Journal of Engineering, Science and Technological Trends (JESTT)

Vol. 2, Issue 2, July 2025
DOI: https://doi.org/10.64060/jestt.v2i2.3

Review

Electrochemical Biosensors for Real-Time Oxidative Stress Monitoring in Saliva

Hafiza Kanza Maryam[1]*, Abdullah[1] and Hafiza Fatima[2]

[1]School of Chemistry, University of the Punjab, Quaid-e-Azam Campus, Lahore, 54590, Pakistan
[2]Department of Chemistry, Lahore College for Women University, Pakistan
* Corresponding Email: k.maryam.edu@gmail.com (H. K. Maryam)

Received: 02 March 2025 / Revised: 27 May 2025 / Accepted: 20 June 2025 / Published online: 25 August 2025 (V-2)

ABSTRACT

Oxidative stress, resulting from an imbalance between reactive oxygen species and antioxidant defences, is a critical factor in the onset and progression of numerous diseases, including cancer, cardiovascular conditions, and neurological disorders. Early detection of oxidative stress biomarkers is essential for timely diagnosis and effective treatment. Saliva has emerged as a highly attractive biofluid for this purpose due to its non-invasive, easily accessible, and cost-effective collection. Recent advancements in electrochemical biosensors have significantly enhanced the sensitivity, selectivity, and reliability of detecting oxidative stress indicators in saliva. These innovative sensing platforms enable real-time monitoring of key biomarkers at low concentrations, offering great potential for clinical and point-of-care applications. However, challenges such as sensor stability, biofouling, and interference from complex salivary components remain to be addressed to ensure robust performance in practical settings. This review summarises the latest developments in electrochemical biosensing of salivary oxidative stress biomarkers, highlights existing limitations, and discusses prospective strategies to overcome current barriers. The continued evolution of this technology promises to facilitate early disease detection and improve patient outcomes through accessible and precise oxidative stress monitoring.

Keywords*:* Disease monitoring; Electrochemical biosensors; Non-invasive diagnostics; Oxidative stress; Point-of-care sensing; Reactive oxygen species

1. Introduction

A pathological state caused by an imbalance between antioxidant defence mechanisms and reactive oxygen/nitrogen species (ROS/RNS), oxidative stress is a major factor in the development and progression of many chronic diseases, such as diabetes, cancer, autoimmune diseases, cardiovascular diseases, and neurodegenerative disorders [1]. Protein folding and oxidative phosphorylation are two examples of regular biological processes that produce reactive oxygen and nitrogen species (ROS and RNS) [2]. These comprise both non-radical (like hydrogen peroxide and hypochlorous acid) and radical (like superoxide, hydroxyl, and nitric oxide) forms, each with unique biological functions and reactivities [3]. Although ROS and RNS are vital for cell signalling, too much of them can lead to oxidative stress and harm various parts of the cell. Even with their acknowledged importance, research is still ongoing to distinguish between their physiological and pathological functions [4]. Despite the critical role of reactive oxygen and nitrogen species (ROS/RNS) in cellular signalling and stress responses, there is a lack of effective tools for their selective and real-time detection in living systems. Electrochemical methods using custom-designed microelectrodes offer promising solutions, enabling direct, in situ monitoring of specific ROS/RNS like hydrogen peroxide (H_2O_2), nitric oxide (NO), peroxynitrite ($ONOO^-$), and superoxide ($O_2^{\bullet-}$) with high spatial and temporal resolution [5].

Under normal conditions, antioxidant systems tightly regulate ROS levels to maintain redox balance. However, both deficiency and excess of ROS can disrupt physiological processes [6]. Low ROS levels impair immune response, wound healing, and cell signaling, while excess ROS leads to oxidative damage of DNA, proteins, and lipids markers such as 3-nitrotyrosine (3-NT), Malondialdehyde (MDA), and 8-Hydroxy-2'-deoxyguanosine (8-OHdG) are often used to assess this damage in clinical samples [7].

Still, these biomarkers reflect downstream effects rather than real-time ROS dynamics and fail to distinguish between specific ROS types. Current analytical techniques like electron paramagnetic resonance and photon-emission spectroscopy are limited by cost, complexity, and low temporal resolution [8]. Thus, there is a pressing need for highly sensitive, selective, and rapid-response tools capable of detecting specific ROS in real-time. Developing such electrochemical sensors remains a key challenge in advancing our understanding of oxidative stress and improving disease diagnostics and treatment evaluation.

Saliva's simplicity of collection, low sample processing requirements, and association with systemic health have made it an attractive non-invasive biological fluid for the identification of oxidative stress indicators [9]. Conventional analytical techniques like GC-MS, ELISA, LC-MS/MS, and HPLC have been used to measure these biomarkers in biological matrices [10]. These methods are less appropriate for point-of-care or real-time monitoring applications, though, because they frequently include drawbacks, including high costs, laborious procedures, the requirement for trained staff, and complicated equipment.

Because of their intrinsic benefits, high sensitivity, specificity, portability, minimal sample volume needs, quick response, and compatibility with wearable formats, electrochemical biosensors present a strong alternative [11]. By boosting active surface area, enhancing conductivity, and facilitating selective molecular recognition, the incorporation of nanomaterials like metal nanoparticles (like AuNPs), graphene oxide nanoribbons (GONRs), multi-walled carbon nanotubes (MWCNTs), and molecularly imprinted polymers (MIPs) has further improved the performance of these sensors [12],[13]. MIP-based electrochemical sensors are particularly well-suited for detecting tiny oxidative stress indicators like 3-NT and 8-OHdG in intricate biological settings like saliva because they replicate antibody-antigen interactions with enhanced stability and reduced manufacturing costs [14].

With an emphasis on 3-NT, 8-OHdG, MDA, and ROS, this review aims to give readers a thorough grasp of saliva as a potentially useful diagnostic fluid, emphasising its capacity to track both mental and physical function. The development of electrochemical biosensors as dependable instruments for their detection is next covered, along with an examination of important oxidative stress indicators. These biosensors are perfect for continuous and non-invasive health monitoring since they have real-time sensing capabilities and can be easily integrated with wearable electronic platforms.

2. Salivary oxidative stress biomarkers

Saliva has drawn interest as a diagnostic fluid since it is simple to collect, requires little training, and can be self-collected, making it available to a variety of people, including young children and the elderly. Samples are convenient since they may be collected in a variety of locations, including at home or work. Biomolecules such as proteins, hormones, and enzymes found in saliva are connected to stress, illness, and general well-being [15]. Saliva-based diagnostic tests for ailments like stress, mental health, and oral disorders have been developed as a result of these advantages. However, there are still issues like pollutants, individual biomarker variance, and temporal lags between blood and saliva changes. Saliva's non-invasiveness, ease of collection, and capacity to track a variety of biomarkers connected to stress, illness, and general health have made it a potential diagnostic fluid.

Proteins, enzymes, and hormones are just a few of the macromolecules found in saliva that represent physiological alterations linked to illness and stress. Salivary α-amylase, chromogranin A (CgA), cortisol, brain-derived neurotrophic factor (BDNF), and immunoglobulin A (IgA) are some of the biomarkers frequently examined in stress research [16],[17],[18]. For example, both acute and chronic stress cause an increase in salivary α-amylase, whereas cortisol levels rise during acute stress but may become dysregulated under chronic stress. Stress usually causes immunoglobulin A levels to drop, which is a sign of immunological suppression. Increased levels of CgA, a protein generated by the adrenal glands under stress, are seen under both acute and chronic stress. CgA is also used to measure alterations associated with stress [19].

Furthermore, stress can affect BDNF, a growth factor implicated in brain plasticity, which exhibits higher levels during acute stress but lower levels under chronic stress [20]. Saliva has a lot of promise for diagnostics; however, there are still issues with biomarker variability because of things like sample collecting techniques, time lags between blood and saliva changes, and individual variations in concentration gradients. Saliva, however, provides an easy-to-use way to track health and stress reactions, and research is being done to maximise its utility in clinical settings.

