Oxidative Stress: Insights into Nutrition, Psychological Stress, Environmental Exposure, and Antioxidants Roles

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Abstract

This comprehensive review describes the intricate realms of oxidative stress, examining its origins in nutrition, psychological stress, environmental exposures, and the vital roles of antioxidants. Nutritional factors, particularly macronutrients and dietary elements, play a dual role in either inducing or preventing oxidative stress, with implications for inflammation, metabolic disorders, and carcinogenesis. The exploration extends to the profound impact of psychological stress, highlighting oxidative imbalance as a "new stress" linked to various diseases, including psychiatric disorders. Environmental exposures, encompassing pollutants and UV radiation, contribute significantly to oxidative stress, emphasizing the need for a comprehensive understanding of these mechanisms. The role of endogenous and exogenous antioxidants is crucial in neutralizing free radicals and maintaining redox homeostasis. This thorough analysis provides insights into potential interventions and underscores the complex relationships between oxidative stress, antioxidants, and human health.

Significance | This review discusses how oxidative stress affects our bodies due to factors like diet, stress, and environment, and how antioxidants help. Understanding this is crucial for fighting diseases like cancer and staying healthy.

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Introduction

The human body, composed of 100 trillion cells engaged in numerous daily reactions, naturally undergoes oxidation by utilizing oxygen to metabolize carbon (Liguori et al., 2018), resulting in oxidative stress. Factors contributing to this stress include inadequate nutrition, chronic psychological stress, environmental pollution, and UV radiation (Kresser, 2018). From inflammation to cancer, oxidative stress, marked by an imbalance in the cell's redox state due to excess reactive oxygen species or malfunctioning antioxidant systems (Gandhi & Abramov, 2012). The consequences may involve damage to cellular components such as DNA, lipids, and proteins. Oxidative stress occurs when there is an imbalance between the formation of free radicals and the cell's capacity to eliminate them. For instance, an excess of hydroxyl radical and peroxynitrite can lead to lipid peroxidation, causing damage to cell membranes and lipoproteins. Cancer initiation and progression have been associated with oxidative stress, contributing to DNA mutations, genome instability, and increased cell proliferation.

In normal biological processes, oxygen (O2) is vital, especially for tissue requirements. Cellular utilization of O2 for energy production generates free radicals as by-products during ATP (adenosine triphosphate) synthesis in the mitochondria.

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Mitochondria, acting as the primary source of endogenous reactive oxygen species (ROS), produce reactive oxygen species (ROS) and reactive nitrogen species (RNS) through cellular redox processes. The electron transport chain, responsible for up to 90 percent of the cell's total O2 consumption, generates reactive oxygen species (ROS) during ATP synthesis, converting O2 to a water molecule as the final electron acceptor through a partial four-electron conversion. Under normal physiological conditions, approximately 0.1–0.5 percent of inhaled O2 is converted to superoxide (O2-) (Tan et al., 2018). Free radicals, unstable atoms capable of causing cellular damage leading to illness and aging, originate from both endogenous and exogenous sources.

1. Nutritional Factors in Oxidative Stress

Diets and nutrition play a dual role in influencing oxidative processes, offering both benefits and potential detriments. Oxidative stress, induced by food intake, is intricately influenced by various factors such as calorie intake, micronutrient forms, antioxidant nutrient intake, and cooking methods. Postprandial oxidative stress emanates primarily from leukocytes and mitochondria, linking it to the persistent occurrence of metabolic and reproductive disorders (Diamanti-Kandarakis et al., 2017). Macronutrients, in excess, may exhibit toxicity and prooxidant properties, contributing to nutritional oxidative stress, defined as a postprandial imbalance between antioxidant protection and prooxidant burden resulting from insufficient or redundant nutrient supply (Saha et al., 2017). The impact of macronutrients on oxidative stress and inflammation is a significant research area, demonstrating that elevated macronutrient doses can trigger oxidative stress through NF-cell signaling pathways (Jia et al., 2013). Notably, dietary carbohydrates, especially those with a high glycemic index (GI) or glycemic load (GL), are implicated in long-term inflammation and the development of conditions like obesity, diabetes, coronary heart disease, and cancer (Piya et al., 2013; Tan et al., 2018). Persistent inflammation resulting from oxidative stress can lead to DNA damage, escalating the risk of cancer (Manan et al., 2015).

