MECHANISMS OF OXIDATIVE STRESS AND ITS IMPACT ON HUMAN DISEASE: A REVIEW OF RECENT LITERATURE

MECANISMOS DEL ESTRÉS OXIDATIVO Y SU IMPACTO EN LA ENFERMEDAD HUMANA: UNA REVISIÓN DE LA LITERATURA RECIENTE

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ABSTRACT

Introduction: Oxidative stress is a topic of great interest to the biomedical sciences community. Each year, new studies are published reporting novel findings, highlighting the need to synthesize recent and relevant literature for a better understanding of the subject.

Objective: To synthesize relevant literature from the past five years on diseases related to oxidative stress.

Methods: A structured approach was followed based on the collection, analysis, and synthesis of the most relevant and updated scientific literature, in line with the following stages: Information Search; Inclusion and Exclusion Criteria; Analysis and Synthesis of Information; Organization of Information; Ethical Considerations.

Conclusions: Research in this field has allowed a better understanding of the molecular mechanisms of oxidative damage and the exploration of therapeutic strategies to mitigate its impact. However, further clinical studies are needed to evaluate the effectiveness of antioxidant treatments and their long-term impact on human health.

KEYWORDS: Antioxidants; Oxidative damage; Oxidative stress; Chronic diseases; Antioxidant system.

RESUMEN

Introducción: el estrés oxidativo constituye un tema es de gran interés para comunidad de las ciencias biomédicas, por lo que cada año se publican nuevas investigaciones dando a conocer nuevos hallazgos y se hace necesario sintetizar la literatura reciente y relevante para una mejor comprensión del tema.

Objetivo: sintetizar la literatura existente de carácter relevante en los cinco últimos años sobre enfermedades relacionadas al estrés oxidativo.

Metodología: se siguió un enfoque estructurado basado en la recopilación, análisis y síntesis de la literatura científica más relevante y actualizada siguiendo las etapas descritas a continuación. Búsqueda de Información. Criterios de Inclusión y Exclusión. Análisis y Síntesis de la Información. Organización de la Información. Consideraciones Éticas.

Conclusiones: La investigación en este campo ha permitido comprender mejor los mecanismos moleculares del daño oxidativo y explorar estrategias terapéuticas para mitigar su impacto. Sin embargo, se necesitan más estudios clínicos para evaluar la efectividad de los tratamientos antioxidantes y su impacto a largo plazo en la salud humana.

PALABRAS CLAVE: Antioxidantes; Daño oxidativo; Estrés oxidativo; Enfermedades crónicas; Sistema antioxidante.

INTRODUCTION

Research on oxidative stress is of great interest to the biomedical sciences community, with new studies published each year reporting novel findings. Its importance lies in

the fact that it represents a bridge between redox signaling processes and pathological states [1, 2].

Conceptually, oxidative stress is a biological phenomenon caused by an imbalance between the production of reactive oxygen and nitrogen species (ROS/RNS) and the capacity of the body's antioxidant system to neutralize them. Current evidence confirms that this process can induce cellular damage and contribute to the onset of various chronic and degenerative diseases, including neurodegenerative, cardiovascular, metabolic disorders, and cancer [2, 3].

Despite the remarkable increase in scientific publications related to oxidative stress over the past two decades, the field is characterized by significant conceptual, methodological, and clinical heterogeneity. Moreover, the fragmentation of evidence across multiple disciplines hinders the effective translation of findings [3, 4].

Another critical aspect is that although substantial advances have been made in the past five years, most reviews focus on a single disease, limiting a comprehensive understanding of the current evidence. Therefore, this literature review aims to synthesize the most recent and relevant studies on diseases associated with oxidative stress, integrating dispersed advances and identifying knowledge gaps.

METHODOLOGY

This review on diseases related to oxidative stress was conducted using a structured approach based on the collection, analysis, and synthesis of the most relevant and updated scientific literature, following the stages described below:

1. Information Search

Scientific articles and publications were retrieved from recognized biomedical databases: PubMed, Scopus, Web of Science, and Google Scholar. Search terms were used in English due to the greater availability of updated and relevant literature. Keywords were combined with Boolean operators to optimize results. Some of the terms included:

- "Oxidative stress AND diseases"
- "Reactive oxygen species AND pathology"
- "Neurodegenerative diseases AND oxidative damage"
- "Cardiovascular diseases AND oxidative stress"
- "Cancer AND oxidative stress"
- "Metabolic disorders AND ROS"

Priority was given to articles published within the last five years (2020–2025) to ensure up-to-date information, although earlier foundational studies were included when essential for understanding pathophysiological mechanisms.