One well-researched ROS that serves as a signalling molecule and an indication of oxidative imbalance is hydrogen peroxide (H_2O_2) [21]. The nitration of tyrosine residues in proteins produces 3-nitrotyrosine (3-NT), a particular marker that indicates oxidative and nitrosative damage [22]. Through their involvement in redox-sensitive signalling cascades, protein phosphorylation levels, which are changed in oxidative environments, also function as indirect indicators. As an indicator of oxidative DNA damage, 8-Hydroxy-2'-deoxyguanosine (8-OHdG) is one of the most researched oxidative stress biomarkers currently being explored. Furthermore, 3-nitrotyrosine (3-NT) has emerged as a crucial indicator of protein nitration, indicating oxidative protein damage [4]. Reactive oxygen species (ROS), which are a direct indicator of oxidative stress levels, and Malondialdehyde (MDA), a byproduct of lipid peroxidation, are also important indicators of oxidative imbalance in the body [23]. The increased attention paid to these biomarkers, in particular, 8-OHdG, 3-NT, and MDA, highlights their potential for real-time oxidative stress monitoring and early disease diagnosis, offering insight into the mechanisms driving stress and related illnesses. Table 2 represents the electrochemical biosensors for Key salivary oxidative stress biomarkers

The pre-analytical stability of saliva oxidative indicators varies greatly with temperature, storage period, and enzymatic activity. Saliva, as opposed to blood, is abundant in enzymes such as amylase and proteases that can hydrolyse biomarkers for MDA, 3-nitrotyrosine, and 8-OHdG as soon as they are sampled. Studies have shown that biomarker concentrations significantly decrease within 30 to 60 minutes if cooling is delayed or protease inhibitors are not added. Effective sample handling requires fast chilling, storage at −20°C or lower, and the absence of freeze-thaw cycles. Accuracy may also be impacted by consistency in salivary flow and collection methods. Hence, standardised methods are important for biosensor-based diagnoses to be reliable.

3. Comparative analysis of the diagnostic accuracy of salivary oxidative stress biomarkers: Saliva vs blood, urine and cerebrospinal fluid (CSF)

Table 1:
Comparative analysis of biofluids for detection of oxidative stress biomarkers.

Parameter	Blood/Serum	Urine	CSF	Saliva
Invasiveness	High	Moderate	High	None
Sample Volume Needed	Moderate to High	Moderate to High	High	Low
Biomarker Stability	High (under storage)	Moderate	High	Low (enzyme activity)
Real-time Monitoring	Difficult	Not practical	Not practical	Easily achievable
Point-of-Care Compatibility	Limited	Moderate	Poor	Excellent
Cost and Simplicity	Expensive	Moderate	Expensive	Low-cost
Clinical Standardization	Established	Partial	Established	Emerging

Saliva offers a practical, easily available, non-invasive biofluid for evaluating oxidative stress biomarkers, but its diagnostic accuracy in comparison to more conventional fluids such as blood, urine, and cerebrospinal fluid (CSF) remains a major problem. Table 1 shows the comparative analysis of biofluids for detection of oxidative stress biomarkers. Because of things like selective diffusion across acinar cells, active transport processes, and enzymatic degradation by salivary enzymes like amylase and peroxidase, the levels of oxidative stress indicators in saliva are often significantly lower than in plasma or CSF. For example, the levels of 8-hydroxy-2′-deoxyguanosine (8-OHdG) in plasma can range from 0.2 to 1.0 ng/mL, whereas in saliva they are normally between 0.05 and 0.3 ng/mL [24]. Malondialdehyde (MDA) and 3-nitrotyrosine can also be found in saliva, although in smaller amounts than in blood. Despite these variations, several studies have demonstrated statistically significant relationships between oxidative stress marker concentrations in serum and saliva in clinical populations, such as patients with neurological disorders, diabetes, and cardiovascular disease [9],[21].

Additionally, saliva can be collected by self-collection to reduce patient discomfort and contamination risk, unlike blood and CSF, which require invasive procedures and specialised care. According to Monosik et al. [11], this makes saliva the best material for repeated or real-time monitoring, especially when paired with electrochemical biosensor technologies that offer great sensitivity and specificity at low analyte concentrations. However, pre-analytical factors such as sample collection method, circadian rhythms, hydration, and food intake can affect biomarker levels, reducing the diagnostic utility of saliva. Furthermore, unless processed or stabilised immediately, saliva may degrade labile biomarkers due to its increased susceptibility to biochemical instability brought on by enzymatic activity and pH fluctuations. However, the detection of salivary oxidative stress biomarkers at clinically relevant concentrations has significantly improved with recent developments in wearable biosensing technologies, molecularly imprinted polymers, and nanomaterials. Saliva-based diagnostics can therefore provide a scalable, affordable, and efficient substitute for traditional fluids with the right standardisation and validation, especially for point-of-care and personalised treatment.

4. Electrochemical Biosensing Principle

The principles of electrochemistry, which investigate the connection between electrical energy and chemical reactions, specifically, redox processes, in which electrons are transported between molecules, form the basis of electrochemical sensing techniques [25]. Since many biological processes, including cellular respiration and neural activity, depend on these reactions, electrochemical techniques are extremely important for use in biomedical and diagnostic settings [26]. The measurement of electrical current produced by redox reactions at electrode surfaces is the fundamental component of electrochemical detection. This current enables accurate quantitative analysis since it is proportional to the target analyte's concentration.

Important methods include electrochemical impedance spectroscopy (EIS), which examines the resistance to charge transfer at the electrode interface; amperometry, which keeps a constant potential to track changes in current in real time; and voltammetry, which varies the potential and the current that results reveals the redox behavior of analytes [27]. These techniques provide great sensitivity, quick reaction, and the capacity to identify biomarkers at trace levels in complicated matrices like blood or saliva, particularly when supplemented with nanomaterials or molecularly imprinted polymers (Figure 1). They are essential instruments in contemporary biosensing because of their versatility and diagnostic capabilities, especially when it comes to identifying disease-associated biomarkers like 3-nitro-L-tyrosine.

4.1. Electrochemical sensing of 8-Hydroxy-2'-deoxyguanosine

Targeting nucleotides, nucleosides, and DNA bases, oxidative stress can cause damage to genomic DNA. Guanine is particularly susceptible because of its low oxidation potential [28]. 8-oxoguanine (8-oxoG) and its deoxynucleoside form, 8-hydroxy-2′-deoxyguanosine (8-OHdG), are the main oxidation products of guanine [29]. Since these substances are the most common and well-established indicators of oxidative DNA damage, 8-OHdG is frequently utilised as an indicator to evaluate oxidative stress at the molecular level. A number of electrochemical platforms have been created to detect 8-oxodG, a biomarker of oxidative DNA damage, with high sensitivity. The sensitive and selective electrochemical detection of 8-oxodG, a crucial indicator of oxidative DNA damage, has been thoroughly investigated using conducting polymers, nanostructured materials (NsM), and biomolecular recognition components. Peak currents were improved and oxidation potentials were shifted to more negative values by electropolymerized films such as poly(3-methylthiophene) (P3MT) and poly(3-acetylthiophene) (P3AT) modified glassy carbon electrodes (GCE). The detection limits of these systems were as low as 0.10 µM and 31.3 nM, respectively [30],[31]. With LODs of 56 nM, mixed DNA–P3MT films likewise showed excellent sensitivity. To improve selectivity for 8-oxoG and guanine, metallopolymers such as $[Os(bpy)_2(PVP)_{10}Cl]^+$ and $[Ru(bpy)_2(PVP)_{10}Cl]^+$ were employed [32]. When 8-oxodG was present during the synthesis of molecularly imprinted polymers (MIPs), highly selective recognition sites were made possible, resulting in LODs as low as 3 nM and even 0.74 pg/mL (≈2.6 pM) [33],[34]. With LODs as low as 100 fg/mL, immunosensors that used 8-oxodG antibodies mounted on electrodes modified with nanomaterials (such as ZnO nanorods or rGO) showed exceptional selectivity and detection capabilities [35]. Because of their non-immunogenic nature, low cost, and great specificity, aptamer-based sensors have become extremely useful in-

