stress, on the other hand, results when ROS generation surpasses the antioxidant defense systems' capacity, causing cell damage and dysfunction (1).

In order to neutralize ROS and preserve redox equilibrium, antioxidants are essential. ROS are changed into less reactive species by endogenous antioxidants, which include enzymes like glutathione peroxidase, catalase, and superoxide dismutase (SOD). By directly scavenging ROS, non-enzymatic

Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about
Review Journal of Neurological & Medical Sciences Review
E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

antioxidants such glutathione, vitamin C, and vitamin E also offer protection (2). Overloading these systems greatly raises the possibility of oxidative damage to macromolecules, which can result in mutations, inflammation, and cellular senescence. Numerous chronic illnesses, including as cancer, cardiovascular disease, and neurodegenerative disorders, can be influenced by this disruption in their onset and progression (3).

Cellular health depends on preserving a sufficient balance between ROS generation and antioxidant capability. It may be possible to reduce the harm caused by oxidative stress and enhance health outcomes by using therapeutic approaches that target ROS levels or strengthen antioxidant defenses.

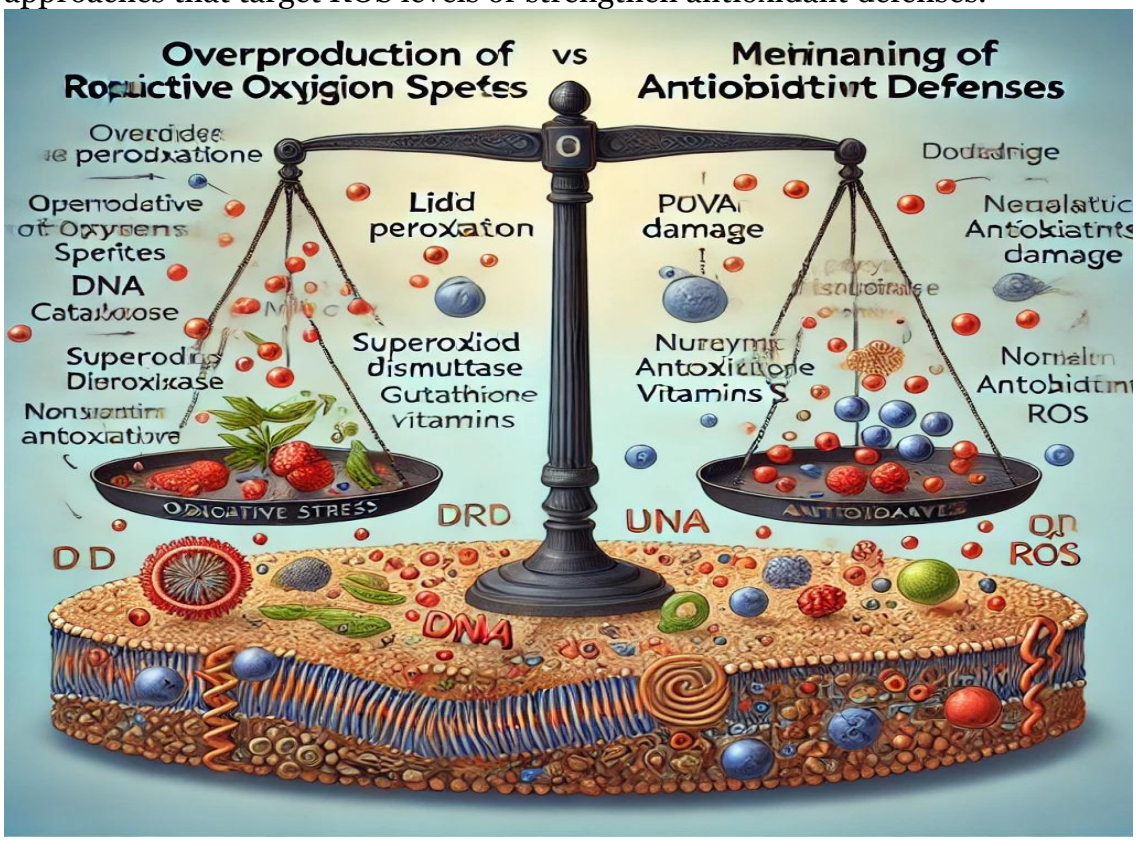


Figure:2 A schematic illustration of the equilibrium between oxidative stress and antioxidant defenses. The image highlights the overproduction of reactive oxygen species (ROS) from endogenous sources like mitochondria and external causes like pollution and UV radiation. This imbalance can cause cellular damage, including lipid peroxidation, DNA alterations, and protein oxidation. The antioxidant defense system, which includes both enzymatic (superoxide dismutase, catalase) and non-enzymatic components (glutathione, vitamins C and E), works to neutralize ROS and restore homeostasis.