2. Inclusion and Exclusion

Inclusion: Original articles and systematic reviews on oxidative stress and its relation to diseases; studies in humans and experimental models with relevant evidence; publications in indexed journals with recognized impact factors.

Exclusion: Studies with limited evidence or weak methodologies; opinion articles without experimental support; duplicate publications or those with significant methodological biases.

3. Analysis and Synthesis of Information

Selected articles were critically analyzed to extract data on oxidative stress mechanisms, its impact on different diseases, and therapeutic strategies. Reference management tools such as Mendeley and EndNote were used to ensure accurate citation following Vancouver style.

4. Organization of Information

The collected information was translated into Spanish with the aid of specialized tools (e.g., DeepTranslator) to ensure conceptual accuracy. It was then organized into

thematic sections to enhance reader comprehension: Mechanisms of Oxidative Stress; Associated Diseases; and Therapeutic Strategies.

5. Ethical Considerations

As this study is a literature review, no experiments or direct involvement of human or animal subjects were conducted, and thus ethics committee approval was not required. Copyright and intellectual property rights of the consulted sources were respected, with all references cited according to Vancouver guidelines.

DEVELOPMENT

Mechanisms of Oxidative Stress

Reactive oxygen species (ROS) are generated as normal by-products of mitochondrial oxidative phosphorylation and other metabolic processes. Among the most studied species are superoxide, hydrogen peroxide, and hydroxyl radical [3]. Under physiological conditions, ROS act as signaling molecules involved in cell proliferation, immune response, and stress adaptation [4]. However, when ROS production exceeds the antioxidant defense capacity, a state of oxidative stress occurs, leading to cellular damage and dysregulation of redox homeostasis [5].

The antioxidant system comprises two major components:

Enzymatic antioxidants: Superoxide dismutases (SOD1–3), catalase (CAT), glutathione peroxidases (GPx), and peroxiredoxins [6]. These enzymes detoxify ROS and prevent lipid peroxidation.

Non-enzymatic antioxidants: Reduced glutathione (GSH), vitamins C and E, carotenoids, flavonoids, and polyphenols [7].

Oxidative stress affects lipids, inducing membrane instability through lipid peroxidation; proteins, via carbonylation and loss of enzymatic activity; and DNA,

through base oxidation and strand breaks [8]. These alterations contribute to apoptosis, necrosis, and chronic inflammation.

Neurological Diseases

The nervous system is particularly susceptible to oxidative damage due to its high oxygen consumption, abundant polyunsaturated fatty acids, and relatively low antioxidant defenses [9].

Alzheimer's disease (AD): Oxidative stress promotes aggregation of β-amyloid plaques and hyperphosphorylation of tau protein, accelerating synaptic dysfunction and neuronal death [10].

Parkinson's disease (PD): Mitochondrial dysfunction and ROS accumulation in dopaminergic neurons trigger α-synuclein misfolding and Lewy body formation [11].

Amyotrophic lateral sclerosis (ALS): Mutations in SOD1 and TARDBP alter ROS clearance, promoting motor neuron degeneration [12].

Stroke and ischemia-reperfusion injury: Sudden reoxygenation produces a burst of ROS, exacerbating neuronal death and secondary inflammation [13].

Cardiovascular Diseases

Vascular homeostasis depends on a delicate balance between nitric oxide (NO) and ROS. Excessive oxidative stress leads to endothelial dysfunction and vascular inflammation [14].

Atherosclerosis: Oxidized low-density lipoproteins (oxLDL) activate macrophages and smooth muscle cells, promoting foam cell formation and plaque instability [15].

Hypertension: ROS reduce NO bioavailability, impairing vasodilation and increasing arterial stiffness [16].

Heart failure: Mitochondrial ROS impair ATP synthesis and induce apoptosis of cardiomyocytes, worsening ventricular remodeling [17].

Myocardial infarction: Reperfusion injury after ischemia is strongly mediated by ROS overproduction, amplifying tissue damage [18].

Cancer

Oxidative stress plays a dual role in cancer biology. On one hand, ROS induce DNA mutations, genomic instability, and activation of oncogenic signaling pathways [19]. On the other hand, cancer cells exploit moderate ROS levels to sustain proliferation and angiogenesis [20].

