https://doi.org/10.70882/mq18cm66

SCIENCE FORUM (JOURNAL OF PURE AND APPLIED SCIENCES) 26, (4) (2026), 737 - 755

Science Forum (Journal of Pure and Applied Sciences)

Journal Homepage: https://atbuscienceforum.com.ng/index.php/jpas

Oxidative Stress and Its Role in Human Disease: Molecular Mechanisms, Biochemical Biomarkers, and Therapeutic Perspectives; as Review Article

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Abstract

Oxidative stress is a dynamic imbalance in cellular redox homeostasis caused by an excess production, accumulation and/or localization of reactive oxygen species (ROS) and/or reactive nitrogen species (RNS) relative to the ability of antioxidant, repair and adaptive systems. At low to moderate concentrations, ROS and RNS are not themselves toxic; they play a role in several signaling, host defense, metabolic, vascular regulatory, and adaptation processes. However, pathological redox imbalance can lead to lipid peroxidation, protein oxidation, damage of nucleic acids, mitochondrial dysfunction, inflammation, changes in cell signaling, senescence and regulated cell death. This review summarizes the most recent research regarding biochemical sources of ROS/RNS, antioxidant defense, glutathione and thiol redox regulation, KEAP1-NRF2 signaling, oxidation of lipids, proteins and DNA, mitochondrial dysfunction, ferroptosis and how redox imbalance contributes to diabetes, cardiovascular, neurodegenerative, hepatic, renal, inflammatory and malignant diseases. Special attention is paid to oxidative stress biomarkers and their analytical shortcomings, and the fact that none of the biomarkers is sufficient to reflect the multidimensional redox state. Current therapeutic strategies such as dietary and pharmacological antioxidants, NRF2 modulation, glutathione directed therapies, mitochondria targeted antioxidants and selective modulation of ROS producing enzymes are critically discussed. The review concludes that future redox medicine should focus on restoration of redox homeostasis in a compartment specific fashion, as opposed to the elimination of reactive species in a non-specific manner, using biomolecules as indicators.

Keywords

Oxidative Stress;
Reactive Oxygen Species;
Reactive Nitrogen Species;
Redox Homeostasis;
Antioxidants; Glutathione;
NRF2;
Biomarkers.

EISSN: 3156-5190 (Online)
ISSN: 1119-4618 (Print)
JPAS
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1. Introduction

Oxidation–reduction reaction is an integral part of life when oxygen is present in the system. Reactive species are constantly generated in mitochondrial respiration, NADPH oxidases, peroxisomal metabolism, endoplasmic-reticulum processes, inflammatory reactions and a number of oxidoreductases. At physiological concentrations, these species act as signaling intermediates, and play a role in immune defence and metabolic adaptation. Oxidative stress is therefore more likely to be viewed as imbalance in a well-regulated oxidant generating-antioxidant recovery and repair mechanism [1-6] rather than merely the presence of free radicals.

Recent studies have corroborated the notion of context dependent redox biology. Depending on what the state of cellular defenses is, the effect of a reactive species will depend on its concentration, lifetime, subcellular location, chemical reactivity and the state of cellular defenses. These factors are responsible for the variable clinical effects of antioxidant supplementation in the general population and the new trend in antioxidant research to correct redox imbalances and pathological oxidant sources [7–10].

This current review combines biochemical mechanisms, disease associations, disease biomarkers, analysis issues, and therapeutic opportunities. It also serves as a valuable guide to new fields like the biomarkers of NRF2, redox proteomics, ferroptosis, spatial redox biology, and precision redox medicine [11–15].

2. Review Methodology

This article is a structured review, which is a narrative review with systematic elements. The source manuscript was critically reorganised, duplicate references were deleted and recent literature from PubMed indexed publications and authoritative reporting guidance were added. Searches were targeted on oxidative stress, ROS, RNS, redox homeostasis, NRF2/KEAP1, glutathione, oxidative stress biomarkers, mitochondrial dysfunction, ferroptosis, antioxidant therapy and major chronic diseases. Peer-reviewed reviews and studies published from 2020 to 2026 that were clinically or mechanistically informative were given priority, as were selected, earlier literature that was needed for biochemical concepts.

The structure is in line with reproducible evidence reporting, for transparency. PRISMA is used as a reporting aid in this manuscript, which details a narrative/structured review rather than a systematic review with quantitative synthesis, but PRISMA has been used as a reporting framework in systematic reviews, and as a claim for registration of a systematic review and meta-analysis [16].

Table 1. Search Strategy, Eligibility Criteria, and Evidence-Synthesis Framework Used in the Structured Narrative Review

Element	Approach
Databases	PubMed; literature indexed through major biomedical databases
Core period	2020–2026, with selected foundational sources when necessary
Concepts	ROS/RNS; redox homeostasis; antioxidants; NRF2; biomarkers; mitochondria; ferroptosis; disease
Priority	Peer-reviewed reviews, mechanistic studies, clinical biomarker evidence
Exclusions	Duplicated references, non-peer-reviewed material, and sources without sufficient bibliographic information
Synthesis	Biochemical mechanisms, disease links, biomarker utility/limitations, and therapeutic translation

3. Biochemical Basis of Oxidative Stress

3.1 Redox Homeostasis

Redox homeostasis is a dynamic equilibrium between generation of oxidants, reduction reactions, antioxidants, repair systems and elimination of damaged molecules. Maintenance of a reducing intracellular environment is a vital function of the glutathione system, thioredoxin and the NADPH system. The GSH/GSSG ratio can be very useful but is very dependent on the conditions of sample collection and analysis, and should be used in conjunction with other markers [17–20].