Impact on Human Diseases

Numerous chronic and degenerative disorders are affected by oxidative stress in human health. Oxidative stress contributes to the onset and progression of

Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about
Review Journal of Neurological & Medical Sciences Review
E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

a number of diseases when the equilibrium between the generation of ROS and antioxidant defenses is upset. Its role in particular disease categories is discussed below.

Neurodegenerative Disorders

The pathophysiology of neurodegenerative illnesses like Huntington's, Parkinson's, and Alzheimer's is known to be influenced by oxidative stress. Oxidative damage aggravates the buildup of tau tangles and amyloid-beta plaques in Alzheimer's disease, resulting in neuronal death and cognitive loss (10). ROS speed up the course of disease by causing mitochondrial malfunction, inflammatory system activation, and apoptosis (11).

Degeneration of dopaminergic neurons in the substantia nigra is a hallmark of Parkinson's disease. Alpha-synuclein is a protein found in Lewy bodies, which are formed in part by oxidative stress. Cell death and motor impairment result from the oxidative alteration of proteins and lipids in these cells (12). Motor, cognitive, and psychiatric symptoms of Huntington's disease are caused by neuronal damage linked to mitochondrial malfunction and elevated ROS generation (13).

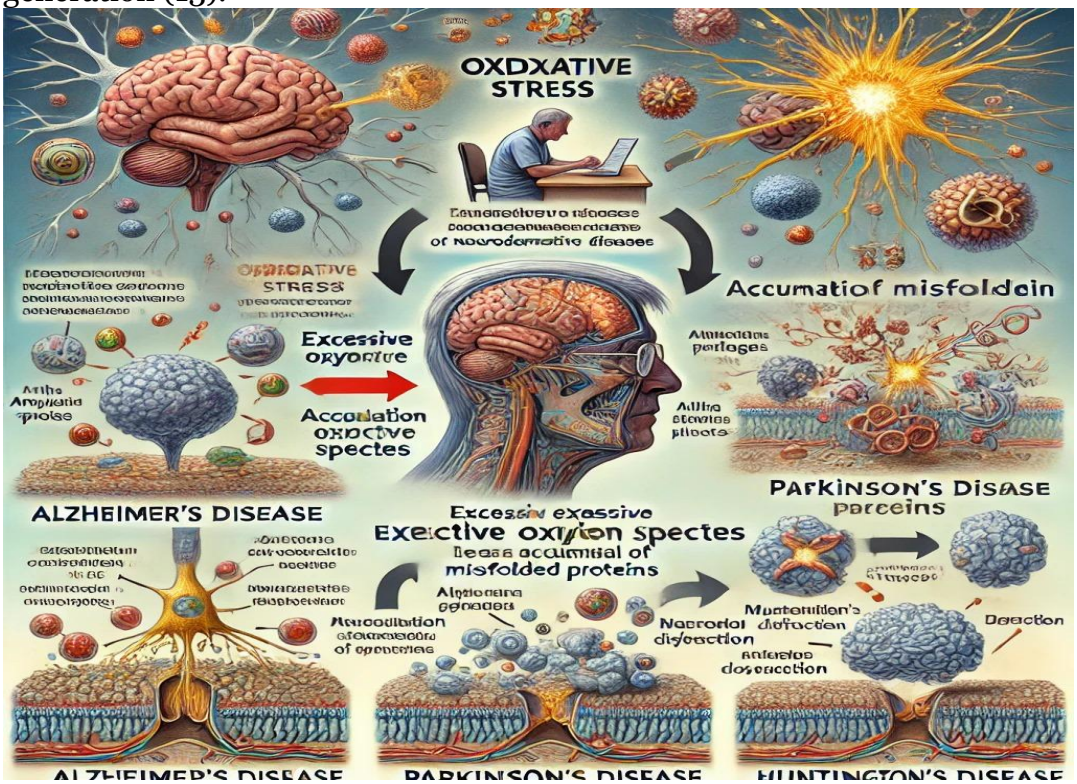


Figure: 3 The figure highlights the impact of reactive oxygen species (ROS) on neuronal damage, mitochondrial dysfunction, and the accumulation of misfolded proteins. Pathways leading to the formation of amyloid plaques, alpha-synuclein aggregates, and neuronal degeneration are depicted to show disease progression

Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about
Review Journal of Neurological & Medical Sciences Review
E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

Cardiovascular Diseases

Atherosclerosis, hypertension, and myocardial infarction are among the cardiovascular diseases those are significantly influenced by oxidative stress. In atherosclerosis, excessive ROS promote the oxidation of low-density lipoprotein (LDL), which is then taken up by macrophages, resulting in foam cell formation and plaque development in the arterial walls (1). In hypertension, oxidative stress also plays a crucial role, as ROS-induced damage to endothelial cells impairs the production of nitric oxide (NO), which lowers vasodilation and increases vascular resistance (14). Similarly, oxidative stress-induced myocardial injury, where ROS contribute to inflammation and apoptosis of cardiac cells, can precipitate myocardial infarction (15).