Oxidative metabolism and redox homeostasis are essential components of aerobic life, serving as protective mechanisms against oxygen derivative damage. However, macronutrients, if present in excessive amounts, can become toxic and prooxidant (Diamanti-Kandarakis et al., 2017). Nutritional oxidative stress, defined as a postprandial imbalance between antioxidant protection and prooxidant burden due to insufficient or redundant nutrient supply, is a critical consideration (Saha et al., 2017). In the context of carcinogenesis, nutrition-mediated oxidative stress assumes a central role. Cells undergo stress due to nutrient overload, surpassing typical physiological responses (Wellen & Thompson, 2010). Both nutrient deficiency and excess can result in cellular stress, emphasizing the delicate balance required for optimal health. Table 1 addresses some of the essential dietary components related to oxidative stress following different aspects of carcinogenesis. The intricate interplay between oxidative stress and dietary components is crucial for understanding the multifaceted relationship between nutrition and health.

2. Psychological Stress and Oxidative Imbalance

Chronic and persistent stress are widely acknowledged triggers for various illnesses, yet the intricate mechanisms driving these effects remain incompletely understood. The term "stress," lacking a precise definition, echoes Hans Selye's observation that, although universally known, its true understanding remains elusive. Stress, whether physical, chemical, or emotional, is broadly defined as a factor causing bodily harm and often leading to disease. Emotional stress is associated with anxiety, depression, and cognitive dysfunction, while physiological stress is tied to conditions like hypertension and cardiovascular issues. The emerging prominence of oxidative stress as the "new stress" aligns with reported links between psychological stress and heightened oxidative damage (Salim, S., 2014).

Severe life stress (SLS) is a significant psychosocial event capable of inducing psychological distress, setting it apart from everyday stressors. Studies on SLS's impact on the central nervous system consistently reveal oxidative stress, marked by increased oxidant production and associated damage (Schiavone et al., 2013). This suggests that prolonged exposure to psychological stressors may heighten the risk of various diseases (Wang et al., 2007). The vulnerable brain, with its high oxygen consumption and free radical production, is particularly prone to oxidative damage. This susceptibility extends to specific psychiatric disorders like anxiety, depression, schizophrenia, and bipolar disorder, where oxidative stress disrupts critical cellular processes. Although the association between oxidative stress and psychiatric disorders is established, determining its causal role remains a challenge (Salim, S., 2014). Emphasizing the delicate balance between pro-oxidants and antioxidants, interventions targeting oxidative stress pathways show promise for innovative treatments. Further exploration of the intricate interplay between free radicals, antioxidants, and cellular mechanisms is needed to unveil the precise role of oxidative stress in neuropsychiatric disorders.

3. Environmental Exposures and Oxidative Stress

Environmental exposures play a pivotal role in inducing oxidative stress, a process with profound implications for human health. In industrialized societies, unavoidable inhalation of toxic substances present in the atmosphere poses a significant risk (Aseervatham et al., 2013). Pesticides and heavy metals contribute to oxidative stress, with organophosphate insecticides (OPs) found on conventionally grown produce activating cytochrome P450 enzymes, disrupting cell redox functions, and impairing cellular energy, rendering cells less capable of neutralizing free radicals (Gassman, 2017). Plastics,

Table 1. The role of different dietary elements in oxidative stress and carcinogenic.