3.2 Reactive Oxygen Species

The major ROSs present are superoxide ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2), hydroxyl radical ($^{\bullet}OH$), peroxyl radicals, alkoxyl radicals, and singlet oxygen. Mitochondrial leakage of electrons, oxidoreductases, such as NOX enzymes, are the sources of superoxide. SOD reduces O_2^- to H_2O_2, which is then dealt with by catalase, glutathione peroxidases and peroxiredoxins. In particular, the formation of hydroxyl radical is very harmful due to its short diffusion length and high reactivity [1,18,21].

3.3 Reactive Nitrogen Species

Nitric oxide is a product of nitric oxide synthases which are physiological signaling molecules. Peroxynitrite could be formed when superoxide meets nitric oxide, which could lead to the oxidation and nitration of proteins, lipids and nucleic acids. Oxidative and nitrosative stress are thus two processes that are linked to each other and not independent [2,22].

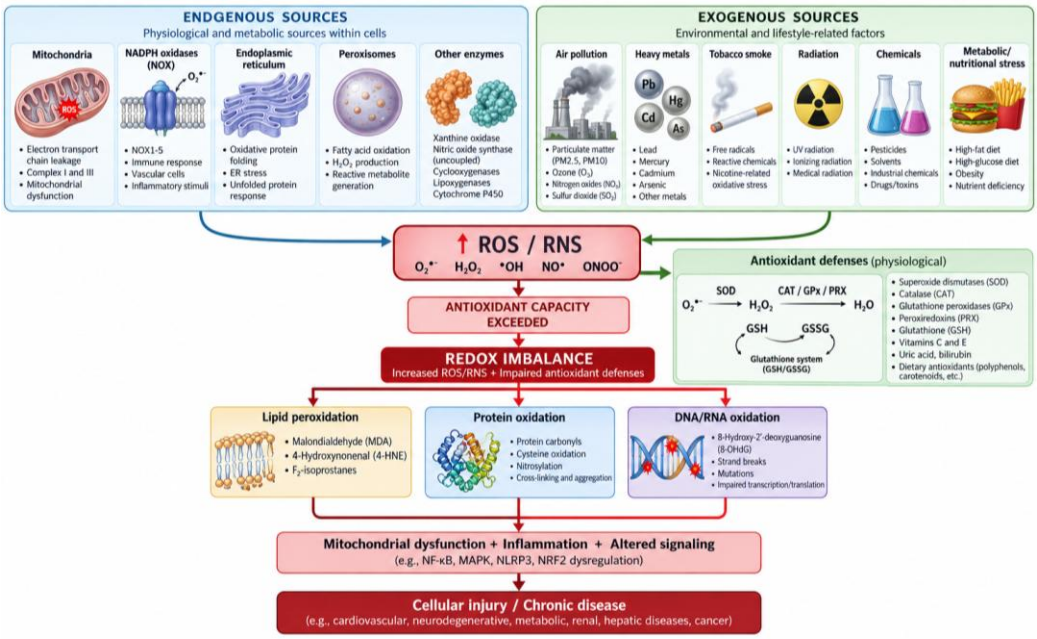

Figure 1. Major endogenous and exogenous sources of ROS/RNS and the progression toward redox imbalance. The diagram is a conceptual synthesis based on the reviewed literature.

4. Cellular Sources of Reactive Species

4.1 Mitochondria

Mitochondria are both producers and consumers of ROS. Excessive oxidant production in the mitochondria can be caused by excessive nutrient supply, changes in the potential, hypoxia/reoxygenation, inflammation, and ageing, and the leakage of electrons during oxidative phosphorylation. Oxidative damage to mitochondrial DNA, proteins, lipids and respiratory complexes could result in further damage of respiratory function and lead to a vicious cycle of exacerbation [23–26].

4.2 NADPH Oxidases

NOX enzymes are specific sources of ROS. The products they produce are involved in signaling, vascular regulation, antimicrobial defense and inflammatory responses. Dysregulated and overactive NOX activity have been linked to cardiovascular and metabolic disease [27,28].

4.3 Endoplasmic Reticulum, Peroxisomes and Xanthine Oxidase

ER protein folding involves regulated oxidative reactions and excess ER stress may lead to higher ROS levels and to interaction with mitochondrial dysfunction. Catalase is an important local defense in this case, since catalase breaks down H_2O_2, which is produced in the peroxisomes during fatty-acid oxidation. During purine metabolism, xanthine oxidoreductase can generate superoxide and H_2O_2, which can play a role in ischemia/reperfusion and vascular oxidative stress [18,29].

5. Antioxidant Defense Systems

Antioxidant protection is a system of systems. The enzymatic defenses consist of SOD, catalase, glutathione peroxidases, glutathione reductase, and peroxiredoxins. Non-enzymatic defenses are GSH, vitamin C, vitamin E, uric acid, bilirubin and dietary antioxidants. They do not have redundant functions [17,30].