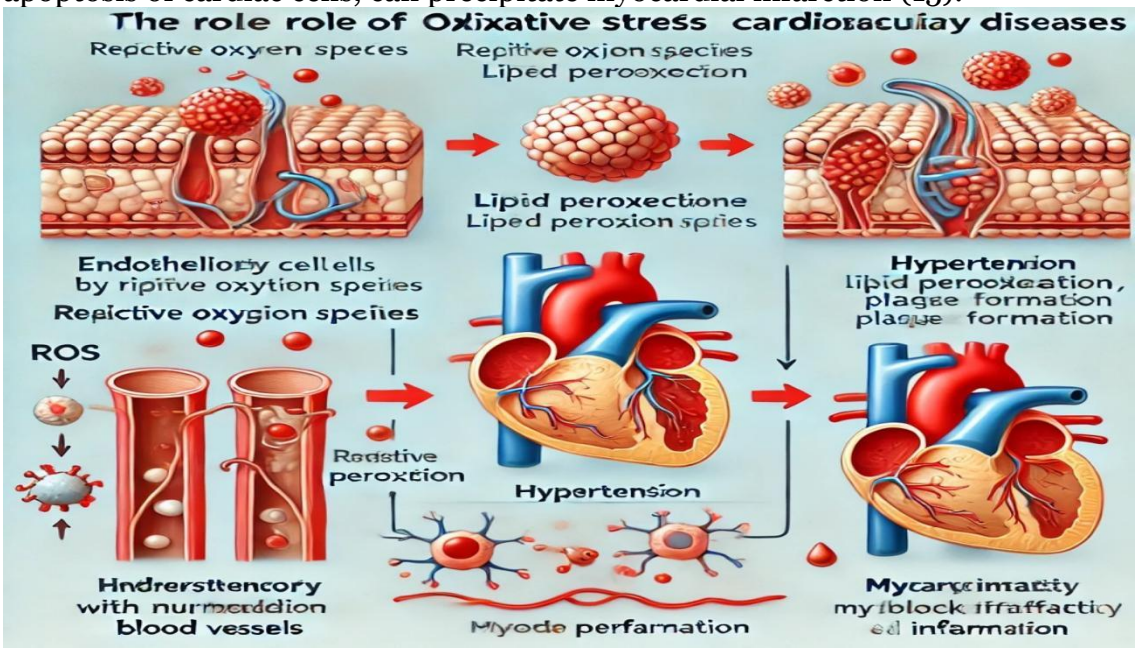
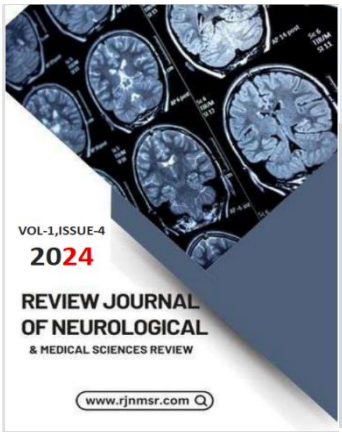


Figure: 4 The figure shows endothelial cell damage caused by reactive oxygen species (ROS), leading to lipid peroxidation, plaque formation, and inflammation. Key conditions such as atherosclerosis, hypertension, and myocardial infarction are highlighted, showing the progression from oxidative stress to cardiovascular damage.

Cancer

Both the development and spread of cancer are influenced by cancer ROS. Elevated ROS levels harm proteins, lipids, and DNA, raising the danger of mutations and the advancement of cancer, but low ROS levels can function as signaling molecules to encourage cell proliferation (3). ROS-induced DNA damage can result in chromosomal instability, oncogene activation, and tumor suppressor gene inactivation—all of which are crucial stages in the development of tumors (16).

Additionally, ROS can change the tumor microenvironment by encouraging angiogenesis, inflammation, and immune evasion—all of which aid in the



Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

growth and metastasis of tumors. By changing the effectiveness of drugs and causing cellular changes, the oxidative environment can also lead to resistance to cancer treatments (16).

