Introduction

Reactive oxygen species (ROS) are chemically reactive molecules containing oxygen that play several beneficial roles for the organism. At low/moderate concentrations, they are needed for physiological activities such as intracellular signaling and homeostasis, cell death, immune defense against pathogens, and induction of mitogenic response [1–5]. These free radicals are produced endogenously as a natural by-product of the normal cellular metabolism of oxygen. Additionally, they can be induced by exogenous sources such as UV light, ionizing radiation, lifestyle, diet, stress, and smoking. Maintaining equilibrium between the reducing and oxidizing states is crucial for proper physiological functions; therefore, living organisms are equipped with antioxidant defense systems, consisting of both enzymatic and nonenzymatic antioxidants, to regulate the levels of these free radicals [6–11].

An imbalance between the production of ROS and the ability of the antioxidant systems to readily detoxify these reactive intermediates results in oxidative stress. Free radicals generated in excessive and uncontrollable amounts under oxidative stress conditions cause damage to DNA, proteins, and lipids, which can severely compromise cell health and contribute to disease development [12–14]. Indeed, in the past years, considerable research has demonstrated that oxidative stress is involved in the natural process of aging as well as a wide variety of human diseases, including...
neurodegenerative disorders, multiple sclerosis, cardiovascular disease, rheumatoid arthritis, and cancer [15–22]. Consistent with this relationship between oxidative stress and human disease, numerous studies have suggested that an increase in dietary antioxidant intake reduces the risk for coronary heart disease [23], Alzheimer’s disease [24–26], Parkinson disease [27], ischemic stroke [28–31], and asthma [32].

Biomarkers of oxidative stress are therefore important tools in the assessment both of disease status and of the health-enhancing effects of antioxidants in humans. In this review, we aim to discuss different methods and approaches used for the evaluation of oxidative stress in clinical samples, as well as to review recent findings of oxidative stress in patients with different types of cancer.

2. Methods and Approaches to Measure Oxidative Stress in Clinical Samples

2.1. Direct Measurement of Reactive Oxygen Species. Reactive oxygen species (ROS) are the key molecules responsible for the deleterious effects of oxidative stress. Direct measurement of their cellular levels is therefore one approach to determine oxidative stress conditions.

One way to estimate the cellular levels of ROS is through the use of fluorogenic probes [33–41]. Hydrogen peroxide (H₂O₂), hydroxyl radicals (OH·), and peroxyl radicals (ROO·) can be measured following staining with 5-(and -6)-carboxy-2′,7′-dichlorodihydrofluorescein diacetate (DCFDA). This membrane-permeable probe diffuses into the cells where it becomes hydrolyzed by intracellular esterase to DCFH. The latter remains trapped within the cells and reacts with H₂O₂, generating the fluorescent 2′,7′-dichlorofluorescein (DCF). Therefore, the amount of peroxide produced by the cells can be estimated by the fluorescence intensity of DCF (λexcitation = 488 nm and λemission = 530 nm) as analyzed by flow cytometry or by employing a fluorescence plate reader [39]. On the other hand, superoxide molecules (O₂⁻) can be detected following staining with another fluorescent probe, dihydroethidium (DHE). The sodium borohydride-reduced form of ethidium bromide is also permeable to viable cells. Inside the cells, DHE is directly oxidized to ethidium bromide by the superoxide anion, which then fluoresces. The red fluorescence, measured using an excitation of 488 nm and an emission of 585 nm, is therefore considered to be proportional to the intracellular superoxide anion levels [34, 38].

Another way to quantify ROS molecules such as hydroperoxides (R-OOH), particularly in serum, is by assessing the derivatives of reactive oxygen metabolites (D-Roms) test, as described by Trotti et al. [42]. In this assay, a small amount of patient serum is dissolved in an acetate-bu

...described by Trotti et al. [42]. In this assay, a small amount of patient serum is dissolved in an acetate-bu
79. While this method determines MDA levels more reproducibly and reliably, the individual sample processing makes it time-consuming, labor-intensive, and impractical.

Alternative, plasma MDA can be measured using high-performance liquid chromatography (HPLC) employing a C18 reversed-phase column [75] as described by Victorino et al. [76] or by gas chromatography-mass spectrometry (GC-MS) on a capillary column following transmethylation with sodium methoxide [77–79]. While this method determines MDA levels more reproducibly and reliably, the individual sample processing makes it time-consuming, labor-intensive, and impractical.

Other lipid peroxidation markers include 8-isoprostaglandin F2α (8-iso-PGF2α), 4-hydroxy-2-nonenal (4-HNE), conjugated dienes (CD), and lipid hydroperoxides (LOOH), providing different reliable approaches for the identification of oxidative damage to the cell’s lipids. 8-ISO-PGF2α, generated as a result of nonenzymatic peroxidation of arachidonic acid in membrane phospholipids, can be measured using rapid ultra-high-performance liquid chromatography-tandem mass spectrometry, noting the limitations of being labor-intensive and requiring specialized and expensive instrumentation [80, 81]. Unsaturated hydroxynalkenal 4-HNE can be investigated in tissues, preferably using immunohistochemistry (IHC), or HPLC [82, 83]. CDs, produced as a consequence of free radical-induced autooxidation of polyunsaturated fatty acids (PUFAs), can be detected according to Suryanarayana Rao and Recknagel, which follows the maximal absorption of UV light at 233 nm by these compounds [84–86]. Finally, LOOHs, which are the primary oxidation products of PUFAs, can be determined by the ferrous oxidation xylenol orange (FOX) assay, based on the ability of LOOH to oxidize ferrous iron in the presence of xylenol orange, leading to the formation of a colored ferric-xylenol orange complex, with an absorbance at 560 nm [87, 88].

