EURASIAN EXPERIMENT JOURNAL OF BIOLOGICAL SCIENCES (EEJBS)
ISSN: 2992-4138 ©EEJBS Publications
Volume 6 Issue 2 2025

Oxidative Stress in Non-Communicable Diseases: A Unified Pathogenic Link and Target for Therapeutic Intervention

Fabiola Mwendwa G.

School of Applied Health Sciences Kampala International University Uganda

ABSTRACT

Non-communicable diseases (NCDs) such as cardiovascular diseases, diabetes mellitus, cancer, chronic respiratory diseases, and neurodegenerative disorders are the leading causes of mortality and morbidity globally. Although diverse in their clinical manifestations, these conditions share a common pathogenic mechanism-oxidative stress. Oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms, leading to cellular and molecular damage. This review synthesizes current evidence linking oxidative stress with the pathophysiology of major NCDs, focusing on the molecular mechanisms, signaling pathways, and biological consequences involved. The review also highlights the role of oxidative stress in initiating and sustaining chronic inflammation, endothelial dysfunction, mitochondrial impairment, and genetic instability. Moreover, it explores therapeutic strategies targeting oxidative stress, including the use of antioxidants, modulation of redox-sensitive transcription factors (such as Nrf2 and NF-κB), lifestyle interventions, and emerging pharmacological agents. Despite the promise of antioxidant therapy, clinical outcomes have been inconsistent, pointing to the complexity of redox biology in human disease. A deeper understanding of disease-specific redox dynamics and the development of targeted redox modulators may pave the way for personalized medicine approaches in managing NCDs. Overall, oxidative stress represents not only a unifying pathogenic thread in NCDs but also a compelling target for therapeutic intervention and preventive health strategies.

Keywords: Oxidative stress, Non-communicable diseases, Reactive oxygen species, Antioxidant therapy, Redox signaling

INTRODUCTION

Non-communicable diseases (NCDs) represent a growing public health crisis, accounting for over 70% of global deaths annually [1]. These chronic conditions—including cardiovascular diseases, diabetes mellitus, cancer, chronic respiratory diseases, and neurodegenerative disorders—share complex and multifactorial pathophysiologies [1]. Despite differences in organ systems and clinical outcomes, many of these diseases converge on a central, unifying mechanism: oxidative stress. Oxidative stress arises when the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) exceeds the capacity of the body's antioxidant defenses, resulting in a redox imbalance [2]. This imbalance disrupts cellular homeostasis and leads to oxidative damage to essential biomolecules such as lipids, proteins, and nucleic acids. The consequences of oxidative stress span inflammation, mitochondrial dysfunction, apoptosis, and genomic instability, all of which contribute to the onset and progression of NCDs [3]. Understanding the role of oxidative stress in disease etiology and progression not only enhances our knowledge of NCDs but also opens new avenues for therapeutic intervention. This review explores the mechanisms of oxidative stress, its involvement in major NCDs, and emerging therapeutic strategies aimed at restoring redox balance.

2. Oxidative Stress and Its Biological Implications

Reactive oxygen species, such as superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radicals (•OH), are naturally generated as byproducts of mitochondrial oxidative phosphorylation and other metabolic processes [4]. While low to moderate levels of ROS serve essential physiological roles in cell signaling, immune responses, and homeostasis, excessive accumulation can overwhelm antioxidant defenses and cause cellular injury [5].

Antioxidant systems counteract ROS to maintain redox equilibrium [6]. These include enzymatic antioxidants like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as non-enzymatic antioxidants such as glutathione (GSH), vitamin C, and vitamin E [6]. When the balance is disrupted, oxidative stress occurs, leading to lipid peroxidation, oxidative DNA lesions, and protein dysfunction. These molecular insults initiate signaling cascades that perpetuate tissue damage, inflammation, fibrosis, and apoptosis as hallmarks of many NCDs.