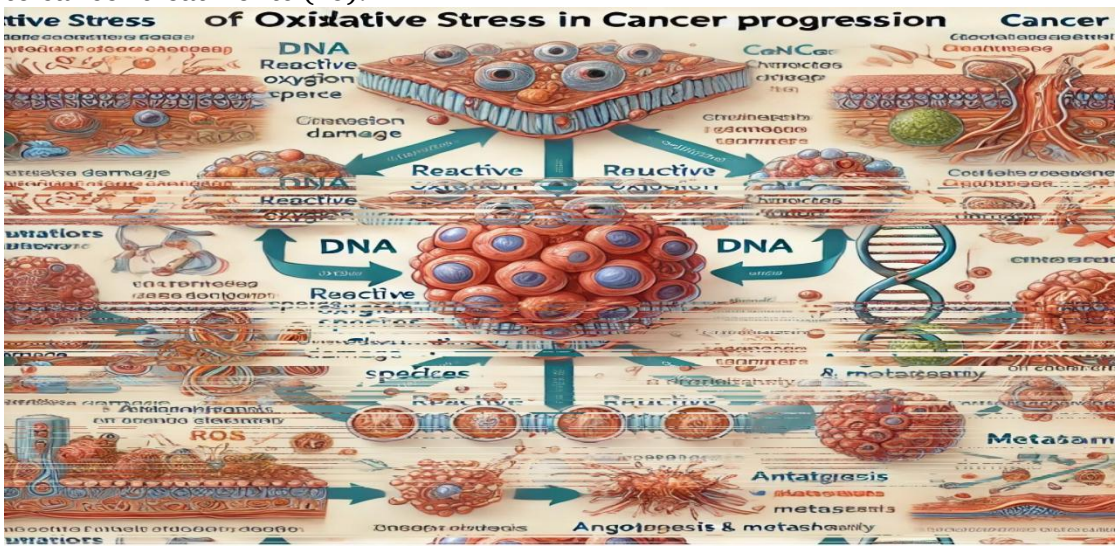


Figure: 5 The figure depicts how reactive oxygen species (ROS) induce DNA damage, leading to mutations and chromosomal instability. Processes such as uncontrolled cancer cell division, angiogenesis, and metastasis driven by ROS are visualized to highlight the link between oxidative stress and tumor development.

Metabolic Disorders

Metabolic Disorders Obesity and diabetes are linked to chronic oxidative damage. In type 2 diabetes, hyperglycemia increases the production of advanced glycation end-products (AGEs), which worsen inflammation and oxidative stress, causing damage to pancreatic β-cells, insulin resistance, and complications like diabetic neuropathy and nephropathy (17). Obesity is also linked to elevated levels of ROS, as adipose tissue in obese people generates pro-inflammatory cytokines and ROS, which fuel systemic inflammation and insulin resistance (18). The chronic oxidative state linked to obesity further predisposes people to metabolic syndrome and cardiovascular problems.

Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about
Review Journal of Neurological & Medical Sciences Review
E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