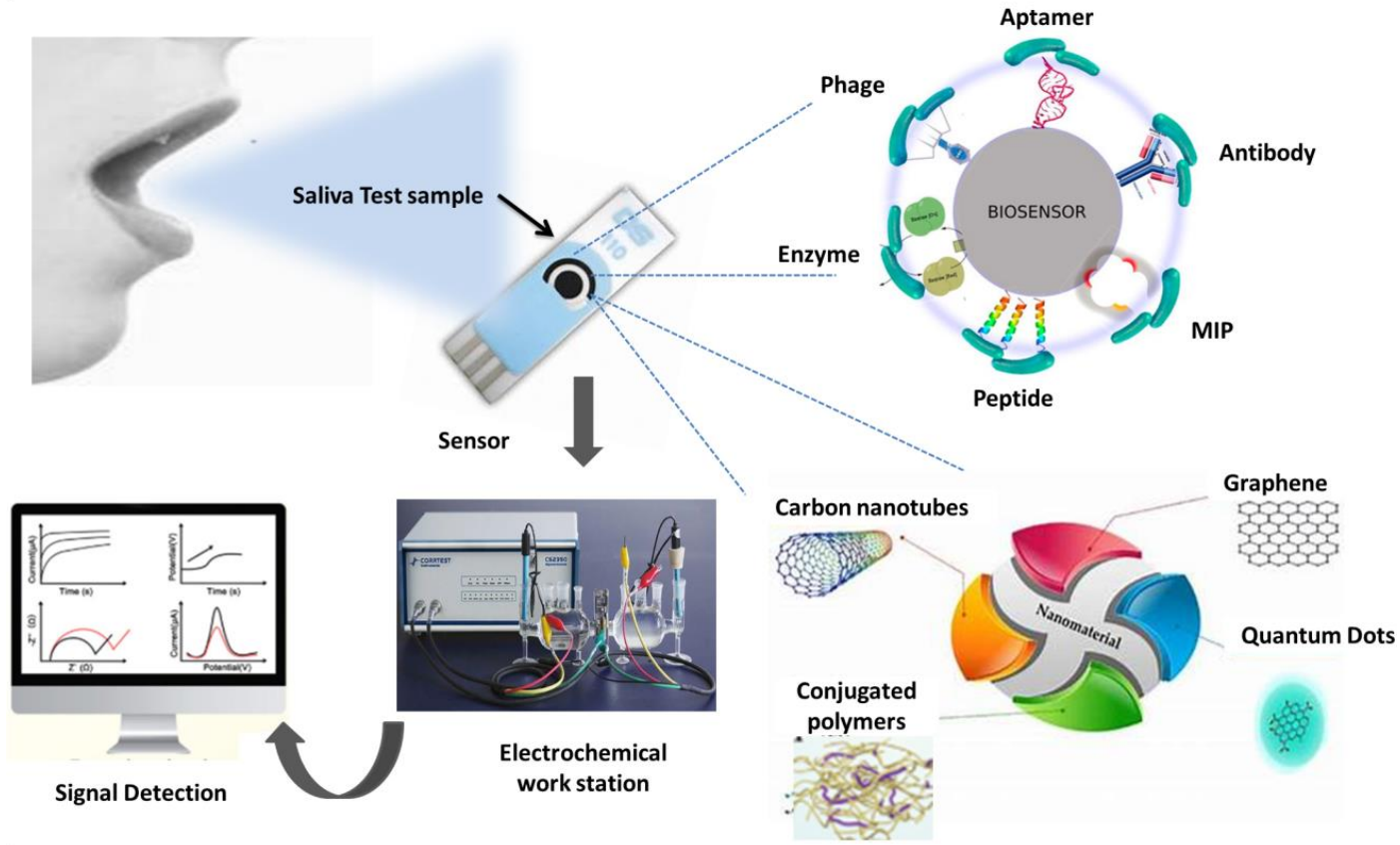

Figure 1. *A visual representation of biosensor for electrochemical detection of oxidative stress biomarkers in saliva*.

struments. Novel designs that combined aptamers with DNAzymes, hybridisation chain reaction (HCR), and other signal amplification techniques produced ultralow LODs down to 24.34 fM while preserving great selectivity against interfering compounds and wide linear ranges [36]. Together, these cutting-edge electrochemical platforms, which include polymers, nanomaterials, MIPs, dendrimers, immunosensors, and aptasensors, provide reliable, sensitive, and specific methods for detecting 8-oxodG in intricate biological matrices, thereby bolstering their potential for use in oxidative stress monitoring and clinical diagnostics.

4.2. Electrochemical sensing of Malondialdehyde

As a byproduct of the oxidation of arachidonic acid (AA), an unsaturated fatty acid, malondialdehyde (MDA) is a key biomarker of lipid peroxidation and oxidative stress. Therefore, it is essential to develop trustworthy techniques for its detection in plasma, serum, and salivary fluid, as monitoring MDA levels in biological systems can be used to determine oxidative stress. Lipid peroxidation products have been identified using both chemical and electrochemical methods. Yuan et al. [37] used multi-walled carbon nanotubes (MWNTs) to create a label-free electrochemical biosensor for MDA detection (Figure 2). After MWNTs and chitosan (CS) were added to a glassy carbon electrode (GCE), glutaraldehyde (GluA), complement factor H (CFH), and bovine serum albumin (BSA) were immobilised to act as links, recognition, and blocking agents, respectively. Every alteration step was validated by cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). While subsequent surface alterations raised resistance and decreased current, suggesting effective layer development, MWNTs improved electron transport. Using differential pulse voltammetry (DPV), the sensor obtained a linear range of 0.1–90 µmol¹ and a detection limit of 0.047 µmol¹; however, stability data were not provided.

Later, a study showed that layer-by-layer nanocomposites made of polymers and nanoparticles performed exceptionally well electroanalytically and in terms of conductivity [38]. MDA was detected in exhaled breath condensate via DPV using quantum dots and polyarginine, with a detection limit of 0.329 nM. For the detection of MDA in breath and serum, Hasanzadeh et al. [23] used a polypurine-modified gold electrode (PT/Au), which produced good stability (90 percent signal retention after 100 analyses), a linear range of 0.78–3.10 mM, and a detection limit of 34 nM. The conductive polymers and nanomaterials' high conductivity, vast surface area, and abundance of active sites are what give these studies their improved performance.

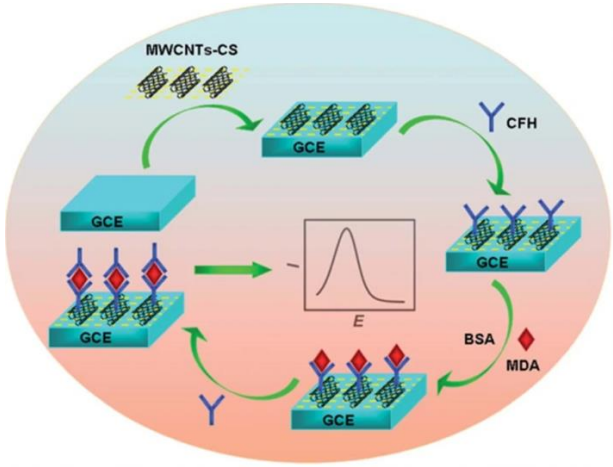

Figure 2. *An illustration showing how the synthesis of label-free biosensors for MDA detection* [37].

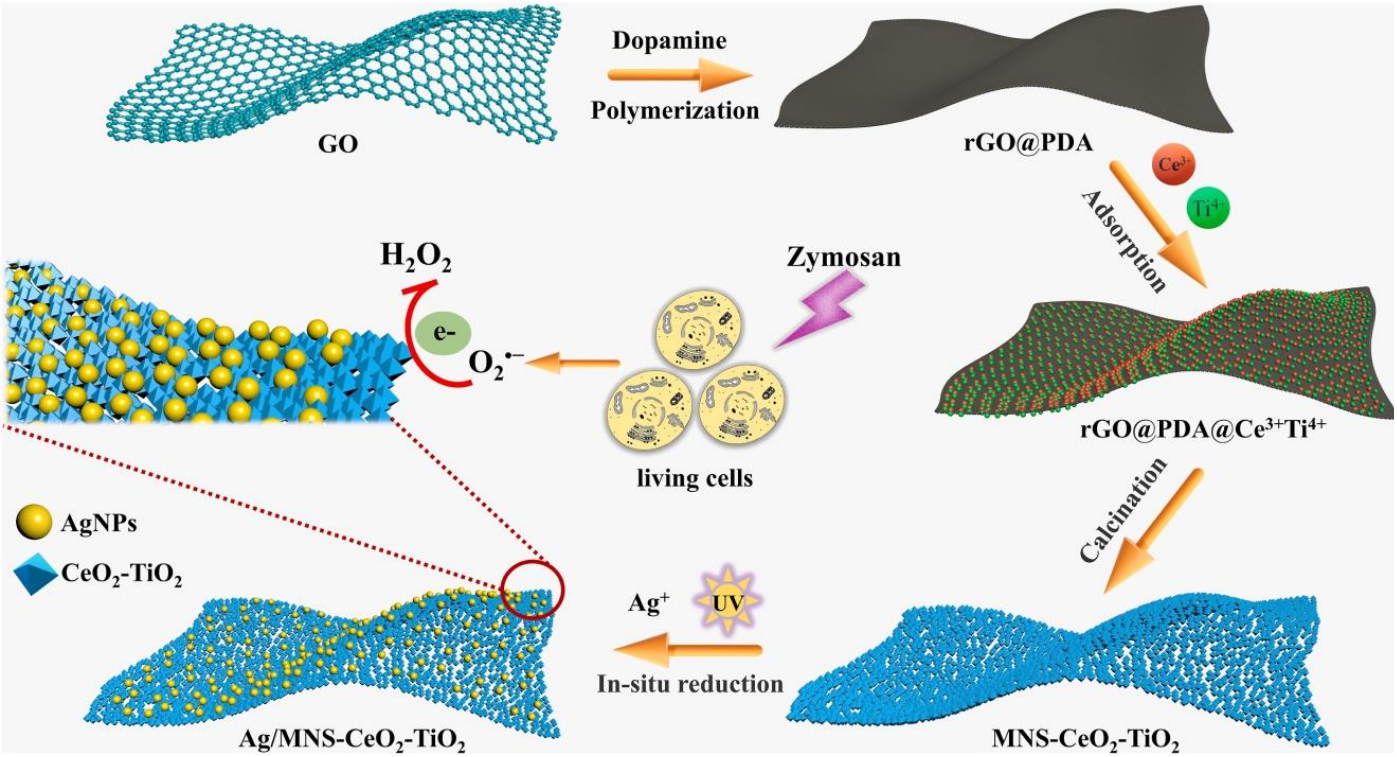

Figure 3. *Development of Ag/MNS-CeO_2-TiO_2 materials and the identification of superoxide anions generated by cells* [42].