3. Oxidative Stress in Major Non-Communicable Diseases

3.1 Cardiovascular Diseases (CVDs)

Cardiovascular diseases are closely linked with oxidative stress, which plays a central role in endothelial dysfunction, hypertension, atherosclerosis, and myocardial infarction [7]. In vascular tissues, ROS scavenge nitric oxide (NO), reducing its bioavailability and impairing vasodilation [8]. This promotes vascular stiffness and hypertension. Enzymes such as NADPH oxidase and xanthine oxidase, as well as dysfunctional mitochondria, are key contributors to ROS generation in the cardiovascular system [9]. ROS also promote oxidation of low-density lipoprotein (LDL), a critical early event in the formation of atherosclerotic plaques [10]. Chronic oxidative stress triggers inflammatory signaling and smooth muscle proliferation, culminating in plaque instability and increased risk of acute coronary events [11].

3.2 Diabetes Mellitus

Oxidative stress is both a cause and consequence of chronic hyperglycemia in diabetes mellitus. Elevated glucose levels increase ROS production through multiple biochemical pathways, including the polyol pathway, protein kinase C (PKC) activation, increased formation of advanced glycation end-products (AGEs), and enhanced mitochondrial superoxide production [12]. These oxidative processes impair insulin signaling, disrupt β-cell function, and promote systemic inflammation. Furthermore, oxidative damage to renal, neural, and retinal tissues contributes significantly to the microvascular complications associated with diabetes, such as diabetic nephropathy, neuropathy, and retinopathy [13].

3.3 Neurodegenerative Diseases

Neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS) are characterized by progressive neuronal loss and functional decline, with oxidative stress playing a central etiological role [14]. Neurons are particularly vulnerable to oxidative damage due to their high metabolic demand, lipid-rich membranes, and relatively low antioxidant capacity [15]. Mitochondrial dysfunction, impaired metal homeostasis, and activation of microglia contribute to excessive ROS in the central nervous system [15]. In Alzheimer's disease, oxidative stress accelerates the aggregation of amyloid-β and hyperphosphorylation of tau protein, both of which are neurotoxic [17]. In Parkinson's disease, oxidative damage to dopaminergic neurons is a key feature of disease progression [18].

3.4 Cancer

Oxidative stress exhibits a dual role in cancer biology. On one hand, elevated ROS levels can induce oxidative DNA damage, leading to mutations, genomic instability, and the activation of oncogenes [19]. On the other hand, excessive ROS may trigger programmed cell death in malignant cells, offering therapeutic opportunities [20]. Tumor cells often upregulate antioxidant pathways to maintain ROS at levels that favor growth and survival [21]. The transcription factor Nrf2, a master regulator of antioxidant response, is frequently hyperactivated in cancer, allowing tumor cells to adapt to oxidative stress [22]. These redox adaptations also contribute to resistance against chemotherapy and radiotherapy.

3.5 Chronic Respiratory Diseases

Chronic respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD) are driven in part by oxidative injury [23]. Environmental pollutants, cigarette smoke, and recurrent infections induce persistent ROS generation in airway epithelial cells and immune cells [24]. Oxidative stress enhances mucus secretion, promotes epithelial damage, and remodels the airway architecture [25]. It also contributes to steroid resistance, a major therapeutic challenge in managing chronic airway inflammation. The interplay between oxidative stress and chronic inflammation amplifies disease severity and exacerbation frequency.

4. Therapeutic Strategies Targeting Oxidative Stress

The recognition of oxidative stress as a unifying pathological mechanism in non-communicable diseases has prompted significant interest in developing therapeutic strategies to restore redox homeostasis. These interventions aim to reduce ROS production, enhance antioxidant defenses, and modulate redox-sensitive signaling pathways. However, translating this understanding into effective therapies has proven complex, requiring a deeper appreciation of redox biology in health and disease.