Dietary Components	Function in Oxidative Stress	Function in Carcinogenesis
Alcohol	Encourages ROS growth, decreasing the abundance of cellular antioxidants, altering the homeostasis among pro- and anti-oxidants, causing oxidative stress in many tissues.	Highly related to breast tumor. The intake and interaction of alcohol genes and the alcohol metabolism elevate the possibility of breast cancer in postmenopausal female.
Carbohydrates	Leads to elevate possibility of atherosclerosis and associated disorders. High-carbon food will cause a greater oxidative stress reaction postprandial.	This may affect the plasma glucose, insulin, also insulin resistance rates of breast cancer. This could rise the possibility of breast cancer when consuming foods with a high insulinogenic content.
Highly Processed Food	Foods high in refined sugars, artificial additives, and trans fats may contribute to oxidative stress and inflammation	Diet high in processed meats, which are often preserved using methods that involve nitrates and nitrites, is associated with an increased risk of colorectal cancer.
High Animal-Based Proteins	Fermentation of the excessive proteins in the gut produces metabolites such as ammonia (NH3) and hydrogen sulfide (H2S), which are compounds known to trigger the toxicity of the mucosa	Intake of well-done red meat cause the formation of carcinogenic HCA and PAH which cause colorectal cancer

Table 2. The roles of common dietary antioxidants.

Dietary Components	Funtion as Antioxidant
Beta-carotene	Has been reported to inhibit directly or suppress radical species and lipid peroxidation in liposomes, thus act as an antioxidant (Packer et al., 1981)
Selenium (Se)	Selenium functions as an antioxidant primarily through its incorporation into selenoproteins, which play crucial roles in defending cells against oxidative stress (Pham-Huy et al., 2008)
Flavonoids	Act as an exogenous antioxidants and undergo direct oxidation by radicals, leading to the formation of less reactive species through four mechanisms: (1) inhibiting nitric oxide synthase activity, (2) suppressing xanthine oxidase activity, (3) influencing channel pathways, or (4) engaging with other enzyme systems (Nijveldt et al., 2001)
Lycopene	One of the most potent antioxidants among the dietary carotenoids mainly due to its many conjugated double bonds (Krishnamoorthy et al., 2013).
Vitamin C	Provides protection against oxidative stress-induced cellular damage by scavenging of reactive oxygen species (Traber & Stevens, 2011).
Vitamin E	Inhibits the production of reactive oxygen species molecules when fat undergoes oxidation and during the propagation of free radical reactions (Traber & Stevens, 2011).
Omega-3 and omega-6 fatty acids	May provide indirect antioxidant benefits by protecting cell membranes from oxidative damage. Their effects on inflammation and cellular function indirectly contribute to a healthier oxidative state (Pham-Huy et al., 2008).

including the ubiquitous chemical BPA, are also implicated in oxidative stress. Free radicals are created by the activation of cytochrome P450 enzymes in the liver attempts to detoxify BPA, a ubiquitous plastic chemical. BPA's induction of free radicals and oxidative stress is thought to make a substantial contribution to this compound's toxicity and carcinogenicity (Gassman, 2017).

Oxidative stress emerges as a central phenomenon in environmental agent toxicology, encompassing a diverse range of contaminants such as oxidant gases, organic compounds, particulate surfaces, and metal ions. Environmental pollutants induce oxidative stress through direct, indirect, or disruptive effects on metabolic and bioenergetic processes regulated by thiol redox switches in cells (Samet & Wages, 2018). UV radiation represents another environmental factor that contributes to oxidative stress by generating reactive oxygen species (ROS), posing potential adverse health impacts. When ROS production surpasses the body's antioxidant defense mechanisms, oxidative stress intensifies. UV radiation can stimulate ROS either directly or through photosensitization mechanisms that affect cellular components. Specifically, UV light influences the catalase enzyme, up-regulates nitric oxide synthase (NOS) synthesis, and may reduce protein kinase C (PKC) expression, leading to increased ROS production. The alterations in DNA and other chromophores induced by UV radiation further contribute to elevated ROS levels. The consequences of elevated ROS levels vary based on the cell's intracellular oxidant status (de Jager et al., 2017). This intricate interplay between environmental exposures and oxidative stress underscores the need for a comprehensive understanding of these mechanisms to mitigate potential health risks.