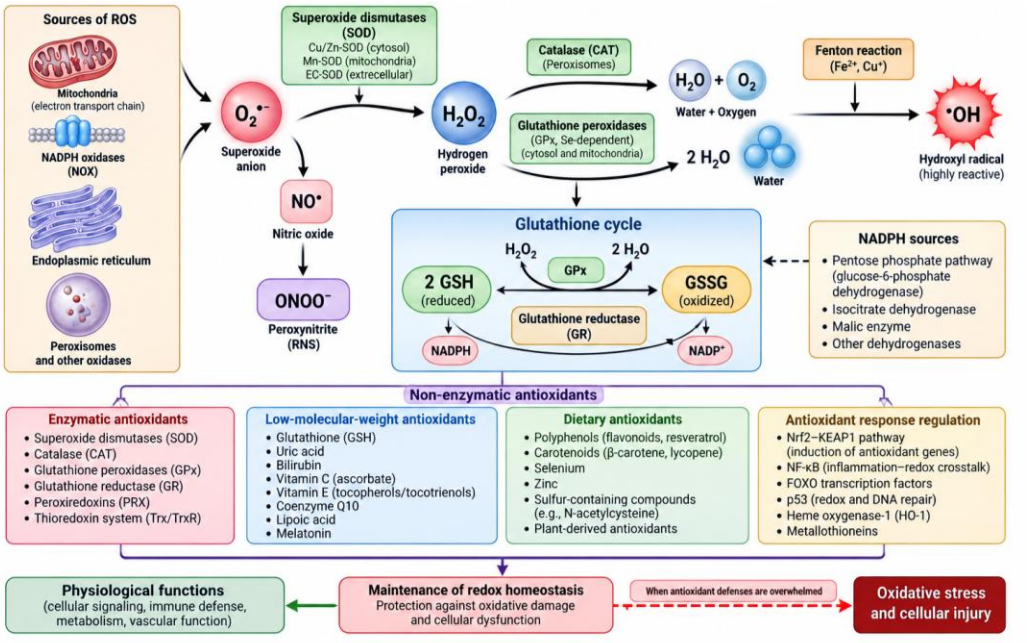

Figure 2. Integrated antioxidant defense network linking superoxide dismutation, peroxide removal, and glutathione recycling.

Table 2. Major Antioxidant Defense Systems, Their Biochemical Functions, and Key Interpretive Considerations

System	Principal function	Major consideration
SOD	Converts $O_2^{\bullet-}$ to H_2O_2	Must be coupled to peroxide-removing systems
Catalase	Converts H_2O_2 to $H_2O + O_2$	High-capacity peroxide removal
GPx	Reduces H_2O_2 and lipid hydroperoxides using GSH	Links antioxidant defense to glutathione
GR	Regenerates GSH from GSSG using NADPH	Maintains reducing capacity
Peroxiredoxins	Remove peroxides and regulate	Important at low H_2O_2

	redox signaling	concentrations
GSH	Major intracellular thiol antioxidant	Sensitive to synthesis, recycling, and compartment
Vitamin C/E	Water- and lipid-phase antioxidant functions	Biological effects depend on context and dose

6. Glutathione and Thiol-Based Redox Regulation

Glutathione is a tripeptide that consists of glutamate, cysteine and glycine. The cysteine sulfohydryl group can reduce the peroxides and preserve the protein thiols. GSH is also involved in the electrophile conjugation by glutathione-S-transferases. The GSH–GPx–GSSG–GR cycle is related to the removal of peroxides and the regeneration of NADPH. In addition to the antioxidant actions, thiol oxidation can also modify signaling proteins in a reversible manner, e.g., by sulfenylation [31-33].

Protein sulfenylation is being recognised as a redox-regulatory modification that is more than just molecular damage. In recent years, controlled oxidation of cysteine has been shown to influence signaling, metabolism, inflammatory processes, and disease processes, highlighting the signaling/damaging properties of ROS [33].

7. Oxidative Damage to Biomolecules

7.1 Lipid Peroxidation

The polyunsaturated fatty acids are oils that are prone to chain reaction oxidation. They are important products such as MDA, 4-HNE, lipid hydroperoxides and F_2-isoprostanes. F_2-isoprostanes are considered to be relatively specific markers of lipid peroxidation, while MDA is considered a general marker which can be influenced by analytical specificity and assay conditions [17,34].

7.2 Protein Oxidation

Protein oxidation can result in the formation of carbonyl groups, oxidized methionine and cysteine residues, disulfide changes, nitration, and sulfenylation. Protein carbonyls are fairly stable markers but cannot encompass all redox modifications [33,35].

7.3 DNA Oxidation

One of the most investigated markers of oxidative DNA damage is 8-hydroxy-2′-deoxyguanosine (8-OHdG/8-oxo-dG). Other oxidative injury effects can also include base modifications, single and double strand breaks, changes in gene expression and genomic instability. The concentrations measured can be materially affected by the analytical and the sampling procedure [17,36].