4.3. Electrochemical sensing of Malondialdehyde

Electrochemical detection of reactive oxygen and nitrogen species (ROS/RNS) is one of the effective methods for tracking oxidative stress in biological fluids, specifically in saliva. ROS and RNS are immediately detected by chemical sensors at their distinctive redox potentials. For instance, the oxygen/superoxide redox pair is detected at about -0.33 V versus NHE, whereas nitric oxide (NO) is oxidised at about 0.8 V vs Ag/AgCl [1]. Amatore et al. [39] and associates' groundbreaking research using platinumized carbon microelectrodes to identify ROS/RNS in individual cells and even inside phagolysosomes. Catalytic materials, such as Prussian blue composites or gold nanocones, are employed to boost sensitivity and further enhance performance. This allows for the detection of hydrogen peroxide (H_2O_2) at low concentrations, even in complicated samples like blood or serum.

In contrast, biological sensors use redox-active proteins that are immobilised on the electrode surface in order to selectively identify the target species. For example, superoxide ($O_2^{-\cdot}$) can be detected using cytochrome c (Cyt C), which facilitates electron

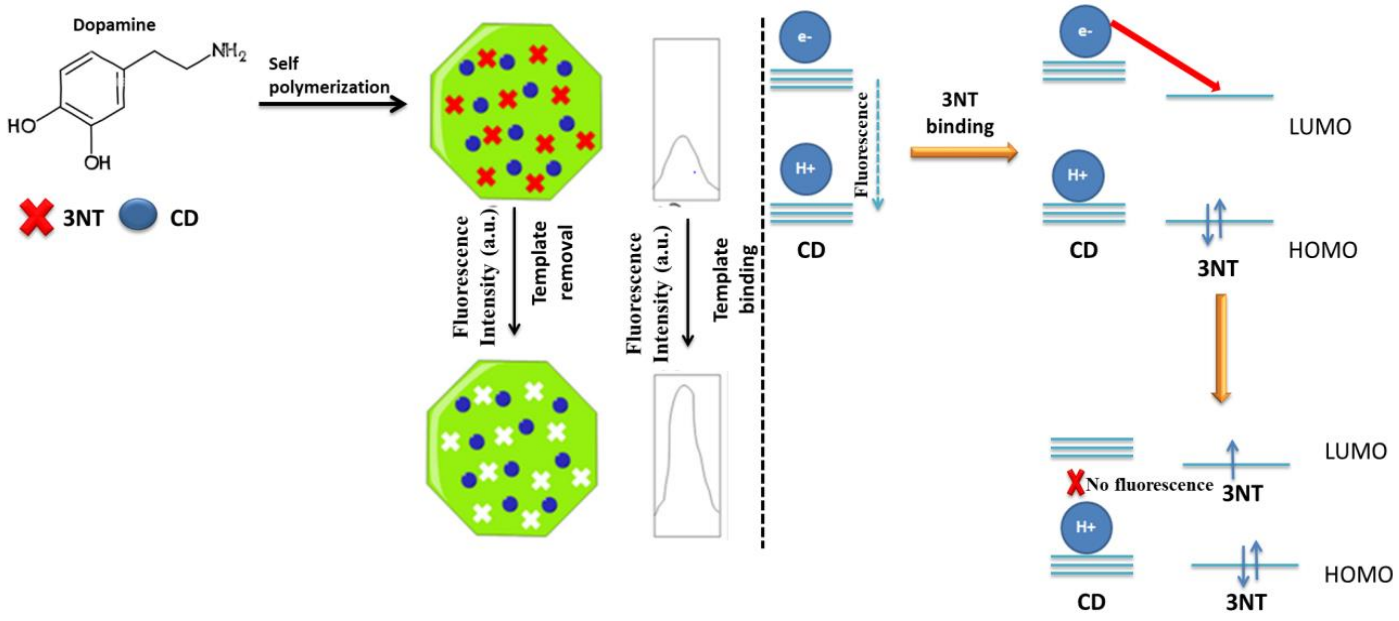

Figure 4. *The BMIP@CDs sensor's fluorescence quenching mechanism* [47].

transfer upon binding and produces a detectable biocatalytic current [40]. Despite the excellent selectivity of these biosensors, their long-term stability and immobilisation complexity can be problematic. More recent methods use hybrid nanomaterials like graphene/AgNP/CeO_2/TiO_2 or enzyme mimetics like $MnTiO_3$ or manganese phosphate (Figure 3) to more robustly simulate enzymatic activity [41],[42].

Because of their short half-life and reactivity, NO and its reactive product, peroxynitrite, require sensors with high sensitivity and fast response [43]. Selectivity is frequently attained by covering CFMEs with selective barriers such as Nafion, chitosan, or o-phenylenediamine since NO oxidises at potentials that overlap with those of other species [44]. Recent developments include Cyt c-modified nanoporous gold electrodes that have low detection limits and great sensitivity for detecting $O_2^{-\cdot}$ in tissues such as skeletal muscle [45]. Even with these developments, further research is required to confirm the specificity of some of the more recent materials, especially in intricate biological settings.

4.3. Electrochemical sensing of 3-Nitrotyrosine (3-NT)

Using a variety of materials and methods, several novel sensors have been created for the detection of 3-nitrotyrosine (3-NT), a crucial indicator of oxidative stress. For precise 3-NT detection in biological fluids, Govindasamy et al. [46] developed an amperometric sensor based on cadmium tungstate nanodots with reduced graphene oxide. This sensor has a low detection limit (LOD) of 3.24 nM, a broad linear range (18.5 nM to 1.84 mM), and good sensitivity. Similar to this, Jalili et al. [47] reported a new molecularly imprinted polymer (MIP) sensor that uses green-light emitting carbon dots (BMIP@CD) showed good serum analysis with high recovery and repeatability (Figure 4). It is less expensive and more resilient than antibody-based sensors.

Additionally, lab-on-a-chip electrochemical paper-based sensors provide a portable, affordable solution for point-of-care diagnostics with a limit of detection of 49.2 nM. In serum from patients with minor hepatic encephalopathy, optical sensors such as a binuclear platinum complex demonstrated remarkable sensitivity (LOD: 4.7×10^{-10} M) and selectivity for 3-NT detection [48]. The LOD of 25.14 pM provided by copper ferrite nanodots embedded in reduced graphene oxide was exceptionally low [49]. While surface acoustic wave (SAW) biosensors in conjunction with electrospray ionisation-mass spectrometry allowed for label-free analysis of nitrated peptides, electrochemical sensors that included MIP-doped gold nanoparticles demonstrated good specificity and sensitivity with a limit of detection of 50 nM [50]. A localised surface plasmon resonance (NDG-LSPR) sensor based on graphene doped with nickel showed good selectivity for 3-NT and a limit of detection of 0.13 pg/mL [51].

Outperforming conventional ELISA techniques, bimetallic Fe/Pd nanoparticles with molecular imprinting provided a durable, affordable, and efficient instrument for 3-NT detection in clinical fluids [52]. Finally, immunofluorescent detection of 3-NT-modified tyrosine residues under oxidative circumstances was made possible by peptide-functionalized fluorescent particles (PFFPs), supporting applications in therapeutic screening and disease monitoring [51]. These new developments demonstrate the expanding potential of sophisticated sensors in the evaluation of clinical oxidative stress.

Table 2:

Electrochemical Biosensors for Key Salivary Oxidative Stress Biomarkers. (ITO: indium tin oxide; AuNTAs: gold nanotriangles arrays; PtNPs: platinum nanoparticles; DPV: differential pulse voltammetry; SWCNT: single-wall carbon nanotubes; GCE: glassy carbon electrode; MWCNT: multiwalled carbon nanotubes; **ErGO**: electrochemically reduced graphene oxide; SWV: square wave voltammetry; CV: cyclic voltammetry; **SPCE**: screen-printed carbon electrode; **MGO**: magnetic graphene oxide; MIPy: molecularly imprinted polypyrrole; $La_2Sn_2O_7$: lanthanum stannate; f−HNT: functionalized halloysite nanotubes; **MIP**: molecularly imprinted polymer; **AMWCNT**: aminated multi-walled carbon nanotubes; **GONRs**: graphene oxide nanoribbons; **MoS_2**: molybdenum disulfide; **$BiVO_4$:** bismuth vanadate; **ZSM-5:** zeolite socony mobil-5; $Mn_3(PO_4)_2$: manganese(II) phosphate; PDDA: Poly(diallyldimethylammonium chloride); AMP: amperometery).