4. Antioxidant as Oxidative Stress Neutralizer

Antioxidants, also known as free radical scavengers, are substances that counteract and neutralize free radicals to prevent cellular damage. The body relies on both endogenous (produced within the body) and exogenous (derived from external sources) antioxidants to combat free radicals. While endogenous antioxidants are internally generated, external sources, particularly diet, contribute significantly to the body's antioxidant pool. Dietary antioxidants are abundant in vegetables, fruits, grains, and are also available as nutritional supplements (Bouayed & Bohn, 2010). Common antioxidants as shown in Table 2 includes beta-carotene, lycopene, and vitamins A, C, and E (alpha-tocopherol). Selenium, classified as a food-based antioxidant, predominantly exerts its antioxidant effects through selenoproteins and enzymes, serving as essential components that counteract peroxides, thereby preventing tissue and DNA damage, inflammation, and associated health issues (Davis et al., 2012).

The mechanism of antioxidants involves neutralizing free radicals by donating electrons. However, this process oxidizes the antioxidant itself, necessitating a continuous replenishment of antioxidant reserves in the body. The effectiveness of a particular antioxidant can vary across different biological systems, and under certain conditions, an antioxidant may exhibit prooxidant properties, generating toxic reactive oxygen species/reactive nitrogen species (ROS/RNS) (Young & Woodside, 2001). Antioxidants can interrupt free radical chain reactions through a process known as the antioxidant cycle. When a free radical steals or releases an electron, it forms the next radical, perpetuating the chain until a chain-breaking antioxidant stabilizes the radical or it transforms into a harmless substance. Lipid peroxidation, a common consequence of oxidative stress, exemplifies such chain reactions (Pham-Huy et al., 2008).

On the other hand, preventing oxidation through antioxidant enzymes is crucial in curbing free radicals and balancing transitional metal radicals like copper and iron. Enzymes such as superoxide dismutase, catalase, and glutathione peroxidase play essential roles in neutralizing oxidative stress (Young & Woodside, 2001). The role of dietary antioxidants is significant in supporting endogenous antioxidants to counteract oxidative stress, preventing various chronic and degenerative diseases linked to nutrient antioxidant deficiencie (Willcox et al., 2004). Each nutrient possesses a unique structure and antioxidant function, emphasizing the importance of a well-balanced and nutrient-rich diet.

5. Conclusion

In conclusion, oxidative stress, stemming from nutrition, psychological stress, environmental exposures, and the interplay of antioxidants, plays a pivotal role in human health. The intricate processes involved, from cellular oxidation to DNA damage, underscore the multifaceted nature of this phenomenon. Factors like dietary choices, chronic stress, and environmental pollutants contribute to oxidative imbalance, influencing various diseases, including cancer. Antioxidants, both endogenous and exogenous, emerge as crucial players in neutralizing free radicals and maintaining redox homeostasis. Understanding the delicate balance between oxidative stress and antioxidants provides insights into potential interventions for mitigating health risks. The complex relationships explored in this comprehensive overview highlight the need for continued research to unravel the precise mechanisms and develop targeted strategies for promoting optimal well-being.

Author contribution

R.B.S.M.N conceptualized, funding acquisition, review & editing. Safany I., drafted, wrote. Saravanan C., edited the article. All authors contributed and read the manuscrpt before publication.

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Competing financial interests

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References

Anon. (2020). Distinguishing benign and malignant growth _ EdCaN (p. 1). Australia Goverment Cancer Australia.

Aseervatham, G. S. B., Sivasudha, T., Jeyadevi, R., & Arul Ananth, D. (2013). Environmental factors and unhealthy lifestyle influence oxidative stress in humans--an overview. In Environmental science and pollution research international (Vol. 20, Issue 7, pp. 4356–4369). https://doi.org/10.1007/s11356-013-1748-0

Bouayed, J., & Bohn, T. (2010). Exogenous antioxidants - Double-edged swords in cellular redox state: Health beneficial effects at physiologic doses versus deleterious effects at high doses. In Oxidative Medicine and Cellular Longevity (pp. 228–237). https://doi.org/10.4161/oxim.3.4.12858

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians, 68(6), 394-424.