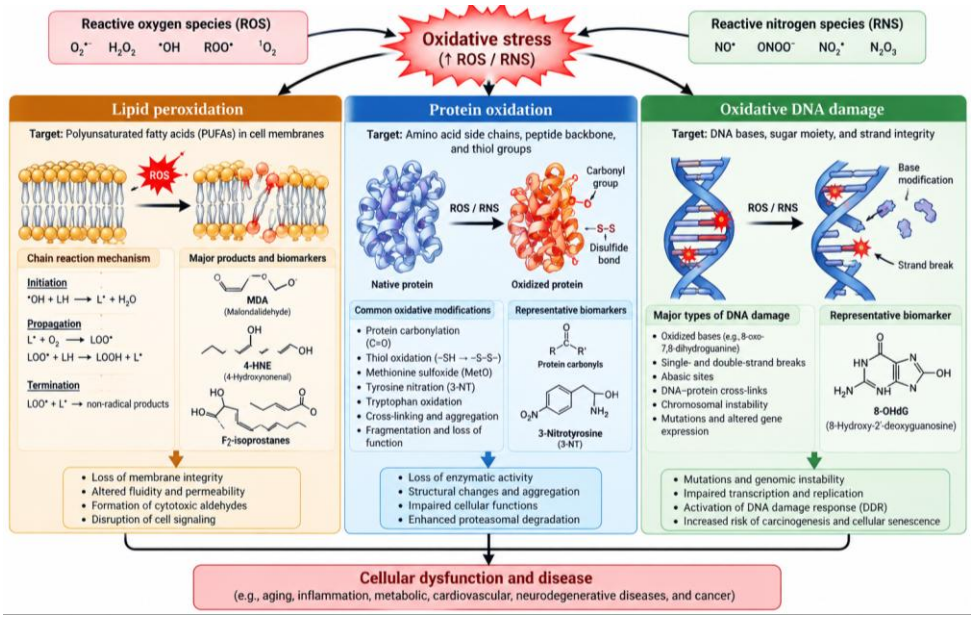

Figure 3. Major molecular consequences of oxidative stress: lipid peroxidation, protein oxidation, and oxidative DNA damage.

8. Oxidative Stress Signaling and the KEAP1–NRF2 Pathway

NRF2 is an important transcriptional regulator of cellular response to electrophilic and oxidative stress. In the basal state, the NRF2 is kept in check by KEAP1 that ubiquitinates and degrades it. The oxidative or electrophilic modification of KEAP1 can lead to the stabilization of NRF2 and its nuclear accumulation and activation of antioxidant response elements. Some key genes associated with NRF2 are NQO1, HMOX1, *GCLC*, *GCLM*, SRXN1 and TXNRD1 [11,37].

Recent studies have highlighted that NRF2 activity should be assessed by measuring multiple target gene/proteins, and not the amount of NRF2 protein. In 2024, a review found that *GCLC*, *GCLM*, HMOX1, NQO1, SRXN1 and TXNRD1 were a good set of genes for measuring NRF2 signaling in a variety of cell and tissue types [11].

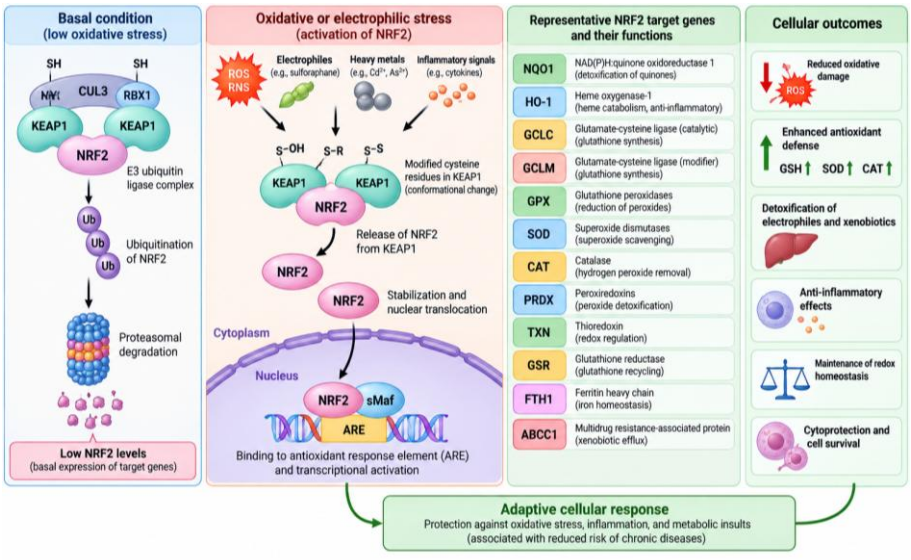

Figure 4. Conceptual KEAP1–NRF2 signaling pathway and representative cytoprotective target genes.

In many normal tissues, NRF2 is a protective player; in cancer, however, sustained activation can lead to a paradoxical role in promoting antioxidant activity, metabolic flexibility, and resistance to therapeutic challenges. NRF2 is protective in many normal tissues but can be detrimental in cancer by maintaining antioxidant activity, metabolic flexibility, and resistance to therapeutic stresses. Therefore, NRF2 should be considered as a context specific therapeutic target, not a path to be pursued in all circumstances [38–40].

9. Oxidative Stress, Mitochondria, Autophagy and Senescence

There is a bidirectional relationship between mitochondrial dysfunction and oxidative stress. Mitochondrial DNA, cardiolipin, respiratory proteins and membranes can be damaged by oxidants which could further contribute to the generation of ROS and a consequent decline in bioenergetic efficiency. Redox imbalance is also associated with other processes such as autophagy and mitochondrial quality control, which could lead to higher oxidative load within a cell in case of failure to remove damaged organelles [23,25,41].