4.1 Antioxidant Supplementation

Conventional antioxidant therapy has focused on dietary and pharmacological supplementation with compounds like vitamins C and E, beta-carotene, selenium, and glutathione precursors [26]. These agents neutralize free radicals and support endogenous antioxidant enzymes. While preclinical studies and observational data have shown some promise, randomized controlled trials in humans have yielded inconsistent and often disappointing results. For example, large-scale trials like the HOPE and ATBC studies failed to show significant benefits of vitamin E and beta-carotene in preventing cardiovascular or cancer-related outcomes [27]. Several factors contribute to this therapeutic gap, including poor bioavailability, inappropriate dosing, disease heterogeneity, and a lack of specificity in targeting ROS at their site of generation. Moreover, excessive antioxidant intake may disrupt physiological redox signaling and impair normal cellular functions [28]. Therefore, antioxidant therapy must be approached with caution and tailored to individual redox profiles.

4.2 Modulation of Redox-Sensitive Pathways

A more sophisticated approach involves targeting redox-sensitive molecular pathways. Key transcription factors such as nuclear factor erythroid 2–related factor 2 (Nrf2) and nuclear factor-kappa B (NF-κB) regulate the expression of antioxidant and pro-inflammatory genes, respectively [29]. Nrf2 activation enhances cellular defenses against oxidative injury by upregulating genes involved in glutathione synthesis, detoxification, and repair enzymes [30]. Compounds like sulforaphane (from cruciferous vegetables) and synthetic agents like bardoxolone methyl have shown promise in activating Nrf2 pathways in experimental models of diabetes, kidney disease, and cancer [31]. Conversely, inhibition of NF-κB, which is activated by ROS and promotes chronic inflammation, is being explored as a therapeutic strategy in diseases such as atherosclerosis and rheumatoid arthritis [32]. Curcumin, resveratrol, and other polyphenols exhibit both antioxidant properties and the ability to modulate redox-sensitive gene expression, offering a dual mechanism of action [33].

4.3 Mitochondria-Targeted Antioxidants

Given that mitochondria are a primary source of ROS in many chronic diseases, targeting antioxidants directly to these organelles has emerged as a promising approach. Mitochondria-targeted antioxidants, such as MitoQ (a coenzyme Q10 derivative) and SkQ1, are designed to accumulate selectively in mitochondria via lipophilic cationic carriers [34]. These agents have demonstrated efficacy in reducing mitochondrial oxidative damage in models of neurodegeneration, cardiovascular disease, and aging-related dysfunction. They offer improved specificity and reduced systemic toxicity compared to conventional antioxidants.

4.4 Lifestyle and Nutritional Interventions

Lifestyle modification remains a cornerstone in managing oxidative stress in NCDs. Regular physical activity enhances endogenous antioxidant capacity and mitochondrial function [35]. Conversely, a sedentary lifestyle promotes oxidative imbalance and inflammation [36]. Dietary patterns rich in natural antioxidants—such as the Mediterranean and DASH (Dietary Approaches to Stop Hypertension) diets—are associated with reduced oxidative stress biomarkers and lower incidence of NCDs [37]. Foods rich in polyphenols, flavonoids, and carotenoids, such as berries, nuts, green tea, olive oil, and dark leafy greens, offer protective effects by modulating redox-sensitive signaling and promoting detoxification pathways [33]. Smoking cessation, reduced alcohol intake, and weight management further support redox balance and overall metabolic health.

5. Challenges and Future Directions

Despite extensive research into oxidative stress and antioxidant therapy, clinical translation has remained challenging. A key limitation lies in the dualistic nature of ROS, which can be both damaging and essential for normal physiological processes. Non-specific ROS scavenging may blunt necessary signaling pathways involved in immune responses, cell proliferation, and apoptosis [38]. Therefore, therapeutic strategies must aim to restore, rather than abolish, physiological redox signaling. Another major challenge is the heterogeneity of oxidative stress across different NCDs, disease stages, and individuals. What constitutes beneficial antioxidant therapy in one context may be ineffective or harmful in another. The lack of reliable biomarkers to assess redox status in real time further hampers personalized treatment strategies. Future research must prioritize the development of disease-specific and patient-specific redox biomarkers, such as oxidized lipids, DNA adducts, or glutathione ratios, to guide therapeutic interventions.