Cooper, G. M., & Hausman, R. E. (2007). The Development and Causes of Cancer. The Cell: A Molecular Approach. https://doi.org/10.1016/j.pbb.2009.09.001

Davis, C. D., Tsuji, P. A., & Milner, J. A. (2012). Selenoproteins and Cancer Prevention. Annual Review of Nutrition, 32, 73–95. https://doi.org/10.1146/annurev-nutr-071811-150740

de Jager, T. L., Cockrell, A. E., & Du Plessis, S. S. (2017). Ultraviolet light induced generation of reactive oxygen species. In Advances in Experimental Medicine and Biology (Vol. 996, pp. 15–23). Springer New York LLC. https://doi.org/10.1007/978-3-319-56017-5_2

Diamanti-Kandarakis, E., Papalou, O., Kandaraki, E. A., & Kassi, G. (2017). Nutrition as a mediator of oxidative stress in metabolic and reproductive disorders in women. In European Journal of Endocrinology (Vol. 176, Issue 2, pp. R79–R99). BioScientifica Ltd. https://doi.org/10.1530/EJE-16-0616

Gandhi, S., & Abramov, A. Y. (2012). Mechanism of oxidative stress in neurodegeneration. In Oxidative Medicine and Cellular Longevity (pp. 1–11). Hindawi Limited. https://doi.org/10.1155/2012/428010

Gassman, N. R. (2017). Induction of oxidative stress by bisphenol A and its pleiotropic effects. In Environmental and Molecular Mutagenesis (Vol. 58, Issue 2, pp. 60–71). John Wiley and Sons Inc. https://doi.org/10.1002/em.22072

Jia, Q. Q., Wang, J. C., Long, J., Zhao, Y., Chen, S. J., Zhai, J. D., Wei, L. B., Zhang, Q., Chen, Y., & Long, H. B. (2013). Sesquiterpene lactones and their derivatives inhibit high glucose-induced NF-κB activation and MCP-1 and TGF-β1 expression in rat mesangial cells. Molecules, 18(10), 13061–13077. https://doi.org/10.3390/molecules181013061

Koju, N., Taleb, A., Zhou, J., Lv, G., Yang, J., Cao, X., Lei, H., & Ding, Q. (2019). Pharmacological strategies to lower crosstalk between nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and mitochondria. In Biomedicine and Pharmacotherapy (Vol. 111, pp. 1478–1498). Elsevier Masson SAS. https://doi.org/10.1016/j.biopha.2018.11.128

Kresser, C. (2018). What really causes oxidative damage. In Kresser Institute (p. 1).

Krishnamoorthy, G., Selvakumar, K., Venkataraman, P., Elumalai, P., & Arunakaran, J. (2013). Lycopene supplementation prevents reactive oxygen species mediated apoptosis in Sertoli cells of adult albino rats exposed to polychlorinated biphenyls. Interdisciplinary Toxicology, 6(2), 83-92.

Liguori, I., Russo, G., Curcio, F., Bulli, G., Aran, L., Della-Morte, D., Gargiulo, G., Testa, G., Cacciatore, F., Bonaduce, D., & Abete, P. (2018). Oxidative stress, aging, and diseases. In Clinical Interventions in Aging (Vol. 13, pp. 757–772). Dove Medical Press Ltd. https://doi.org/10.2147/CIA.S158513

Manan, A. A., Tamin, N. S. I., Abdullah, N. H., & Wahab, M. (2015). The Malaysian National Cancer Registry Report (MNCR) 2007-2011 – From the Desk of the Director-General of Health Malaysia (pp. 2007–2011).

Nagao, M., Honda, M., Seino, Y., Yahagi, T., & Sugimura, T. (1977). Mutagenicities of smoke condensates and the charred surface of fish and meat. Cancer Letters, 2(4–5), 221–226. https://doi.org/10.1016/S0304-3835(77)80025-6

Nijveldt, R. J., Van Nood, E. L. S., Van Hoorn, D. E., Boelens, P. G., Van Norren, K., & Van Leeuwen, P. A. (2001). Flavonoids: a review of probable mechanisms of action and potential applications. The American journal of clinical nutrition, 74(4), 418-425.

OSU. (2001). Selenium | Linus Pauling Institute | Oregon State University. In Linus Pauling Institute (p. Magnesium).