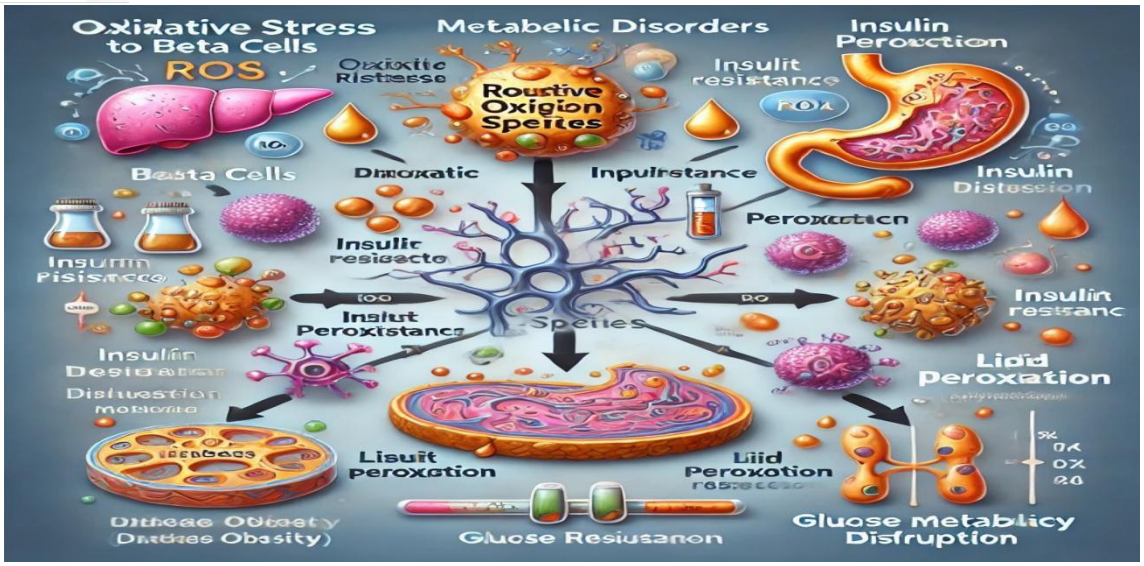


Figure: 6 The figure illustrates how reactive oxygen species (ROS) induce oxidative damage to pancreatic beta cells, leading to impaired insulin secretion and resistance. It also highlights lipid peroxidation and inflammation in adipose tissue as contributing factors to metabolic dysfunctions.

Other Diseases

In respiratory conditions like asthma, where elevated ROS production in the airways leads to inflammation, airway hyperresponsiveness, and tissue damage, oxidative stress has consequences (19).

Through the generation of ROS and the modification of cellular communication, oxidative stress contributes to immune cell activation and tissue damage in autoimmune illnesses such as rheumatoid arthritis (RA) (20).

Increased oxidative stress throughout the aging process itself causes cellular senescence, a decrease in regenerative ability, and the emergence of age-related illnesses such sarcopenia and osteoporosis (3).

Antioxidant Systems

Antioxidant Systems

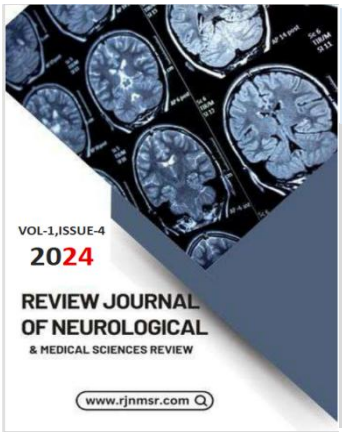
Antioxidants serve an important function in balancing ROS generation and oxidative stress, thereby preserving cells from harm. They are generically classified as endogenous antioxidants, dietary antioxidants, and synthetic antioxidant therapy.

Endogenous Antioxidants

Endogenous antioxidants are naturally created by the body and are essential for neutralizing ROS. These antioxidants are further classified into enzymatic and non-enzymatic types:

Enzymatic Antioxidants: The body generates numerous important enzymes that help neutralize ROS.

Superoxide Dismutase (SOD): Superoxide Dismutase (SOD) converts



Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

superoxide radicals into hydrogen peroxide and oxygen. It is an important initial line of defense against oxidative stress (21).

Catalase: Catalase is a protein that converts hydrogen peroxide into water and oxygen, minimizing the possibility of cellular component damage (22).

Glutathione Peroxidase (GPx): Glutathione Peroxidase (GPx) is an enzyme that lowers hydrogen peroxide and organic hydroperoxides, hence guarding against oxidative damage (23).

Non-enzymatic Antioxidants: These tiny compounds directly scavenge ROS:

Glutathione

Glutathione (GSH) is a tripeptide that neutralizes free radicals and aids in the regeneration of other antioxidants (24).

Dietary Antioxidants

Dietary antioxidants are derived from food and contribute to the body's antioxidant defenses.

Vitamins: Vitamin C (ascorbic acid) is a water-soluble antioxidant that can transfer electrons to counteract ROS and replenish other antioxidants (25).

Vitamin E (tocopherol) is a fat-soluble antioxidant that protects cell membranes from oxidative damage by removing lipid peroxides (26).

Polyphenols: Fruits, vegetables, tea, and red wine all contain polyphenols, which are bioactive substances. They have antioxidant action by scavenging free radicals and regulating oxidative stress signaling pathways (27).

Carotenoids: Carotenoids, including beta-carotene, lutein, and zeaxanthin, are pigments found in colorful fruits and vegetables. They aid to prevent oxidative damage by neutralizing ROS and protecting against photooxidative stress (28).