No.	Biomarker	Material	Technique	LOD	Reference(s)
1	8-OHdG	ITO/AuNTAs/PtNPs portable electrochemical device	DPV	10 ng/mL–100 µg/mL	[53]
2	8-OHdG	SWCNT-Nafion/GCE	DPV	0.03–1.25 µM	[54]
3	8-OHdG	MWCNT/ErGO/GCE	(SWV)	3–75 µM	[55]
4	MDA	GCE/MWCNTs	CV	0.02–40 µM	[37]
5	MDA	SPCE/MGO@MIPy	DPV	0.01–100 µM	[56]
6	3-NT	$La_2Sn_2O_7$/f−HNT	DPV	0.5–214 µM	[57]
7	3-NT	MIP/AMWCNT@GONRs	DPV	0.2–50.0 µM	[50]
8	3-NT	MoS_2@$BiVO_4$	CV	0.001–526.3 µM	[58]
9	ROS	ITO/ZSM-5, $Mn_3(PO_4)_2$, PDDA	Amp	5.0×10^{7} – 1.2×10^{3} dm^2/L	[59]
10	ROS	Ceria-nanoparticle nanozyme on SPCE	CV	1- 100 µM	[60]

5. Recent Advances in Saliva-Based Electrochemical Biosensors

More attention must be paid to emerging illnesses associated with oxidative stress, especially in light of quick and easy diagnostics. Improvements in biosensor technology, such as the creation of wearable and mouthguard-based electrochemical biosensors, are desperately needed. For point-of-care (POC) applications, these cutting-edge technologies have great potential since they enable the early and non-invasive detection of oxidative stress indicators, which is essential for prompt diagnosis and efficient disease management.

Enhancing the sensitivity, selectivity, and mobility of electrochemical biosensors for a salivary oxidative stress indicator has been the main focus of recent advancements. The electrochemical characteristics of sensor platforms have been greatly improved by the introduction of nanostructured materials such as graphene oxide, carbon nanotubes, and gold nanoparticles. Furthermore, biomarker recognition has improved with the use of molecularly imprinted polymers (MIPs), particularly for 3-nitrotyrosine and 8-OHdG. The prohibitive expense of high-end nanomaterials such as gold nanoparticles and graphene constrains the mass production of salivary electrochemical biosensors [61]. Although the cost of synthesis and purification is significant, these materials function exceptionally well [62]. To combat this, research is being done on low-cost substitutes such as metal oxides, polymer nanocomposites, and carbon produced from biomass, which show comparable sensitivity at a lower cost [63]. Similarly, green solvents and electropolymerization are used to optimise molecularly imprinted polymers (MIPs), reducing production costs [64]. For point-of-care applications, pairing with screen-printed electrodes and paper-based platforms also makes mass production affordable.

Real-time monitoring of salivary biomarkers linked to oxidative stress has been transformed by the combination of wearable technology with electrochemical biosensing. The goal of these developments is to offer continuous, non-invasive, and customised health monitoring options.

Mouthguard biosensors that can identify salivary metabolites have been developed thanks to creative designs. An instrumented mouthguard that non-invasively measures salivary uric acid levels was demonstrated by Kim et al. [65]. To enable real-time wireless data transfer to smartphones and other devices, this device combines a uricase-modified screen-printed electrode system with miniature electronics, such as a potentiostat, microprocessor, and Bluetooth Low Energy (BLE) transmitter. OECTs have the potential to be used in wearable biosensors, providing enhanced sensitivity and signal amplification for the detection of low-abundance analytes, as demonstrated by Duan et al. [66]. These gadgets make it easier to track salivary biomarkers in real-time, which improves point-of-care diagnostic performance. Wearable biosensors can be seamlessly integrated with cell phones thanks to the use of wireless connection modules. Proactive health management is supported by this connectivity, which allows consumers to share data with healthcare providers, follow health measures over time, and get rapid feedback.

Wearable electrochemical biosensors for salivary analysis are now much more functional and user-friendly thanks to the development of wireless and microfluidic technology. Figure 5 shows the evolution of wearable electrochemical sensors based on bioreceptors. Wearable biosensors have integrated microfluidic devices to effectively handle tiny amounts of saliva. These technologies make it easier to handle samples precisely, use fewer reagents, and allow multiplexed detection of different biomarkers. For instance, wearable technology with microfluidic channels can track salivary metabolites like uric acid and lactate over time, giving important information about a person's level of oxidative stress.

6. Challenges and Limitations

Age, food, oral health, circadian rhythm, and other physiological and lifestyle factors all affect the baseline levels of oxidative stress indicators in saliva [67]. Age-related alterations in redox metabolism can alter the levels of oxidative stress markers; older individuals often exhibit higher levels of MDA and 8-OHdG due to accumulated oxidative damage and weakened antioxidant defences [68]. Another crucial factor is nutrition; for example, consuming

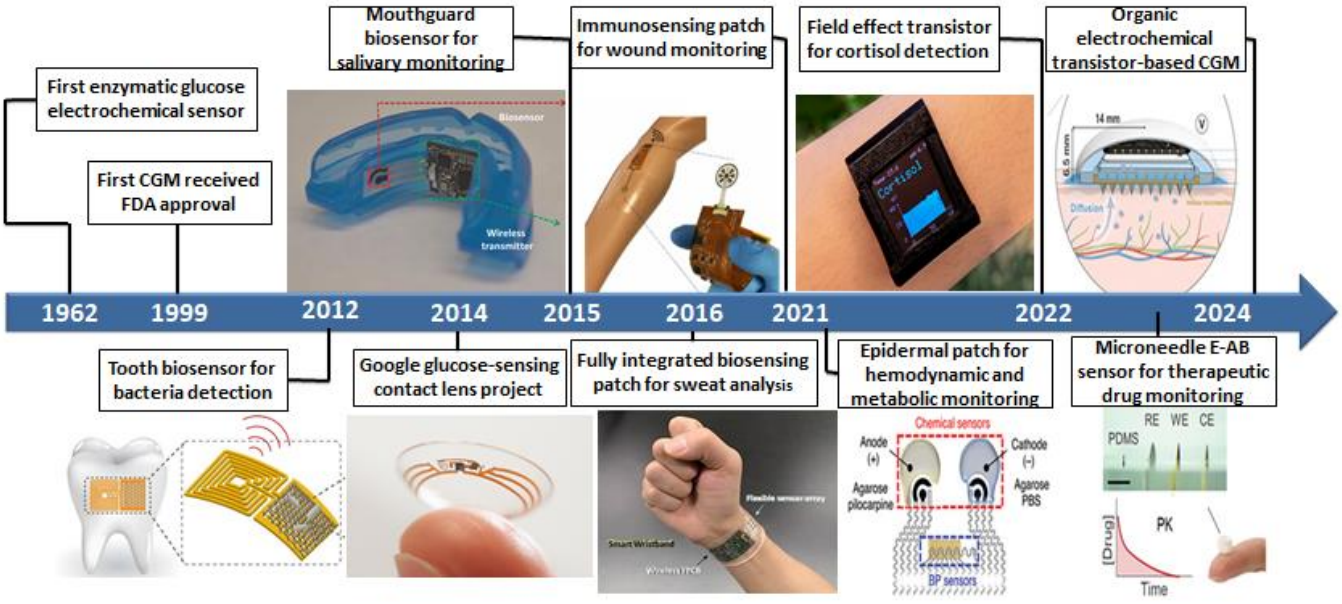

Figure 5. *The evolution of wearable electrochemical sensors based on bioreceptors* [66].

too many processed foods or polyunsaturated fats can increase lipid

peroxidation and, in turn, MDA levels, whereas diets high in antioxidants have been demonstrated to suppress the production of biomarkers. Another important factor is oral health; independent of systemic health, gingivitis or periodontitis can cause local oxidative stress and artificially raise salivary ROS and 3-nitrotyrosine levels. Salivary biomarkers have also been shown to exhibit circadian rhythms; for example, cortisol and 8-OHdG are two analytes that peak in the morning and then decline throughout the day. False-positive or false-negative diagnoses are more likely when these physiological variations are not taken into consideration. Therefore, it is essential to standardise sample timing of collection and account for individual physiological characteristics to provide valid clinical interpretation and calibration of biosensors.

A number of significant restrictions and difficulties prevent saliva-based electrochemical biosensors for oxidative stress indicators from being widely used in clinical settings and being commercialised. Target biomarkers like 3-nitrotyrosine (3-NT), 8-hydroxy-2′-deoxyguanosine (8-OHdG), Malondialdehyde (MDA), and reactive oxygen species (ROS) are among the most important problems. These biomarkers are frequently found in saliva at nanomolar to picomolar concentrations, which calls for ultra-sensitive detection techniques. Saliva's complex and varied composition, which includes variations in pH, protein content, viscosity, and enzyme activity brought on by dietary changes, circadian rhythms, or personal health conditions, can also have a substantial impact on sensor performance, resulting in inconsistent and poor reproducibility [24].