Pham-Huy, L. A., He, H., & Pham-Huy, C. (2008). Free radicals, antioxidants in disease and health. In International Journal of Biomedical Science (pp. 89–96).

Packer, J. E., Mahood, J. S., Mora-Arellano, V. O., Slater, T. F., Willson, R. L., & Wolfenden, B. S. (1981). Free radicals and singlet oxygen scavengers: reaction of a peroxy-radical with β-carotene, diphenyl furan and 1, 4-diazobicyclo (2, 2, 2)-octane. Biochemical and biophysical research communications, 98(4), 901-906.

Piya, M. K., McTernan, P. G., & Kumar, S. (2013). Adipokine inflammation and insulin resistance: The role of glucose, lipids and endotoxin. In Journal of Endocrinology (Vol. 216, Issue 1, pp. T1–T15). https://doi.org/10.1530/JOE-12-0498

Ricordi, C., Garcia-Contreras, M., & Farnetti, S. (2015). Diet and inflammation: possible effects on immunity, chronic diseases, and life span. Journal of the American College of Nutrition, 34(sup1), 10-13.

Rizzo, A. M., Berselli, P., Zava, S., Montorfano, G., Negroni, M., Corsetto, P., & Berra, B. (2010). Endogenous antioxidants and radical scavengers. Advances in Experimental Medicine and Biology, 698, 52–67. https://doi.org/10.1007/978-1-4419-7347-4_5

Saha, S. K., Lee, S. Bin, Won, J., Choi, H. Y., Kim, K., Yang, G. M., Dayem, A. A., & Cho, S. G. (2017). Correlation between oxidative stress, nutrition, and cancer initiation. In International Journal of Molecular Sciences (Vol. 18, Issue 7, p. 1544). MDPI AG. https://doi.org/10.3390/ijms18071544

Salim, S. (2014). Oxidative stress and psychological disorders. Current neuropharmacology, 12(2), 140-147.

Samet, J. M., & Wages, P. A. (2018). Oxidative stress from environmental exposures. In Current Opinion in Toxicology (Vol. 7, pp. 60–66). Elsevier B.V. https://doi.org/10.1016/j.cotox.2017.10.008

Schiavone, S., Jaquet, V., Trabace, L., & Krause, K. H. (2013). Severe life stress and oxidative stress in the brain: From animal models to human pathology. Antioxidants and Redox Signaling, 18(12), 1475–1490. https://doi.org/10.1089/ars.2012.4720

Tan, B. L., Norhaizan, M. E., Liew, W. P. P., & Rahman, H. S. (2018). Antioxidant and oxidative stress: A mutual interplay in age-related diseases. In Frontiers in Pharmacology (Vol. 9, Issue OCT, p. 1162). Frontiers Media S.A. https://doi.org/10.3389/fphar.2018.01162

Traber, M. G., & Stevens, J. F. (2011). Vitamins C and E: beneficial effects from a mechanistic perspective. Free radical biology and medicine, 51(5), 1000-1013.

Wang, L., Muxin, G., Nishida, H., Shirakawa, C., Sato, S., & Konishi, T. (2007). Psychological stress-induced oxidative stress as a model of sub-healthy condition and the effect of TCM. Evidence-Based Complementary and Alternative Medicine, 4(2), 195–202. https://doi.org/10.1093/ecam/nel080

Wang, Y., Chun, O. K., & Song, W. O. (2013). Plasma and dietary antioxidant status as cardiovascular disease risk factors: A review of human studies. In Nutrients (Vol. 5, Issue 8, pp. 2969–3004). MDPI AG. https://doi.org/10.3390/nu5082969

Wellen, K. E., & Thompson, C. B. (2010). Cellular Metabolic Stress: Considering How Cells Respond to Nutrient Excess. In Molecular Cell (pp. 323–332). https://doi.org/10.1016/j.molcel.2010.10.004

Young, I. S., & Woodside, J. V. (2001). Antioxidants in health and disease. In Journal of Clinical Pathology (pp. 176–186). https://doi.org/10.1136/jcp.54.3.176