Antioxidant Therapies

Antioxidant therapies employ synthetic chemicals to fight oxidative stress and are used in a variety of health applications:

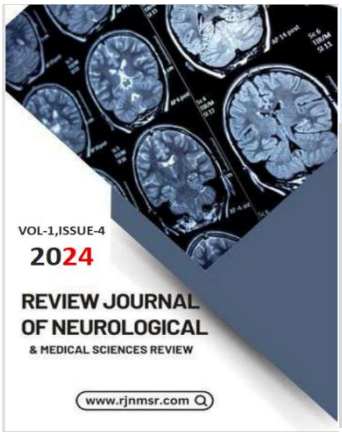
Synthetic antioxidants

N-acetylcysteine (NAC): NAC is a precursor to glutathione and has been used clinically to treat oxidative stress diseases such as chronic obstructive pulmonary disease (COPD) and acetaminophen overdose (29).

Alpha-lipoic acid (ALA): Alpha-lipoic acid (ALA) is a powerful antioxidant that can help diabetics reduce oxidative damage and improve insulin sensitivity (30).

Coenzyme Q10 (CoQ10): CoQ10 promotes mitochondrial activity and protects against oxidative damage, making it particularly effective for cardiovascular and neurological illnesses (31).

Applications of Antioxidant Therapies: Synthetic antioxidants are now being used to treat chronic diseases, cancer, and aging-related problems, in addition to clinical treatments. While some studies have found advantages, others indicate that excessive antioxidant supplementation may interfere with natural oxidative signaling pathways (32).



Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

Challenges and Limitations

Despite the well-established role of antioxidants and oxidative stress in human health, there are numerous hurdles and constraints to study and clinical use in this area. This section addresses some of the major issues and gaps in existing knowledge.

Controversies and Overuse of Supplements

One of the biggest issues in the study of oxidative stress and antioxidant therapy is the abuse and misuse of antioxidant supplements. While antioxidants can help reduce oxidative damage, excessive supplementation may have negative consequences and disrupt natural redox signaling mechanisms. High concentrations of antioxidants, such as vitamin E and beta-carotene, have been related to unfavorable health effects, including an increased risk of specific diseases and interference with normal cellular signaling (33).

For example, large-scale clinical trials have demonstrated that high-dose beta-carotene supplementation can raise the risk of lung cancer in smokers (34). Similarly, vitamin E supplements have been linked to an increased risk of hemorrhagic stroke and other consequences (35). These findings highlight the necessity of a well-balanced antioxidant consumption, as well as the need for additional research to discover the optimal supplement amounts.

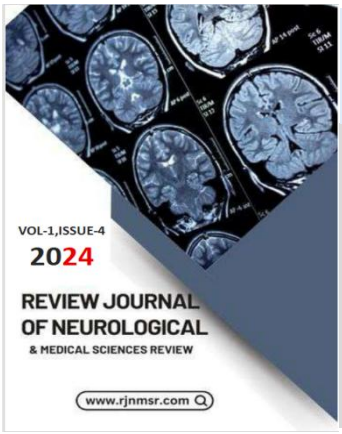
Gaps in Understanding Oxidative Stress's Role in Certain Diseases

While the role of oxidative stress in numerous diseases is widely known, there are still major gaps in knowing its precise processes and the amount to which it contributes to disease progression. While oxidative damage is known to have a role in neurodegenerative illnesses, the precise molecular pathways and connections with other factors like as genetics, inflammation, and protein misfolding are unknown (1).

ROS's dual activity as oncogenic and tumor-suppressive agents complicates comprehension of their role in various stages of cancer formation (35). This duality hampers treatment efforts that seek to target oxidative stress while preserving healthy cellular processes.

Cardiovascular diseases are yet another area with severe understanding gaps. While oxidative stress is recognized to play a role in atherosclerosis and hypertension, it is unknown how different ROS sources contribute to specific disease stages or interact with lifestyle and genetic factors (36). Furthermore, there is little understanding of how antioxidants interact with other medications or illnesses, complicating treatment regimens for people with numerous health problems.

Finally, research on metabolic disorders like diabetes and obesity is frequently focused on short-term results, with few studies looking at the long-term effects of oxidative stress and antioxidants on disease progression and consequences.



Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

Future Directions

To address these issues, more focused study is required to better understand the processes of oxidative stress in diverse diseases and to identify safe and effective antioxidant therapies. Precision medicine advancements could help personalize antioxidant therapy to individual patients based on their genetic and environmental backgrounds. Furthermore, better-designed clinical trials that consider long-term effects and combinations with other medications are required to produce comprehensive antioxidant guidelines.

Conclusion

Oxidative stress is a major element in the development of many chronic diseases, and antioxidant systems play an important role in alleviating its effects. However, it is difficult to determine optimal antioxidant concentrations and comprehend how they interact with other medical treatments. To address these issues, future research should concentrate on precision medicine approaches that adapt antioxidant therapy to individuals' genetic and environmental profiles. Longitudinal investigations and clinical trials to determine the long-term safety and efficacy of antioxidant supplements are critical. Mechanistic research should continue to investigate the routes by which ROS contribute to disease progression and uncover potential treatment targets. We can improve human health outcomes by optimizing the use of antioxidants in disease prevention and therapy, thanks to improvements in personalized medicine.