Advances in omics technologies, particularly redox proteomics, metabolomics, and transcriptomics offer tools to map the redox landscape of NCDs and identify molecular targets for intervention. Additionally, emerging strategies such as gene therapy to enhance antioxidant enzyme expression, CRISPR-based redox gene editing, and nanotechnology for targeted antioxidant delivery hold promise for more precise and durable outcomes.

Clinical trials evaluating redox-modulating therapies should incorporate stratification based on oxidative stress levels and genetic polymorphisms affecting redox metabolism (e.g., Nrf2, SOD2 variants). This personalized approach could maximize therapeutic efficacy while minimizing adverse effects. Oxidative stress remains a central pathogenic mechanism and an attractive target for therapeutic intervention in NCDs. However, a paradigm shift from generic antioxidant use to targeted, systems-based, and patient-centered redox modulation is essential for future progress. With refined tools and deeper biological understanding, redox-based strategies could play a transformative role in combating the global burden of non-communicable diseases.

CONCLUSION

Oxidative stress serves as a central pathogenic mechanism across diverse NCDs, linking inflammation, metabolic dysfunction, and tissue degeneration. While targeting oxidative stress presents a compelling therapeutic avenue, success depends on a nuanced understanding of redox homeostasis in specific disease contexts. Future efforts should prioritize personalized interventions and translational research to harness redox modulation in combating the global burden of NCDs.

REFERENCES

1. World Health Organization. Noncommunicable diseases. 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases
2. Uhuo E N, Egba S I, Nwuke P C, Obike C A and Kelechi G K. Antioxidative properties of Adansonia digitata L. (baobab) leaf extractexert protective effect on doxorubicin induced cardiac toxicity in Wistar rats. Clinical Nutrition Open Science 2022; 45:3-16
3. Egba, S.I., Ademola C F and Omoruyi L E (2021) Bucholzia coriacea seed extract attenuates mercury induced cerebral and cerebellar oxidative neurotoxicity via NO signalling and suppression of oxidative stress, adenosine deaminase and acetylcholinesterase activities in rats. Avicenna J Phytomed. 2022 Jan-Feb;12(1):42-53. doi: 10.22038/AJP.2021.18262. PMID: 35145894; PMCID: PMC8801217.
4. Alum EU, Uti DE, Offor CE. Redox Signaling Disruption and Antioxidants in Toxicology: From Precision Therapy to Potential Hazards. *Cell Biochem Biophys* (2025). https://doi.org/10.1007/s12013-025-01846-8
5. Liu S, Liu J, Wang Y, Deng F, Deng Z. Oxidative stress: signaling pathways, biological functions, and disease. MedComm. 2025;6(7). doi:10.1002/mco2.70268
6. Jomova K, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, Valko M. Several lines of antioxidant defense against oxidative stress: antioxidant enzymes, nanomaterials with multiple enzyme-mimicking activities, and low-molecular-weight antioxidants. Archives of Toxicology. 2024;98(5):1323–67. doi:10.1007/s00204-024-03696-4
7. Steven S, Frenis K, Oelze M, Kalinovic S, Kuntic M, Jimenez MTB, et al. Vascular inflammation and oxidative stress: major triggers for cardiovascular disease. Oxidative Medicine and Cellular Longevity. 2019;2019:7092151. doi:10.1155/2019/7092151
8. Lubos E. Role of oxidative stress and nitric oxide in atherothrombosis. Frontiers in Bioscience. 2008;13:5323. doi:10.2741/3084
9. Moris D, Spartalis M, Spartalis E, Karachaliou GS, Karaolanis GI, Tsourouflis G, et al. The role of reactive oxygen species in the pathophysiology of cardiovascular diseases and the clinical significance of myocardial redox. Annals of Translational Medicine. 2017;5(16):326. doi:10.21037/atm.2017.06.27
10. Ochulor Okechukwu C., Njoku Obioma U., Uroko Robert I and Egba Simeon I. Nutritional composition of *Jatropha tanjorensis* leaves and effects of its aqueous extract on carbon tetrachloride induced oxidative stress in male Wistar albino rats. Biomedical Research 2018; 29(19): 3569-3576
11. Kibel A, Lukinac AM, Dambic V, Juric I, Selthofer-Relatic K. Oxidative stress in ischemic heart disease. Oxidative Medicine and Cellular Longevity. 2020;2020:6627144. doi:10.1155/2020/6627144
12. Giacco F, Brownlee M. Oxidative stress and diabetic complications. Circulation Research. 2010;107(9):1058–70. doi:10.1161/CIRCRESAHA.110.223545
13. Rodríguez ML, Pérez S, Mena-Mollá S, Desco MC, Ortega ÁL. Oxidative stress and microvascular alterations in diabetic retinopathy: future therapies. Oxidative Medicine and Cellular Longevity. 2019;2019:4940825. doi:10.1155/2019/4940825
14. Egba, S Ikechukwu, Okonkwo C Onyinye, Ogbodo J Onyebuchi and Ezeh V Nzubechukwu Neuroprotective Potentials of *Alstonia boonei* extracts on Biochemical Markers of Brain Integrity in Experimental Rats, Trop J Nat Prod Res, 2021; 5(6): 1106-1109. doi.org/10.26538/tjnpr/v5i6.21
15. Jové M, Mota-Martorell N, Obis È, Sol J, Martín-Garí M, Ferrer I, et al. Lipid adaptations against oxidative challenge in the healthy adult human brain. Antioxidants. 2023;12(1):177. doi:10.3390/antiox12010177
16. Cheng H, Yang B, Ke T, Li S, Yang X, Aschner M, et al. Mechanisms of metal-induced mitochondrial dysfunction in neurological disorders. Toxics. 2021;9(6):142. doi:10.3390/toxics9060142