The non-specific adsorption of salivary proteins and other interfering chemicals onto the sensor surface is another significant drawback. This can lead to electrode fouling, signal instability, and a gradual decrease in sensitivity [69]. The absence of defined procedures for the collection, handling, and processing of saliva further complicates matters, making it challenging to compare findings across several platforms or research studies. Additionally, selectivity is still problematic, especially when sensors exhibit cross-reactivity with compounds that share structural similarities, leading to erroneous results.

Furthermore, a lot of biosensors depend on biological recognition components like enzymes or antibodies, which are naturally unstable and have short shelf lives, particularly in environments with variable humidity or temperature [70]. Although it holds promise for real-time, non-invasive diagnostics, the incorporation of these sensors into wearable platforms introduces another level of complexity because it necessitates robust miniaturisation, power efficiency, wireless data transmission, and biocompatibility, all of which raise production costs and technical obstacles. Lastly, batch-to-batch variability frequently plagues sensor fabrication techniques, especially those employing nanomaterials or molecularly imprinted polymers. This compromises repeatability and restricts scalability for mass production. All of these drawbacks point to the necessity of ongoing advancements in sensor design, fabrication methods, and materials to fully utilise saliva-based electrochemical biosensors in oxidative stress diagnostics.

7. Future Perspectives

The area of electrochemical biosensing based on saliva is on the brink of major change, fueled by material sciences development, wearable technology, and integration into digital health. The incorporation of biosensors into Internet of Things (IoT) systems and smart wearables is the main focus of future development. This will enable wireless data transfer and remote clinician input, enabling continuous real-time monitoring of biomarkers for oxidative stress. Early disease identification and proactive healthcare will be made possible by this. Meanwhile, advancements in next-generation low-cost nanomaterials such as carbon quantum dots, metal-organic frameworks (MOFs), and biodegradable polymers are expected to enhance sensor performance while permitting ecologically benign, large-scale manufacture. When combined with hybrid detection modes (electrochemical, optical, and enzymatic), multiplex biosensors that can simultaneously detect multiple oxidative stress indicators such as 3-nitrotyrosine, 8-OHdG, MDA, and ROS will yield more comprehensive diagnostic data, improving analytical accuracy and cross-validation.

With the help of artificial intelligence (AI) and machine learning (ML), data interpretation will be transformed into pattern recognition and real-time health analytics. This includes the possibility of profiling an individual's oxidative stress based on their physiology, lifestyle, and medical history. Furthermore, to comply with regulatory standards and facilitate commercialisation, future progress will be fueled by overcoming current constraints through the standardisation of sample harvest, calibration processes, and clinical verification. Miniaturising biosensors based on self-powered systems, such as triboelectric nanogenerators (TENGs) or biofuel cells, is another exciting avenue. This will eliminate the need for external power sources and allow for the creation of completely autonomous, non-invasive devices. With the potential to significantly improve public health through early diagnosis, tailored treatment, and real-time health monitoring, these novel developments collectively position saliva-based electrochemical biosensors as a cornerstone of next-generation non-invasive diagnostics.

8. Conclusion

In conclusion, saliva-based electrochemical biosensors have a lot of promise for real-time, non-invasive monitoring of oxidative stress biomarkers, providing a viable path toward early disease detection and individualised health care. The sensitivity, selectivity, and convenience of these biosensors have been significantly improved by the combination of wearable technology, molecularly imprinted polymers, and sophisticated nanomaterials. Recent advances, such as mouthguard biosensors and microfluidic systems, have shown impressive progress despite obstacles such as biomarker variability, sample collection problems, and the requirement for device uniformity. These advancements, especially in wearable technology, have the potential to revolutionise the diagnostics industry by facilitating ongoing health monitoring using user-friendly, accessible gadgets. Saliva-based electrochemical biosensors, which provide a non-invasive, effective way to monitor oxidative stress and enhance health outcomes, are set to play a significant part in the future of personalised healthcare as research and technology develop.

Declaration

Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical Issues: There are no ethical issues. All data in this paper is publicly available.

Author Contribution Statement: H.K.M, A.A. and H.F. conceived the idea and designed the research; analysed and interpreted the data and wrote the paper.

Funding Statement: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Consent to Publish: All authors have agreed to publish the version of the manuscript in this journal.