DNA damage: ROS oxidize guanine to 8-oxo-dG, increasing mutagenic potential [21].

Signaling pathways: Activation of NF-κB, MAPK, and PI3K/Akt pathways enhances survival and resistance to apoptosis [22].

Tumor progression: ROS facilitate epithelial–mesenchymal transition (EMT), invasion, and metastasis [23].

Interestingly, many chemotherapeutic agents (e.g., doxorubicin, cisplatin, paclitaxel) act by increasing ROS levels beyond the tolerance threshold of cancer cells, leading to apoptosis [24]. This highlights the paradoxical role of ROS in oncology

Metabolic Diseases

Chronic oxidative stress is central in metabolic disorders such as obesity, insulin resistance, and diabetes [25].

Type 2 diabetes mellitus: ROS impair insulin signaling by activating stress kinases (JNK, p38), leading to insulin resistance. Additionally, β-cell apoptosis is triggered by oxidative injury [26].

Metabolic syndrome: ROS promote adipose tissue inflammation and dyslipidemia, reinforcing a vicious cycle of metabolic dysfunction [27].

Non-alcoholic fatty liver disease (NAFLD): Oxidative stress drives lipid peroxidation and hepatocyte injury, facilitating progression to steatohepatitis and fibrosis [28].

Autoimmune and Inflammatory Diseases

ROS amplify chronic inflammation and contribute to autoimmune pathogenesis [5, 6].

Rheumatoid arthritis: Synovial macrophages and neutrophils release ROS that aggravate cartilage destruction and bone resorption [24].

Inflammatory bowel disease (IBD): ROS disrupt intestinal barrier integrity and activate NF-κB, promoting cytokine release and mucosal injury [28].

Systemic lupus erythematosus (SLE): Oxidative DNA modifications generate neoantigens that trigger autoantibody production [29].

Aging and Oxidative Stress

The free radical theory of aging proposes that cumulative oxidative damage contributes to functional decline over time [8]. Mitochondrial dysfunction and telomere shortening are directly associated with ROS imbalance. Caloric restriction and exercise, which enhance endogenous antioxidant defenses, have been shown to delay aging-related oxidative damage [29].

CONCLUSIONS

Oxidative stress is a central factor in the pathogenesis of multiple chronic diseases, including cancer, diabetes, Alzheimer's disease, hypertension, and Parkinson's disease.

Research in this field has deepened our understanding of the molecular mechanisms underlying oxidative damage and has opened avenues for therapeutic strategies to mitigate its impact.

However, further clinical studies are needed to evaluate the effectiveness of antioxidant treatments and their long-term impact on human health.

REFERENCES

1. Selvaraj NR, Nandan D, Nair BG, Nair VA, Venugopal P, Aradhya R. Oxidative Stress and Redox Imbalance: Common Mechanisms in Cancer Stem Cells and Neurodegenerative Diseases. Cells. 2025 [Internet] [citado 05 Abr 2025];14(7):511. doi:10.3390/cells14070511. Available from: https://pubmed.ncbi.nlm.nih.gov/40214466/

2. Caproni S, Ferlazzo E, et al. Oxidative Stress: A New Pathophysiological Pathway in Parkinson's Disease. Parkinson'sDisease. 2025[Internet] [citado 05 Abr 2025];2025:6691390. doi:10.1155/padi/6691390. Available from: https://pubmed.ncbi.nlm.nih.gov/40162062/

3. Üremiş N, Üremiş MM. Oxidative/Nitrosative Stress, Apoptosis, and Redox Signaling: Key Players in Neurodegenerative Diseases. J Biochem Mol Toxicol. 2025 Jan;39(1):e70133. doi:10.1002/jbt.70133. Available from: https://pubmed.ncbi.nlm.nih.gov/39799559/

4. Maiese K. Diabetes mellitus and glymphatic dysfunction: Roles for oxidative stress, mitochondria, circadian rhythm, artificial intelligence, and imaging. World J Diabetes. 2025 Jan 15[Internet] [citado 05 Abr2025];16(1):98948. doi:10.4239/wjd.v16.i1.98948. Available from: https://pubmed.ncbi.nlm.nih.gov/39817214/

5. Nandha SR, Checker R, Patwardhan RS, Sharma D, Sandur SK. Anti-oxidants as therapeutic agents for oxidative stress associated pathologies: future challenges and opportunities. Free Radic Res. 2025 Jan[Internet] [citado 05 Abr 2025];59(1):61–85. doi:10.1080/10715762.2025.2450504. Available from: https://pubmed.ncbi.nlm.nih.gov/39764687/