Chronic inflammation and tissue dysfunction can be associated with redox imbalance due to persistent oxidative stress which can lead to cellular senescence and senescence-associated secretory phenotype. These interlinked processes may provide a method to understand why oxidative stress is often seen in seemingly unrelated chronic diseases [42].

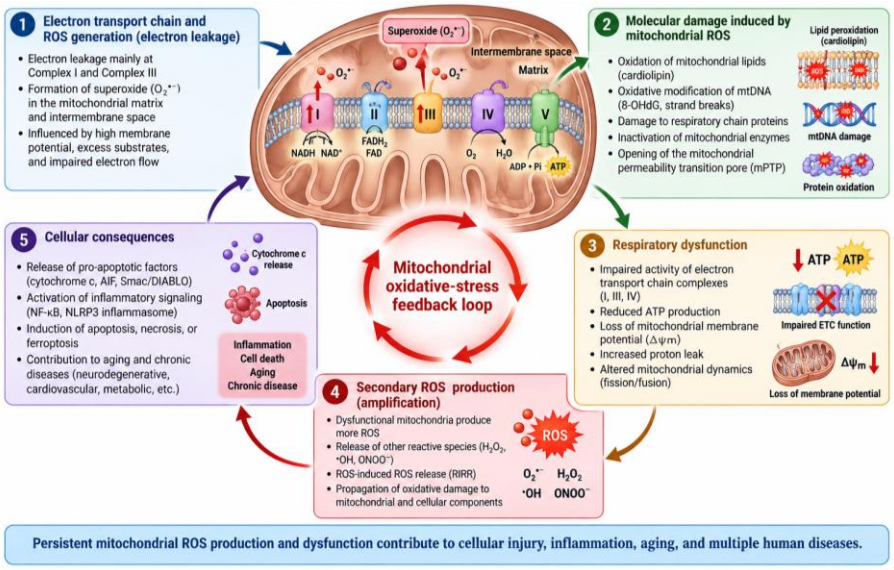

Figure 5. Mitochondrial oxidative-stress feedback loop: electron leakage, molecular damage, respiratory dysfunction, and secondary ROS production. The course is designed to examine the mechanisms and consequences of oxidative stress in major human diseases.

10. Oxidative Stress and Major Human Diseases

10.1 Diabetes and Metabolic Syndrome

Hyperglycemia can lead to increase in ROS via several mechanisms: mitochondrial dysfunction, activation of the polyol pathway, activation of protein kinase C, formation of advanced glycation end products, and the hexosamine pathway. Inflammatory pathways adds to the oxidative pressure, and ROS can disrupt insulin signaling and β-cell function. Oxidative stress remains a mechanism that is still supported by recent reviews as a link between metabolic dysfunction and diabetic complications [43,44].

10.2 cardiovascular disease

In the vasculature, the superoxide can decrease nitric-oxide bioavailability by the formation of peroxynitrite which can lead to endothelial dysfunction. Vascular inflammation and the oxidative modification of LDL can lead to the initiation of atherosclerosis. The research of biomarkers has gone beyond the scope of measuring the overall antioxidant capacity and has started to focus on the targets of oxidation reactions [45,46].

10.3 neurodegenerative diseases

The brain is susceptible to oxidative injury due to the high metabolic rate of oxygen consumption, presence of polyunsaturated lipids and specific metabolic demands. That oxidative stress and mitochondrial dysfunction, protein misfolding, and neuroinflammation, and metal homeostasis are interrelated in Alzheimer's and Parkinson's disease [47–49].

10.4 Liver and Kidney Diseases

As a result of its metabolic and detoxifying functions, the liver is constantly subjected to endogenous and xenobiotic oxidants. Kidney disease involves oxidative stress that is linked to inflammation, endothelial dysfunction, uremic toxins, mitochondrial dysfunction, and dysfunction of the antioxidant defense system [50,51].

10.5 Cancer

Cancer cells have increased oxidative stress. Oxidative stress is often increased in cancer cells. Moderate ROS encourages cell growth and adaptation, while high ROS levels can cause DNA damage and cell death. In the context of oncology, the activation of NRF2 may become beneficial for normal cells, but also for the survival and drug resistance of tumors, depending on the context [38–40].

10.6 Chronic Inflammation and Other Disorders

ROS/RNS and inflammation feed on each other; ROS activation of immune cells leads to production of ROS/RNS, and ROS activation of inflammatory signaling leads to activation of immune cells. The relationship is bi-directional and is significant in inflammatory bowel disease, skin disease, ocular disease and other chronic diseases [52-55].