References

1. S. Deshpande, W. Muraoka, and S. Andreescu, "Electrochemical sensors for oxidative stress monitoring," Curr. Opin. Electrochem., vol. 29, p. 100809, Oct. 2021, doi: 10.1016/j.coelec.2021.100809.
2. M. P. Murphy et al., "Unraveling the Biological Roles of Reactive Oxygen Species," Cell Metab., vol. 13, no. 4, pp. 361–366, Apr. 2011, doi: 10.1016/j.cmet.2011.03.010.
3. M. Schrader and H. D. Fahimi, "Peroxisomes and oxidative stress," Biochim. Biophys. Acta BBA - Mol. Cell Res., vol. 1763, no. 12, pp. 1755–1766, Dec. 2006, doi: 10.1016/j.bbamcr.2006.09.006.
4. K. M. Nash, A. Rockenbauer, and F. A. Villamena, "Reactive Nitrogen Species Reactivities with Nitrones: Theoretical and Experimental Studies," Chem. Res. Toxicol., vol. 25, no. 8, pp. 1581–1597, Aug. 2012, doi: 10.1021/tx200526y.
5. H. Sies and D. P. Jones, "Reactive oxygen species (ROS) as pleiotropic physiological signalling agents," Nat. Rev. Mol. Cell Biol., vol. 21, no. 7, pp. 363–383, Jul. 2020, doi: 10.1038/s41580-020-0230-3.
6. Y. Chen, M. B. Azad, and S. B. Gibson, "Superoxide is the major reactive oxygen species regulating autophagy," Cell Death Differ., vol. 16, no. 7, pp. 1040–1052, Jul. 2009, doi: 10.1038/cdd.2009.49.
7. A. Andries, J. Rozenski, P. Vermeersch, D. Mekahli, and A. Van Schepdael, "Recent progress in the LC–MS/MS analysis of oxidative stress biomarkers," ELECTROPHORESIS, vol. 42, no. 4, pp. 402–428, 2021, doi: 10.1002/elps.202000208.
8. H. Togashi, M. Aoyama, and K. Oikawa, "Imaging of reactive oxygen species generated in vivo," Magn. Reson. Med., vol. 75, no. 3, pp. 1375–1379, 2016, doi: 10.1002/mrm.25582.
9. M. A. Javaid, A. S. Ahmed, R. Durand, and S. D. Tran, "Saliva as a diagnostic tool for oral and systemic diseases," J. Oral Biol. Craniofacial Res., vol. 6, no. 1, pp. 67–76, Jan. 2016, doi: 10.1016/j.jobcr.2015.08.006.
10. W. V. Giannobile, T. Beikler, J. S. Kinney, C. A. Ramseier, T. Morelli, and D. T. Wong, "Saliva as a diagnostic tool for periodontal disease: current state and future directions," Periodontol. 2000, vol. 50, pp. 52–64, 2009, doi: 10.1111/j.1600-0757.2008.00288.x.
11. R. Monošík, M. Stred'anský, and E. Šturdík, "Application of Electrochemical Biosensors in Clinical Diagnosis," J. Clin. Lab. Anal., vol. 26, no. 1, pp. 22–34, 2012, doi: 10.1002/jcla.20500.
12. M. U. Javed et al., "Metal-Organic Framework/Polymer Composites for Solid State Electrolytes-A Critical Review," J. Power Sources, vol. 640, p. 236720, Jun. 2025, doi: 10.1016/j.jpowsour.2025.236720.
13. F. J. Iftikhar, A. Shah, Q. Wali, and T. Kokab, "Advancements in Nanofiber-Based Electrochemical Biosensors for Diagnostic Applications," Biosensors, vol. 13, no. 4, Art. no. 4, Apr. 2023, doi: 10.3390/bios13040416.
14. Y. Li, "Molecularly imprinted polymer-based electrochemical biosensors for biomarkers detection," Doctoral, UCL (University College London), 2024. Accessed: May 17, 2025. [Online]. Available: https://discovery.ucl.ac.uk/id/eprint/10195540/
15. I. D. Mandel, "Sialochemistry in Diseases and Clinical Situations Affecting Salivary Glands," CRC Crit. Rev. Clin. Lab. Sci., vol. 12, no. 4, pp. 321–366, Jan. 1980, doi: 10.3109/10408368009108733.
16. U.-M. Bailey, C. Punyadeera, J. J. Cooper-White, and B. L. Schulz, "Analysis of the extreme diversity of salivary alpha-amylase isoforms generated by physiological proteolysis using liquid chromatography–tandem mass spectrometry," J. Chromatogr. B, vol. 911, pp. 21–26, Dec. 2012, doi: 10.1016/j.jchromb.2012.10.023.
17. Y. Kanamaru, Kikukawa ,Azusa, and K. and Shimamura, "Salivary chromogranin-A as a marker of psychological stress during a cognitive test battery in humans," Stress, vol. 9, no. 3, pp. 127–131, Jan. 2006, doi: 10.1080/14769670600909594.
18. F. P. Idris, Y. Wan, X. Zhang, and C. Punyadeera, "Within-Day Baseline Variation in Salivary Biomarkers in Healthy Men," OMICS J. Integr. Biol., vol. 21, no. 2, pp. 74–80, Feb. 2017, doi: 10.1089/omi.2016.0168.
19. M. A. D'amico, B. Ghinassi, P. Izzicupo, L. Manzoli, and A. D. Baldassarre, "Biological function and clinical relevance of chromogranin A and derived peptides," Jun. 2014, doi: 10.1530/EC-14-0027.
20. A. L. Mandel, Ozdener ,Hakan, and V. and Utermohlen, "Brain-Derived Neurotrophic Factor in Human Saliva: Elisa Optimization and Biological Correlates," J. Immunoassay Immunochem., vol. 32, no. 1, pp. 18–30, Jan. 2011, doi: 10.1080/15321819.2011.538625.
21. D. Tsikas, "Analytical methods for 3-nitrotyrosine quantification in biological samples: the unique role of tandem mass spectrometry," Amino Acids, vol. 42, no. 1, pp. 45–63, Jan. 2012, doi: 10.1007/s00726-010-0604-5.
22. S. Maheshwaran et al., "An Ultra-sensitive Electrochemical Sensor for the Detection of Oxidative Stress Biomarker 3-Nitro-l-tyrosine in Human Blood Serum and Saliva Samples Based on Reduced Graphene Oxide Entrapped Zirconium (IV) Oxide," J. Electrochem. Soc., vol. 167, no. 6, p. 066517, Apr. 2020, doi: 10.1149/1945-7111/ab847d.
23. M. Hasanzadeh, F. Mokhtari, V. Jouyban-Gharamaleki, A. Mokhtarzadeh, and N. Shadjou, "Electrochemical monitoring of malondialdehyde biomarker in biological samples via electropolymerized amino acid/chitosan nanocomposite," J. Mol. Recognit., vol. 31, no. 8, p. e2717, 2018, doi: 10.1002/jmr.2717.
24. J. Wang, H. M. Schipper, A. M. Velly, S. Mohit, and M. Gornitsky, "Salivary biomarkers of oxidative stress: A critical review," Free Radic. Biol. Med., vol. 85, pp. 95–104, Aug. 2015, doi: 10.1016/j.freeradbiomed.2015.04.005.
25. H. A. Saputra, "Electrochemical sensors: basic principles, engineering, and state of the art," Monatshefte Für Chem. - Chem. Mon., vol. 154, no. 10, pp. 1083–1100, Oct. 2023, doi: 10.1007/s00706-023-03113-z.
26. D. Grieshaber, R. MacKenzie, J. Vörös, and E. Reimhult, "Electrochemical Biosensors - Sensor Principles and Architectures," Sensors, vol. 8, no. 3, Art. no. 3, Mar. 2008, doi: 10.3390/s80314000.
27. J. Baranwal, B. Barse, G. Gatto, G. Broncova, and A. Kumar, "Electrochemical Sensors and Their Applications: A Review," Chemosensors, vol. 10, no. 9, Art. no. 9, Sep. 2022, doi: 10.3390/chemosensors10090363.
28. A. M. Oliveira-Brett, J. A. P. Piedade, L. A. Silva, and V. C. Diculescu, "Voltammetric determination of all DNA nucleotides," Anal. Biochem., vol. 332, no. 2, pp. 321–329, Sep. 2004, doi: 10.1016/j.ab.2004.06.021.
29. R. N. Goyal and G. Dryhurst, "Redox chemistry of guanine and 8-oxyguanine and a comparison of the peroxidase-catalyzed and electrochemical oxidation of 8-oxyguanine," J. Electroanal. Chem. Interfacial Electrochem., vol. 135, no. 1, pp. 75–91, Apr. 1982, doi: 10.1016/0022-0728(82)90006-7.
30. T.-H. Li, W.-L. Jia, H.-S. Wang, and R.-M. Liu, "Electrochemical performance of 8-hydroxy-2′-deoxyguanosine and its detection at poly(3-methylthiophene) modified glassy carbon electrode," Biosens. Bioelectron., vol. 22, no. 7, pp. 1245–1250, Feb. 2007, doi: 10.1016/j.bios.2006.05.005.
31. X. Sun et al., "Electrochemical detection of 8-hydroxy-2′-deoxyguanosine as a biomarker for oxidative DNA damage in HEK293 cells exposed to 3-chloro-1,2-propanediol," Anal. Methods, vol. 7, no. 16, pp. 6664–6671, Aug. 2015, doi: 10.1039/C5AY01246E.
32. A. Mugweru, B. Wang, and J. Rusling, "Voltammetric Sensor for Oxidized DNA Using Ultrathin Films of Osmium and Ruthenium Metallopolymers," Anal. Chem., vol. 76, no. 18, pp. 5557–5563, Sep. 2004, doi: 10.1021/ac049375j.
33. N. Kumar, Rosy, and R. N. Goyal, "A melamine based molecularly imprinted sensor for the determination of 8-hydroxydeoxyguanosine in human urine," Talanta, vol. 166, pp. 215–222, May 2017, doi: 10.1016/j.talanta.2017.01.058.
34. G. V. Martins, A. C. Marques, E. Fortunato, and M. G. F. Sales, "8-hydroxy-2′-deoxyguanosine (8-OHdG) biomarker detection down to picoMolar level on a plastic antibody film," Biosens. Bioelectron., vol. 86, pp. 225–234, Dec. 2016, doi: 10.1016/j.bios.2016.06.052.
35. A. M. Faria, E. B. M. I. Peixoto, C. B. Adamo, A. Flacker, E. Longo, and T. Mazon, "Controlling parameters and characteristics of electrochemical biosensors for enhanced detection of 8-hydroxy-2′-deoxyguanosine," Sci. Rep., vol. 9, no. 1, p. 7411, May 2019, doi: 10.1038/s41598-019-43680-y.
36. L.-P. Jia et al., "Enzyme-free and triple-amplified electrochemical sensing of 8-hydroxy-2′-deoxyguanosine by three kinds of short pDNA-driven catalyzed hairpin assemblies followed by a hybridization chain reaction," Analyst, vol. 145, no. 10, pp. 3605–3611, May 2020, doi: 10.1039/D0AN00233J.
37. L. Yuan, Y. Lan, M. Han, J. Bao, W. Tu, and Z. Dai, "Label-free and facile electrochemical biosensing using carbon nanotubes for malondialdehyde detection," Analyst, vol. 138, no. 11, pp. 3131–3134, May 2013, doi: 10.1039/C3AN00041A
38. M. Jamshidi, A. Walcarius, M. Thangamuthu, M. Mehrgardi, and A. Ranjbar, "Electrochemical approaches based on micro- and nanomaterials for diagnosing oxidative stress," Microchim. Acta, vol. 190, no. 4, p. 117, Mar. 2023, doi: 10.1007/s00604-023-05681-7.
39. C. Amatore, S. Arbault, M. Guille, and F. Lemaître, "Electrochemical Monitoring of Single Cell Secretion: Vesicular Exocytosis and Oxidative Stress," Chem. Rev., vol. 108, no. 7, pp. 2585–2621, Jul. 2008, doi: 10.1021/cr068062g.