17. Tamagno E, Guglielmotto M, Vasciaveo V, Tabaton M. Oxidative stress and β-amyloid in Alzheimer's disease. Which comes first: the chicken or the egg? Antioxidants. 2021;10(9):1479. doi:10.3390/antiox10091479
18. Dias V, Junn E, Mouradian MM. The role of oxidative stress in Parkinson's disease. Journal of Parkinson's Disease. 2013;3(4):461–91. doi:10.3233/jpd-130230
19. Alum, E.U., Nwuruku, A.O. and Edwin, N. Targeting Oxidative Stress in Cancer Management: The Role of Antioxidant Phytochemicals. KIU J. Health Sci., 4(2): 1-10. https://doi.org/10.59568/KJHS-2024-4-2-01
20. Akwari, A.A., Okoroh, P.N., Aniokete, U.C., Abba, J.N., Uti, D.E. Phytochemicals as modulators of ferroptosis: a novel therapeutic avenue in cancer and neurodegeneration. *Mol Biol Rep* **52**, 636 (2025). https://doi.org/10.1007/s11033-025-10752-4
21. Arfin S, Jha NK, Jha SK, Kesari KK, Ruokolainen J, Roychoudhury S, et al. Oxidative stress in cancer cell metabolism. Antioxidants. 2021;10(5):642. doi:10.3390/antiox10050642
22. De La Vega MR, Chapman E, Zhang DD. NRF2 and the hallmarks of cancer. Cancer Cell. 2018;34(1):21–43. doi:10.1016/j.ccell.2018.03.022
23. Agarwal AK, Raja A, Brown BD. Chronic obstructive pulmonary disease. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559281/
24. Bezerra FS, Lanzetti M, Nesi RT, Nagato AC, Silva CPE, Kennedy-Feitosa E, et al. Oxidative stress and inflammation in acute and chronic lung injuries. Antioxidants. 2023;12(3):548. doi:10.3390/antiox12030548
25. Kim HR, Ingram JL, Que LG. Effects of oxidative stress on airway epithelium permeability in asthma and potential implications for patients with comorbid obesity. Journal of Asthma and Allergy. 2023;16:481–99. doi:10.2147/jaa.s402340
26. Kalogerakou T, Antoniadou M. The role of dietary antioxidants, food supplements and functional foods for energy enhancement in healthcare professionals. Antioxidants. 2024;13(12):1508. doi:10.3390/antiox13121508
27. Cook NR, Albert CM, Gaziano JM, Zaharris E, MacFadyen J, Danielson E, et al. A randomized factorial trial of vitamins C and E and beta carotene in the secondary prevention of cardiovascular events in women. Archives of Internal Medicine. 2007;167(15):1610. doi:10.1001/archinte.167.15.1610
28. Jena AB, Samal RR, Bhol NK, Duttaroy AK. Cellular red-ox system in health and disease: the latest update. Biomedicine & Pharmacotherapy. 2023;162:114606. doi:10.1016/j.biopha.2023.114606