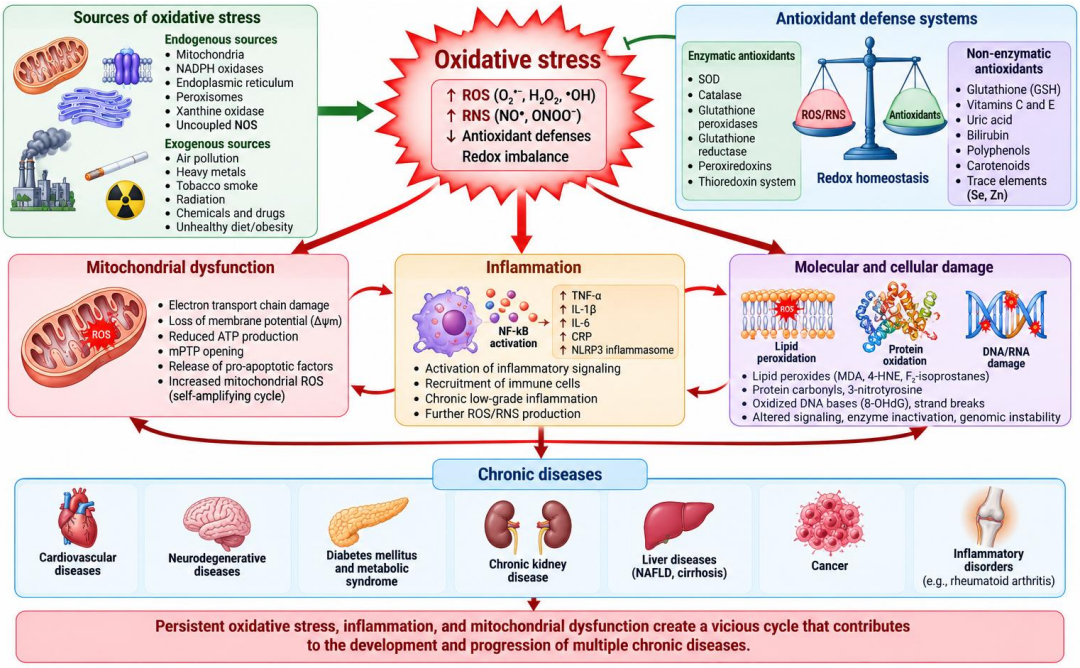

Figure 6. Oxidative stress as a shared biochemical mechanism linking redox imbalance, inflammation, mitochondrial dysfunction, and chronic disease.

Table 3. Major Human Diseases Associated with Oxidative Stress: Principal Redox Mechanisms and Representative Biomarkers

Disease	**Major redox mechanism**	**Representative biomarkers/targets**
Type 2 diabetes	Hyperglycemia, mitochondrial ROS, AGE–RAGE signaling	MDA, 8-OHdG, GSH/GSSG, SOD/GPx
Cardiovascular disease	NOX activation, NO depletion, LDL oxidation	F_2-isoprostanes, oxidized LDL, protein carbonyls
Neurodegeneration	Mitochondrial dysfunction, neuroinflammation	8-OHdG, lipid peroxidation products, GSH
Liver disease	Lipid accumulation and lipid peroxidation	MDA, 4-HNE, GSH, antioxidant enzymes
Kidney disease	Uremic stress, mitochondrial dysfunction, inflammation	MDA, protein carbonyls, GSH/GSSG
Cancer	DNA damage, redox adaptation, NRF2 activation	8-OHdG, NRF2 targets, GSH/GPX4
Chronic inflammation	Immune-cell ROS/RNS and inflammatory signaling	MDA, protein oxidation, antioxidant enzymes

11. Biochemical Biomarkers of Oxidative Stress

Measuring ROS/RNS directly is frequently technically challenging, due to their short term existence and compartmentalization. Therefore, typical markers of oxidative damage or antioxidants are measured and are relatively stable products. Multiparametric approach is more informative than single marker approach [17,56].

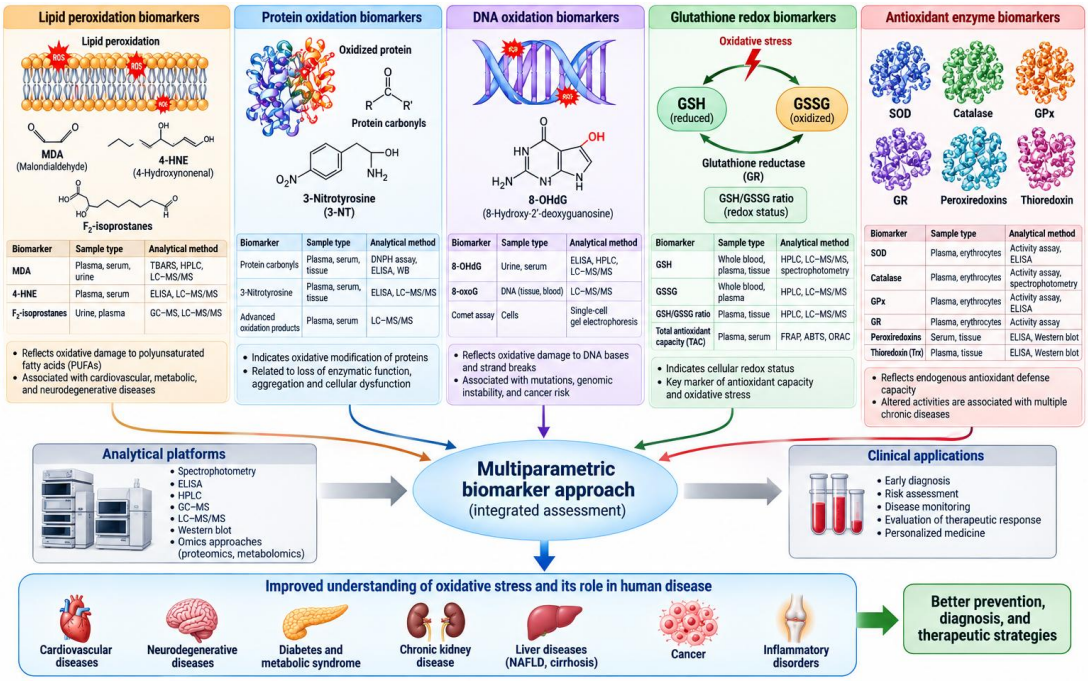

Figure 7. Multiparametric biomarker strategy covering lipid, protein, DNA, glutathione, and enzymatic domains.