References

1. Giles, G. I., Nasim, M. J., Ali, W., & Jacob, C. (2017). The reactive sulfur species concept: 15 years on. *Antioxidants*, *6*(2), 38.
2. Pham-Huy, L. A., He, H., & Pham-Huy, C. (2008). Free radicals, antioxidants in disease and health. *International journal of biomedical science: IJBS*, *4*(2), 89.
3. Liguori, I., Russo, G., Curcio, F., Bulli, G., Aran, L., Della-Morte, D., ... & Abete, P. (2018). Oxidative stress, aging, and diseases. *Clinical interventions in aging*, 757-772.
4. Dawson, D. M. (1993). Entrapment neuropathies of the upper extremities. *New England Journal of Medicine*, *329*(27), 2013-2018.
5. Chen, X. J., & An, N. (2021). Long noncoding RNA ATB promotes ovarian cancer tumorigenesis by mediating histone H3 lysine 27 trimethylation through binding to EZH2. *Journal of Cellular and Molecular Medicine*, *25*(1), 37-46.
6. Bedard, K., & Krause, K. H. (2007). The NOX family of ROS-generating NADPH oxidases: physiology and pathophysiology. *Physiological reviews*, *87*(1), 245-313.
7. Vousden, K. H., & Lane, D. P. (2007). p53 in health and disease. *Nature reviews Molecular cell biology*, *8*(4), 275-283.

Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

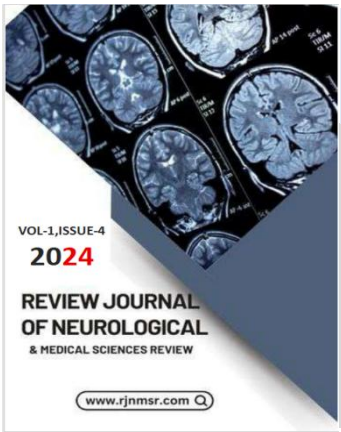
8. Daiber, A., & Münzel, T. (2020). Special Issue" Impact of environmental pollution and stress on redox signaling and oxidative stress pathways". *Redox Biology*, *37*.
9. Zhao W, Robbins ME. Inflammation and chronic oxidative stress in radiation-induced late normal tissue injury: therapeutic implications. Curr Med Chem. 2009;16(2):130-43. doi: 10.2174/092986709787002790. PMID: 19149566.
10. Moriconi, C., Di Castro, M. A., Fucile, S., Eusebi, F., & Grassi, F. (2010). Mechanism of verapamil action on wild-type and slow-channel mutant human muscle acetylcholine receptor. *Journal of neurochemistry*, *114*(4), 1231-1240.
11. Gupta, A., Beg, M., Kumar, D., Shankar, K., Varshney, S., Rajan, S., ... & Gaikwad, A. N. (2017). Chronic hyper-leptinemia induces insulin signaling disruption in adipocytes: Implications of NOS2. *Free Radical Biology and Medicine*, *112*, 93-108.
12. Jenner, P., & Olanow, C. W. (1996). Oxidative stress and the pathogenesis of Parkinson's disease. *Neurology*, *47*(6_suppl_3), 161S-170S.
13. Dutta, D., Kundu, M., Mondal, S., Roy, A., Ruehl, S., Hall, D. A., & Pahan, K. (2019). RANTES-induced invasion of Th17 cells into substantia nigra potentiates dopaminergic cell loss in MPTP mouse model of Parkinson's disease. *Neurobiology of disease*, *132*, 104575.
14. Faria, A., et al. (2014). *The role of oxidative stress in hypertension*. Hypertension Research, 37(4), 243–250. https://doi.org/10.1038/hr.2013.124
15. Hori, M., & Nishida, K. (2009). Oxidative stress and left ventricular remodelling after myocardial infarction. *Cardiovascular research*, *81*(3), 457-464.
16. Sosa, V., Moliné, T., Somoza, R., Paciucci, R., Kondoh, H., & LLeonart, M. E. (2013). Oxidative stress and cancer: an overview. *Ageing research reviews*, *12*(1), 376–390. https://doi.org/10.1016/j.arr.2012.10.004
17. Jakuš, V., & Rietbrock, N. (2004). Advanced glycation end-products and the progress of diabetic vascular complications. *Physiological research*, *53*(2), 131-142.
18. Roberts, C. K., & Sindhu, K. K. (2009). Oxidative stress and metabolic syndrome. *Life sciences*, *84*(21-22), 705–712. https://doi.org/10.1016/j.lfs.2009.02.026
19. Sahiner, U. M., Birben, E., Erzurum, S., Sackesen, C., & Kalayci, O. (2011). Oxidative stress in asthma. *The World Allergy Organization journal*, *4*(10), 151–158. https://doi.org/10.1097/WOX.0b013e318232389e
20. Brewer, S. M., Brubaker, S. W., & Monack, D. M. (2019). Host inflammasome defense mechanisms and bacterial pathogen evasion strategies. *Current opinion in immunology*, *60*, 63-70.
21. Alscher, R. G., Erturk, N., & Heath, L. S. (2002). Role of superoxide dismutases (SODs) in controlling oxidative stress in plants. *Journal of experimental botany*, *53*(372), 1331-1341.

Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

22. Cao, C., Leng, Y., & Kufe, D. (2003). Catalase activity is regulated by c-Abl and Arg in the oxidative stress response. *Journal of Biological Chemistry*, *278*(32), 29667-29675.
23. Ahmadzada, T., Kao, S., Reid, G., Boyer, M., Mahar, A., & Cooper, W. A. (2018). An update on predictive biomarkers for treatment selection in non-small cell lung cancer. *Journal of Clinical Medicine*, *7*(6), 153.
24. Veillet, F., Perrot, L., Guyon-Debast, A., Kermarrec, M. P., Chauvin, L., Chauvin, J. E., ... & Nogué, F. (2020). Expanding the CRISPR toolbox in P. patens using SpCas9-NG variant and application for gene and base editing in solanaceae crops. *International Journal of Molecular Sciences*, *21*(3), 1024.
25. Bendich, A., Machlin, L. J., Scandurra, O., Burton, G. W., & Wayner, D. D. M. (1986). The antioxidant role of vitamin C. *Advances in Free Radical Biology & Medicine*, *2*(2), 419-444.
26. Liebler, D. C. (1993). The role of metabolism in the antioxidant function of vitamin E. *Critical reviews in toxicology*, *23*(2), 147-169.
27. Boelsma, E., & Kloek, J. (2010). IPP-rich milk protein hydrolysate lowers blood pressure in subjects with stage 1 hypertension, a randomized controlled trial. *Nutrition Journal*, *9*, 1-7.
28. Judge, M. P., Casavant, S. G., Dias, J. A., & McGrath, J. M. (2016). Reduced DHA transfer in diabetic pregnancies: mechanistic basis and long-term neurodevelopmental implications. *Nutrition Reviews*, *74*(6), 411-420.
29. Kelly, G. S. (1998). Clinical applications of N-acetylcysteine. *Alternative medicine review: a journal of clinical therapeutic*, *3*(2), 114-127.
30. Grebinyk, A., Grebinyk, S., Prylutska, S., Ritter, U., Matyshevska, O., Dandekar, T., & Frohme, M. (2018). C60 fullerene accumulation in human leukemic cells and perspectives of LED-mediated photodynamic therapy. *Free Radical Biology and Medicine*, *124*, 319-327.
31. Sarter, B. (2002). Coenzyme Q10 and cardiovascular disease: a review. *Journal of Cardiovascular Nursing*, *16*(4), 9-20.
32. Bray, T. M. (1999). Antioxidants and oxidative stress in health and disease: introduction. *Proceedings of the Society for experimental biology and Medicine*, *222*(3), 195-195.
33. Khalil, H. (2012). The effect of antioxidant supplements for preventing mortality in patients with various diseases. *Australian Pharmacist*, *31*(5), 370.
34. Alpha-Tocopherol Beta Carotene Cancer Prevention Study Group. (1994). The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *New England Journal of Medicine*, *330*(15), 1029-1035.
35. Cheng, P., Wang, L., Ning, S., Liu, Z., Lin, H., Chen, S., & Zhu, J. (2018). Vitamin E intake and risk of stroke: a meta-analysis. *British journal of nutrition*, *120*(10), 1181-1188.



Vol. 2 No. 4 (2024): October - December
https://rjnmsr.com/index.php/rjnmsr/about

Review Journal of Neurological & Medical Sciences Review

E(ISSN) : 3007-3073
P(ISSN) : 3007-3065

36. Rütti, S., & Widmann, C. (2015). Genetics and molecular biology: HDL plasticity and diversity of functions. *Current opinion in lipidology*, *26*(6), 596-597.