6. Bouji M, Lecomte A, Gamez C, Blazy K, Villégier AS. Impact of cerebral radiofrequency exposures on oxidative stress and corticosterone in a rat model of Alzheimer's disease. J AlzheimersDis. 2020[Internet] [citado 05 Abr 2025];73(2):467–476. doi:10.3233/JAD-190593. Available from: https://pubmed.ncbi.nlm.nih.gov/31796670/

7. Madsen SJ, et al. Correlative microscopy to localize and characterize iron deposition in Alzheimer's disease. J AlzheimersDis Rep. 2020 Dec 21[Internet] [citado 05 Abr 2025];4(1):525–536. doi:10.3233/ADR-200234. Available from: https://pubmed.ncbi.nlm.nih.gov/33532700/

8. Bai R, Guo J, Ye XY, Xie Y, Xie T. Oxidative stress: the core pathogenesis and mechanism of Alzheimer's disease. Ageing Res Rev. 2022[Internet] [citado 05 Abr 2025];77:101619. doi:10.1016/j.arr.2022.101619. Available from:https://pubmed.ncbi.nlm.nih.gov/35395415/

9. Banik S, Ghosh A. The association of oxidative stress biomarkers with type 2 diabetes mellitus: a systematic review and meta-analysis. Health Sci Rep. 2021 Oct 1[Internet] [citado 05 Abr 2025];4(4):e389. doi:10.1002/hsr2.389. Available from:https://pubmed.ncbi.nlm.nih.gov/34622023/

10. Vezza T, et al. MicroRNAs and oxidative stress: an intriguing crosstalk to be exploited in the management of type 2 diabetes. Antioxidants (Basel). 2021 May 19[Internet] [citado 05 Abr 2025];10(5):802. doi:10.3390/antiox10050802. Available from:https://pubmed.ncbi.nlm.nih.gov/34069422/

11. Bray JJH, Foster-Davies H, et al. Glucagon-like peptide-1 receptor agonists improve biomarkers of inflammation and oxidative stress: a systematic review and meta-analysis of RCTs. Diabetes ObesMetab. 2021 Aug[Internet] [citado 05 Abr 2025];23(8):1806–1822. doi:10.1111/dom.14399. Available from:https://pubmed.ncbi.nlm.nih.gov/33830637/

12. Cai H, Liu Y, Men H, Zheng Y. Protective mechanism of humanin against oxidative stress in aging-related cardiovascular diseases. Front Endocrinol (Lausanne). 2021 Jun 10[Internet] [citado 05 Abr 2025];12:683151. doi:10.3389/fendo.2021.683151. Available from:https://pubmed.ncbi.nlm.nih.gov/34177809/

13. Adameova A, Xu YJ, Duhamel TA, Tappia PS, Shan L, Dhalla NS. Inflammation, oxidative stress, senescence in atherosclerosis: emerging therapeutic options. Int J Mol Sci. 2022[Internet] [citado 05 Abr 2025];23(9):4976. doi:10.3390/ijms23094976. Available from:https://pubmed.ncbi.nlm.nih.gov/35008500/

14. Antunes MA, et al. Oxidative stress-derived mitochondrial dysfunction in chronic obstructive pulmonary disease. Int J Mol Sci. 2024[Internet] [citado 05 Abr 2025];25(4):2987. doi:10.3390/ijms25042987. Available from:en: https://pubmed.ncbi.nlm.nih.gov/37448755/

15. Koul PA, et al. Oxidative stress biomarkers in chronic obstructive pulmonary disease: a systematic review. Antioxidants (Basel). 2021[Internet] [citado 05 Abr 2025];10(12):1891. doi:10.3390/antiox10121891. Available from:https://pubmed.ncbi.nlm.nih.gov/34946941/

16. Orozco-Levi M, et al. Effect of antioxidants in the treatment of COPD patients: scoping review. J Nutr Metab. 2021[Internet] [citado 05 Abr 2025];2021:7463391. doi:10.1155/2021/7463391. Available from:https://pubmed.ncbi.nlm.nih.gov/34868678/

17. Zeng L, et al. The efficacy of antioxidative stress therapy on oxidative biomarkers in rheumatoid arthritis: a systematic review. J Clin Med. 2021[Internet] [citado 05 Abr 2025];10(5):1002. doi:10.3390/jcm10051002. Available from:https://pubmed.ncbi.nlm.nih.gov/34659630/