Table 4. Biochemical Biomarkers of Oxidative Stress: Molecular Domains, Analytical Strengths, and Key Limitations

Biomarker	Target/domain	Strength	Key limitation
MDA	Lipid peroxidation	Inexpensive; widely used	Limited specificity in some assays
4-HNE	Lipid peroxidation	Biologically active lipid aldehyde	Sampling/analytical complexity
F₂-isoprostanes	Lipid peroxidation	Relatively specific in vivo marker	Specialized instrumentation
Protein carbonyls	Protein oxidation	Relatively stable	Does not capture all PTMs
8-OHdG	DNA oxidation	Widely investigated	Sampling and assay dependence
GSH/GSSG	Cellular redox state	Directly linked to thiol balance	Highly sensitive to handling
SOD/CAT/GPx/GR	Antioxidant response	Functional information	Activity may represent adaptation or dysregulation
NRF2 target genes	Adaptive redox response	Mechanistic information	Requires tissue/cell context

12. Analytical Methods for Oxidative-Stress Biomarkers

Validity of the biomarkers is key in their analytical interpretation. Spectrophotometric assays are available but may be interfered with and are not as specific. ELISA is easy to use for certain protein products, but requires antibody specificity. More certain chemical separation and identification for a few lipid and nucleic-acid oxidation products is provided by HPLC and LC–MS/MS. The sensitivity or specificity of the GC–MS may be very high, but a derivatization may be needed. Site-specific characterization of amino acid oxidation and thiol modifications is possible by using redox proteomics and targeted mass spectrometry, respectively, in growing number and increasing detail [17,33,56].

Pre-analytical variables are of the same importance. Changes in redox sensitive measurements such as GSH/GSSG may occur during sample type, storage at different temperatures, processing time, use of different anticoagulants, freeze–thaw cycles, and exposure to oxygen. Thus, standardization of collection and analytical procedures in biomarker studies should be reported and complementary biomarkers should be used for various molecular domains, if possible.

The aforementioned principle is demonstrated by the rise in use of NRF2 biomarker panels where only measuring one transcription factor is not necessarily a good reflection of pathway activity, but a validated panel of downstream genes/proteins are a better indicator of pathway engagement [11].

13. Ferroptosis and Redox-Dependent Cell Death

Ferroptosis is a regulated cell death that is dependent on iron and involves the build-up of lipid peroxides. This GSH–GPX4 axis is an important protective system as GPX4 will consume lipid hydroperoxides with GSH. Thus GSH depletion or reduced GPX4 activity may lead to an increase in lipid peroxide levels and ferroptosis [57–59].

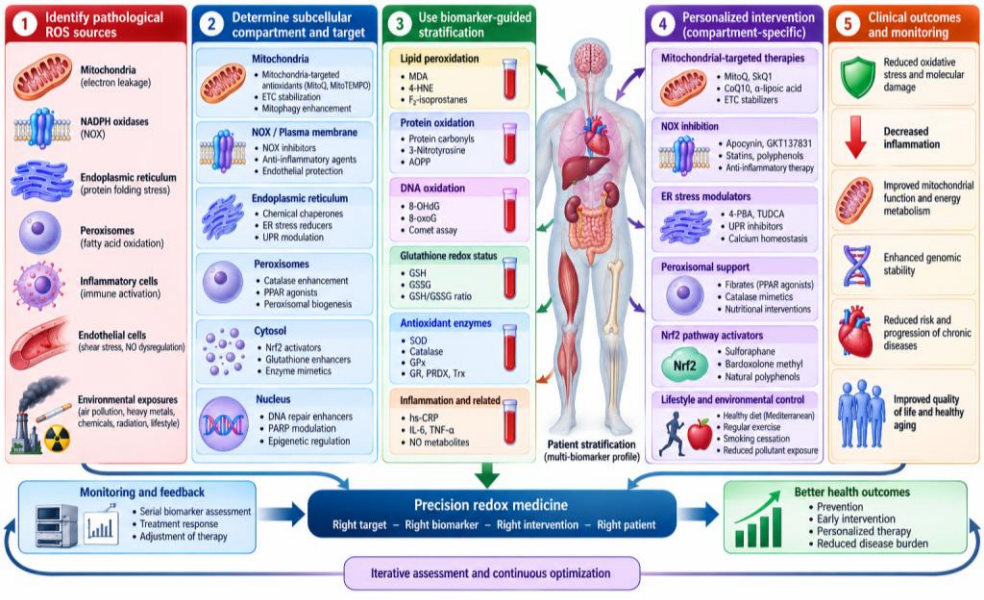

Figure 8. Redox precision-medicine framework linking identification of pathological ROS sources to compartment-specific, biomarker-guided intervention.

14. Therapeutic Perspectives

The therapeutic manipulation of oxidative stress is complex as ROS also play a critical role in normal signaling and host defense. In clinical practice, it has been found that antioxidant supplementation does not always benefit. The efficacy is a function of the dose, bioavailability, state of the disease, distribution in the tissues and targetedness of the involved oxidant source [7,60].