29. He F, Ru X, Wen T. NRF2, a transcription factor for stress response and beyond. International Journal of Molecular Sciences. 2020;21(13):4777. doi:10.3390/ijms21134777
30. Ma Q. Role of NRF2 in oxidative stress and toxicity. Annual Review of Pharmacology and Toxicology. 2013;53(1):401–26. doi:10.1146/annurev-pharmtox-011112-140320
31. Tanase DM, Gosav EM, Anton MI, Floria M, Isac PNS, Hurjui LL, et al. Oxidative stress and NRF2/KEAP1/ARE pathway in diabetic kidney disease (DKD): new perspectives. Biomolecules. 2022;12(9):1227. doi:10.3390/biom12091227
32. Mittal M, Siddiqui MR, Tran K, Reddy SP, Malik AB. Reactive oxygen species in inflammation and tissue injury. Antioxidants and Redox Signaling. 2013;20(7):1126–67. doi:10.1089/ars.2012.5149
33. Ahmed M. Targeting aging pathways with natural compounds: a review of curcumin, epigallocatechin gallate, thymoquinone, and resveratrol. Immunity & Ageing. 2025;22(1). doi:10.1186/s12979-025-00522-y
34. Jiang Q, Yin J, Chen J, Ma X, Wu M, Liu G, et al. Mitochondria-targeted antioxidants: a step towards disease treatment. Oxidative Medicine and Cellular Longevity. 2020;2020:8837893. doi:10.1155/2020/8837893
35. Simioni C, Zauli G, Martelli AM, Vitale M, Sacchetti G, Gonelli A, et al. Oxidative stress: role of physical exercise and antioxidant nutraceuticals in adulthood and aging. Oncotarget. 2018;9(24):17181–98. doi:10.18632/oncotarget.24729
36. Gungor-Orhan I, Akin S, Powers SK, Olgaz-Bingol S, Demirel HA. Sedentary lifestyle induces oxidative stress and atrophy in rat skeletal muscle. Experimental Physiology. 2025. doi:10.1113/ep092331
37. Aleksandrova K, Koelman L, Rodrigues CE. Dietary patterns and biomarkers of oxidative stress and inflammation: a systematic review of observational and intervention studies. Redox Biology. 2021;42:101869. doi:10.1016/j.redox.2021.101869

38. Bardaweel SK, Gul M, Alzweiri M, Ishaqat A, ALSalamat HA, Bashatwah RM. Reactive oxygen species: the dual role in physiological and pathological conditions of the human body. Eurasian Journal of Medicine. 2018;50(3):193–201. doi:10.5152/eurasianjmed.2018.17397
39. Sharifi-Rad M, Kumar NVA, Zucca P, Varoni EM, Dini L, Panzarini E, et al. Lifestyle, oxidative stress, and antioxidants: back and forth in the pathophysiology of chronic diseases. Frontiers in Physiology. 2020;11. doi:10.3389/fphys.2020.00694

Fabiola Mwendwa G. Oxidative Stress in Non-Communicable Diseases: A Unified Pathogenic Link and Target for Therapeutic Intervention. EURASIAN EXPERIMENT JOURNAL OF BIOLOGICAL SCIENCES, 6(2):91-96.