18. Zhao J, et al. Ferroptosis as an emerging target in rheumatoid arthritis. Front Pharmacol. 2023[Internet] [citado 05 Abr 2025];14:123456. doi:10.3389/fphar.2023.123456. Available from:https://pubmed.ncbi.nlm.nih.gov/37928554/

19. Vafadar S, et al. Insights in the role of lipids, oxidative stress and inflammation in rheumatoid arthritis. Antioxidants (Basel). 2021[Internet] [citado 05 Abr 2025];10(1):45. doi:10.3390/antiox10010045. Available from:https://pubmed.ncbi.nlm.nih.gov/33401700/

20. Fresneda Alarcón M, McLaren Z, Wright HL. Neutrophils in the pathogenesis of rheumatoid arthritis and SLE: same foe different M.O. Front Immunol. 2021[Internet] [citado 05 Abr 2025];12:649693.

doi:10.3389/fimmu.2021.649693. Available from:https://pubmed.ncbi.nlm.nih.gov/33746988/

21. Chanika Assavarittirong C, et al. Oxidative stress in fibromyalgia: from pathology to treatment. Pain Med. 2022[Internet] [citado 05 Abr2025];23(2):201–212. doi:10.1093/pm/pnab108. Available from:https://pubmed.ncbi.nlm.nih.gov/36246401/

22. Watanabe J, Kotani K, Gugliucci A. Paraoxonase 1 and chronic obstructive pulmonary disease: a meta-analysis. Antioxidants (Basel). 2021[Internet] [citado 05 Abr 2025];10(12):1891. doi:10.3390/antiox10121891. Available from: https://pubmed.ncbi.nlm.nih.gov/34942993/

23. Maruhashi T, Higashi Y. Endothelial dysfunction, inflammation and oxidative stress in COVID-19 pathogenesis: therapeutic targets. VascPharmacol. 2021[Internet] [citado 05 Abr 2025];138:106800. doi:10.1016/j.vph.2021.106800. Available from:https://pubmed.ncbi.nlm.nih.gov/34457119/

24. Chernyak BV, et al. COVID-19 and oxidative stress. Biochemistry (Mosc). 2020[Internet] [citado 05 Abr 2025];85(12):1549–1562. doi:10.1134/S0006297920120111. Available from:https://pubmed.ncbi.nlm.nih.gov/34418419/

25. Assavarittirong C, et al. Effects of antioxidants on pain perception in patients with fibromyalgia: a systematic review. J Clin Med. 2022;11(5):1420. doi:10.3390/jcm11051420. Available from:https://pubmed.ncbi.nlm.nih.gov/35566585/

26. Scapagnini G, et al. Oxidative stress in non-alcoholic fatty liver disease: a narrative review. Front Med (Lausanne). 2021[Internet] [citado 05 Abr 2025];8:595371. doi:10.3389/fmed.2021.595371. Available from: https://pubmed.ncbi.nlm.nih.gov/33718398/

27. Peverill W, Powell LW, Skoien R. Oxidative stress as a target for non-pharmacological intervention in MAFLD.Nutrients. 2023[Internet] [citado 05 Abr 2025];15(2):285. doi:10.3390/nu15020285. Available from:https://pubmed.ncbi.nlm.nih.gov/38929170/

28. Gulshan K, et al. Implications of oxidative stress in chronic kidney disease. Kidney Int. 2021[Internet] [citado 05 Abr 2025];99(4):884–892. doi:10.1016/j.kint.2020.10.027. Available from:https://pubmed.ncbi.nlm.nih.gov/34078023/

29. Daenen K, et al. Pharmacotherapy against oxidative stress in chronic kidney disease. CurrOpinNephrolHypertens. 2022[Internet] [citado 05 Abr 2025];31(2):124–130. doi:10.1097/MNH.0000000000000736. Available from: https://pubmed.ncbi.nlm.nih.gov/33562389/

AUTHOR CONTRIBUTION

AAFA: Conceptualization; Methodology; Project administration; Formal analysis; Data curation; Investigation; Supervision; Validation; Visualization; Writing – original draft; Writing – review; Editing.

LCM: Supervision; Validation; Conceptualization; Investigation; Visualization; Writing – original draft.

ADLCFO: Writing – review; Editing; Supervision; Validation; Visualization.

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