40. M. K. Beissenhirtz, F. W. Scheller, and F. Lisdat, “A Superoxide Sensor Based on a Multilayer Cytochrome c Electrode,” Anal. Chem., vol. 76, no. 16, pp. 4665–4671, Aug. 2004, doi: 10.1021/ac049738f.
41. Z. Wang, H. Zhao, Q. Gao, K. Chen, and M. Lan, “Facile synthesis of ultrathin two-dimensional graphene-like CeO2–TiO2 mesoporous nanosheet loaded with Ag nanoparticles for non-enzymatic electrochemical detection of superoxide anions in HepG2 cells,” Biosens. Bioelectron., vol. 184, p. 113236, Jul. 2021, doi: 10.1016/j.bios.2021.113236.
42. S. Zhao, Z. Shi, C. X. Guo, and C. M. Li, “A high-energy-state biomimetic enzyme of oxygen-deficient MnTiO3 nanodiscs for sensitive electrochemical sensing of the superoxide anion,” Chem. Commun., vol. 55, no. 54, pp. 7836–7839, Jul. 2019, doi: 10.1039/C9CC02679G.
43. E. Dumitrescu, K. N. Wallace, and S. Andreescu, “Real time electrochemical investigation of the release, distribution and modulation of nitric oxide in the intestine of individual zebrafish embryos,” Nitric Oxide, vol. 74, pp. 32–38, Apr. 2018, doi: 10.1016/j.niox.2018.01.002.
44. R. E. Özel, K. N. Wallace, and S. Andreescu, “Chitosan coated carbon fiber microelectrode for selective in vivo detection of neurotransmitters in live zebrafish embryos,” Anal. Chim. Acta, vol. 695, no. 1, pp. 89–95, Jun. 2011, doi: 10.1016/j.aca.2011.03.057.
45. G. Ferrer-Sueta and R. Radi, “Chemical Biology of Peroxynitrite: Kinetics, Diffusion, and Radicals,” ACS Chem. Biol., vol. 4, no. 3, pp. 161–177, Mar. 2009, doi: 10.1021/cb800279q.
46. M. Govindasamy, S. Manavalan, S.-M. Chen, R. Umamaheswari, and T.-W. Chen, “Determination of oxidative stress biomarker 3-nitro-l-tyrosine using CdWO4 nanodots decorated reduced graphene oxide,” Sens. Actuators B Chem., vol. 272, pp. 274–281, Nov. 2018, doi: 10.1016/j.snb.2018.05.138.
47. R. Jalili and M. Amjadi, “Bio-inspired molecularly imprinted polymer–green emitting carbon dot composite for selective and sensitive detection of 3-nitrotyrosine as a biomarker,” Sens. Actuators B Chem., vol. 255, pp. 1072–1078, Feb. 2018, doi: 10.1016/j.snb.2017.08.145.
48. G. V. Martins, A. C. Marques, E. Fortunato, and M. G. F. Sales, “Wax-printed paper-based device for direct electrochemical detection of 3-nitrotyrosine,” Electrochimica Acta, vol. 284, pp. 60–68, Sep. 2018, doi: 10.1016/j.electacta.2018.07.150.
49. S.-M. Chen et al., “Hierarchically structured CuFe2O4 ND@RGO composite for the detection of oxidative stress biomarker in biological fluids,” Inorg. Chem. Front., vol. 5, no. 4, pp. 944–950, Apr. 2018, doi: 10.1039/C7QI00799J.
50. S. Wang et al., “Constructing a novel composite of molecularly imprinted polymer-coated AuNPs electrochemical sensor for the determination of 3-nitrotyrosine,” Electrochimica Acta, vol. 259, pp. 893–902, Jan. 2018, doi: 10.1016/j.electacta.2017.11.033.
51. S. P. Ng, G. Qiu, N. Ding, X. Lu, and C.-M. L. Wu, “Label-free detection of 3-nitro-l-tyrosine with nickel-doped graphene localized surface plasmon resonance biosensor,” Biosens. Bioelectron., vol. 89, pp. 468–476, Mar. 2017, doi: 10.1016/j.bios.2016.04.017.
52. X. Wang, M. Zhu, H. Liu, J. Ma, and F. Li, “Modification of Pd–Fe nanoparticles for catalytic dechlorination of 2,4-dichlorophenol,” Sci. Total Environ., vol. 449, pp. 157–167, Apr. 2013, doi: 10.1016/j.scitotenv.2013.01.008.
53. Y. Bai and S. Li, “Oxidative Stress Sensing System for 8-OHdG Detection Based on Plasma Coupled Electrochemistry by Transparent ITO/AuNTAs/PtNPs Electrode,” Biosensors, vol. 13, no. 6, p. 643, Jun. 2023, doi: 10.3390/bios13060643.
54. L. Yang, B. Wang, H. Qi, Q. Gao, C. Li, and C. Zhang, “Highly Sensitive Electrochemical Sensor for the Determination of 8-Hydroxy-2′-deoxyguanosine Incorporating SWCNTs-Nafion Composite Film,” J. Sens., vol. 2015, no. 1, p. 504869, 2015, doi: 10.1155/2015/504869.
55. Rosy and R. N. Goyal, “Determination of 8-Hydroxydeoxyguanosine: A potential biomarker of oxidative stress, using carbon-allotropic nanomaterials modified glassy carbon sensor,” Talanta, vol. 161, pp. 735–742, Dec. 2016, doi: 10.1016/j.talanta.2016.09.038.
56. P. Montoro-Leal, M. Zougagh, A. Sánchez-Ruiz, Á. Ríos, and E. Vereda Alonso, “Magnetic graphene molecularly imprinted polypyrrole polymer (MGO@MIPy) for electrochemical sensing of malondialdehyde in serum samples,” Microchem. J., vol. 178, p. 107377, Jul. 2022, doi: 10.1016/j.microc.2022.107377.
57. B. Sriram, S. Kogularasu, S.-F. Wang, and G.-P. Chang-Chien, “The Fabrication of a La2Sn2O7/f-HNT Composite for Non-Enzymatic Electrochemical Detection of 3-Nitro-l-tyrosine in Biological Samples,” Biosensors, vol. 13, no. 7, Art. no. 7, Jul. 2023, doi: 10.3390/bios13070722.
58. B. Sriram, J. N. Baby, Y.-F. Hsu, S.-F. Wang, and M. George, “In Situ Synthesis of a Bismuth Vanadate/Molybdenum Disulfide Composite: An Electrochemical Tool for 3-Nitro-l-Tyrosine Analysis,” Inorg. Chem., vol. 61, no. 35, pp. 14046–14057, Sep. 2022, doi: 10.1021/acs.inorgchem.2c02037.
59. F. X. Hu et al., “Living Cells Directly Growing on a DNA/Mn3(PO4)2-Immobilized and Vertically Aligned CNT Array as a Free-Standing Hybrid Film for Highly Sensitive In Situ Detection of Released Superoxide Anions,” Adv. Funct. Mater., vol. 25, no. 37, pp. 5924–5932, 2015, doi: 10.1002/adfm.201502341.
60. Z. Zhai et al., “Robust nanozyme with dense crystalline-amorphous interfaces for efficient detection of reactive oxygen species in saliva,” Sens. Actuators B Chem., vol. 435, p. 137571, Jul. 2025, doi: 10.1016/j.snb.2025.137571.
61. U. Afzal et al., “Chemical engineering for advanced flexible sensors: Novel carbon-metal oxide nanocomposites with superior multi-sensing behavior,” Sens. Actuators B Chem., vol. 431, p. 137449, May 2025, doi: 10.1016/j.snb.2025.137449.
62. Z. Xu et al., “A wearable sensor based on multifunctional conductive hydrogel for simultaneous accurate pH and tyrosine monitoring in sweat,” Biosens. Bioelectron., vol. 234, p. 115360, Aug. 2023, doi: 10.1016/j.bios.2023.115360.
63. A. Khan, E. DeVoe, and S. Andreescu, “Carbon-based electrochemical biosensors as diagnostic platforms for connected decentralized healthcare,” May 2023, doi: 10.1039/D2SD00226D.
64. C. Mwanza, W.-Z. Zhang, K. Mulenga, and S.-N. Ding, “Advancing green chemistry in environmental monitoring: the role of electropolymerized molecularly imprinted polymer-based electrochemical sensors,” Green Chem., vol. 26, no. 23, pp. 11490–11517, Nov. 2024, doi: 10.1039/D4GC03250K.
65. J. Kim et al., “Wearable salivary uric acid mouthguard biosensor with integrated wireless electronics,” Biosens. Bioelectron., vol. 74, pp. 1061–1068, Dec. 2015, doi: 10.1016/j.bios.2015.07.039.
66. H. Duan et al., “Wearable Electrochemical Biosensors for Advanced Healthcare Monitoring,” Adv. Sci. Weinh. Baden-Wurtt. Ger., vol. 12, no. 2, p. e2411433, Jan. 2025, doi: 10.1002/advs.202411433.
67. R. Diab, A. Choufani, J. Dagher, and N. Chahine, “The Influence of Circadian Rhythm on the Antioxidant Capacity of Saliva in Periodontal Diseases,” Cureus, vol. 16, no. 3, p. e56174, Mar. 2024, doi: 10.7759/cureus.56174.
68. S. Watanabe, Y. Kawasaki, and K. Kawai, “Diurnal variation of salivary oxidative stress marker 8-hydroxyguanine,” Genes Environ., vol. 41, no. 1, p. 20, Dec. 2019, doi: 10.1186/s41021-019-0138-3.
69. J. F. Hernández-Rodríguez, D. Rojas, and A. Escarpa, “Electrochemical Sensing Directions for Next-Generation Healthcare: Trends, Challenges, and Frontiers,” Anal. Chem., vol. 93, no. 1, pp. 167–183, Jan. 2021, doi: 10.1021/acs.analchem.0c04378.
70. P. V. V. Romanholo, C. A. Razzino, P. A. Raymundo-Pereira, T. M. Prado, S. A. S. Machado, and L. F. Sgobbi, “Biomimetic electrochemical sensors: New horizons and challenges in biosensing applications,” Biosens. Bioelectron., vol. 185, p. 113242, Aug. 2021, doi: 10.1016/j.bios.2021.113242.