14.1 Dietary Antioxidants and Phytochemicals

There are many vitamins and polyphenols, such as vitamin C, vitamin E, the carotenoids, curcumin, resveratrol, quercetin, epigallocatechin gallate and sulforaphane, which have received extensive study. Several phytochemicals seem to mediate their activity partially via modulation of endogenous signaling as well as by simple direct radical scavenging [61].

14.2 NRF2 Modulation

The activation of NRF2 may increase the levels of antioxidants, cytoprotective mechanisms, enzymes for detoxification and synthesis of glutathione. In some cancers, however, the prolonged activation may be a negative aspect, as NRF2 mediated adaptation may promote both the survival and drug resistance of tumors. However, the blockade of NRF2 selectively in tumors with constitutively activated pathway is being studied [38-40].

14.3 Mitochondria-Targeted Antioxidants

Targeting antioxidants to the mitochondria is an attractive idea since ROS are both sources and targets in the mitochondria. These approaches could offer a higher level of local activity than traditional antioxidants, but would need to be proven to be distributed to the correct tissue and beneficial to patients [25,62].

14.4 Modulating Glutathione and GPX4/Ferroptosis

Regulating the availability of cysteine, GSH synthetic activity, or GPX4 activity or transport systems could affect ferroptosis and redox balance. These strategies are especially important for cancer and neurodegenerative diseases, but must be carefully regulated, as ferroptosis and redox signaling are not only pathological processes, but also play an important role in the biology [57-59].

In general, future interventions should shift from generic antioxidant supplementation to redox precision medicine, which is the identification of the pathological source of the problem, targeting the specific tissue and compartment, choice of a mechanism-specific intervention and monitoring of the molecular response through the use of validated biomarkers [7,60].

15. Critical Discussion

While oxidative stress is a key mechanism that links metabolism, inflammation, mitochondrial dysfunction, molecular damage and chronic diseases, the field should not consider oxidative stress as a single measurable factor. One of the drawbacks is that isolated biomarkers are used as the total redox system. For example, MDA can be used to screen lipid peroxidation, but it is only chemically similar to a measure of ROS

production and not actually ROS. Likewise, the greater the antioxidant-enzyme activity, the better the adaption or the more the stress response is compensating [17,56].

The second big problem is that of cause and effect. Oxidative stress can trigger a disease process, exacerbate an ongoing disease process or merely reflect damage to the tissue. To draw causal inferences, however, the use of longitudinal studies, tissue-specific measurements, mechanistic biomarkers, and intervention studies is warranted. The variable clinical outcomes of antioxidant therapy highlight the importance of compartment-specific and disease-specific therapies [7,63].

A case in point is NRF2. NRF2 protects cells against oxidative stress and cellular injury in healthy cells. However, in certain cancers, the NRF2 is aberrantly active and has the opposite effect, protecting against cell death and resistance to therapy. Thus, the real therapeutic dilemma lies in what, when, and in how much a pathway should be modulated, rather than whether to modulate it in all instances [11,38–40].

16. Limitations and Future Directions

This review is in the form of a structured narrative synthesis, and is not a registered systematic review, formal risk of bias or meta-analysis. There is some heterogeneity in the definitions of biomarkers, sample types, analytical methods, disease stages and clinical endpoints in the literature. These restrictions make it difficult to make direct comparisons between studies.

Future studies should be directed at the following:

- the use of standardized panels of biomarkers;
- longitudinal sampling of biomarkers;
- validated LC–MS/MS and redox-proteomic biomarker measures;
- measures of the biomarkers within the various cellular compartments;
- linkage of redox measures with the other omics (genomics, transcriptomics, proteomics, metabolomics, and lipidomics); and
- redox biomarker-driven clinical trials for redox interventions.

Such strategies can contribute to the next advancement in the science of oxidative stress, one moving from an association to a mechanism-based clinical medicine [11,56].

17. Conclusion

Oxidative stress is a dynamic imbalance in redox homeostasis which connects metabolism, inflammation, mitochondrial dysfunction, cellular signaling, molecular damage and chronic disease. ROs and RNS must be present at certain concentrations but can be harmful if they are produced too quickly, remain for too long or accumulate in an area beyond the adaptive and repair capacity. Antioxidant systems, such as SOD, catalase, GPx, glutathione, glutathione reductase, peroxiredoxins and thioredoxin systems, are not linear pathways, but rather a network.

KEAP1–NRF2 pathway is a key regulator of cellular adaptation, and glutathione and GPX4 are key to protection from lipid oxidation and ferroptosis. None of these markers individually reflects the whole redox state but there is complementary information available by the use of biomarkers including

MDA, 4-HNE, F_2-isoprostanes, protein carbonyls, 8-OHdG, GSH/GSSG, antioxidant enzymes, and NRF2-associated targets. The best direction is thus multiparametric, standardized and compartment aware assessment.

Therapeutic approaches should aim at restoring the redox imbalance in the pathological state, but not to remove all the reactive species. These are promising areas, but will rely on disease context, timing, tissue targeting, and validated molecular monitoring for success: NRF2 modulation, interventions that target the glutathione system, interventions that target the mitochondria, selective NOX modulation, and ferroptosis-related strategies. Redox precision medicine provides a more biologically-based system to translate biochemical information into clinically relevant strategies and interventions.

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