Oxidized levels of low-density lipoproteins (LDL) are also sometimes measured in human serum or plasma as established biosensors of oxidative stress, using a sandwich ELISA based on the proprietary mouse monoclonal antibody 4E6, which is directed against a conformational epitope in oxidized ApoB-100. However, this method may fall short on antibody specificity for oxLDL as native LDL may also be detected [89–91].

2.2.3. DNA Damage. 8-Hydroxy-2’-deoxyguanosine (8-OHdG) is one of the major oxidative modifications in DNA that is generated by hydroxylation of the deoxyguanosine residues. 8-OHdG residues can be excised from the DNA by enzymatic repair systems, leading to their circulation in the blood and subsequent excretion in the urine [92]. Levels of 8-OHdG in blood and/or urine of patients can therefore be measured as a marker of oxidative DNA damage. 8-OHdG is frequently examined using HPLC coupled with an electrochemical detector (ECD) [93–96] based on the procedures elaborated by Shigenaga et al. [97], Toyokuni et al. [98], or Helbock et al. [99]. In spite of its sensitivity and accuracy, the HPLC-ECD method is not very convenient for analyzing 8-OHdG contents in clinical samples because of its cost, technical involvement, and low throughput [100]. Alternative and simpler ways to measure this DNA damage marker include the enzyme-linked immunosorbent assay (ELISA) [55, 82, 100–102] and immunohistochemical analysis [82, 101–105]. 8-oxoG can also be identified by OxyDNA-FITC conjugate binding followed by analysis by flow cytometry for fluorescence at λexcitation = 495 nm and λemission = 515 nm [36].

Thymidine glycol (TG) is another principal DNA lesion caused by oxidative stress. TG is a more specific marker for oxidative DNA damage because thymidine, unlike guanosine, is not incorporated into RNA. Moreover, TG is sustained in tissues while 8-OHdG is rapidly excised from DNA and excreted in urine. Therefore, TG is an appropriate marker for oxidative DNA damage in tissue specimens. Accumulation of TG in tissues can be examined immunohistochemically using the streptavidin-biotin-peroxidase complex method [44].

Single- or double-stranded breaks within the DNA are also generated during oxidative stress conditions. These oxidative DNA lesions can be identified using the comet assay, which is based on the ability of cleaved DNA fragments to migrate out of the nucleus when an electric field is applied, unlike the undamaged DNA which migrates slower and remains within the nucleoid. Assessment of the DNA “comet” tail shape and migration pattern can therefore be used to evaluate DNA damage within cells [35, 36].

More generally, various modified DNA bases in clinical samples can also be measured using gas chromatography-mass spectrometry with selected ion monitoring (GC/MS-SIM) as described by Dizdaroglu [106]. Here, the quantification of these products is done by isotope-dilution mass spectrometry using their stable isotope-labeled analogues as internal standards. It is worth mentioning that the DNA base modifications detected with all these methods, although very important, do not provide information as to whether the damage is in active genes or in quiescent DNA. However, it seems likely that the “exposed” and active DNA would be more sensitive to oxidative damage than that packaged into condensed chromatin.

Alternatively, DNA repair enzymes, such as human 8-oxoguanine-DNA-glycosylase (hOGG) and apurinic/apyrimidinic endonuclease (APE), which repair the endogenous DNA damage induced by increased ROS levels, can be evaluated to estimate oxidative damage in clinical samples. Their levels can be determined by IHC analysis [107, 108] or HPLC [109] while the activity of the hOGG enzyme can be assessed according to the method of Yamamoto et al. [110], which uses a double-stranded 22 bp oligonucleotide substrate containing one 8-OHdG paired with deoxyctydine at the complementary strand and labeled with FITC.

2.3. Assessment of Antioxidant Status. The human body is equipped with an antioxidant system that serves to counterbalance the deleterious effects of oxidative free radicals. When the balance between antioxidants and ROS species, referred to as redox homeostasis, is disturbed, oxidative stress can occur. The disturbance of this prooxidant and antioxidant balance
can be a result of increased free radical production, antioxidant enzyme inactivation, or excessive antioxidant consumption. Assessment of the antioxidant status can thereby be correlated to the extent of oxidative stress in clinical samples.

Redox homeostasis is regulated by two arms of antioxidant machineries: enzymatic components and nonenzymatic, low molecular compounds. Several approaches have been developed to measure the different activities or levels of these antioxidants. Alternatively, the total antioxidant status can be evaluated to assess the oxidative state of clinical samples.

2.3.1. Enzymatic Antioxidants

(1) Superoxide Dismutase. Superoxide dismutase (SOD) is a family of antioxidant enzymes that regulate ROS levels by catalyzing the conversion of superoxide to hydrogen peroxide and molecular oxygen [61].

Their total activity can be determined using a method described by McCord and Fridovich [111] or Misra and Fridovich [112]. The basis of this method is the ability of SOD to inhibit the autoxidation of adrenaline to adrenochrome in a basic medium, which can be measured at an absorption of \( \lambda = 480 \text{ nm} \) [66, 67]. Another method to directly measure the activity of SOD has been established by Marklund and Marklund [113] and described by Roth and Gilbert [114] and is based on a similar principle. Instead of epinephrine autoxidation, their method conversely investigates the ability of SOD to inhibit the autoxidation of pyrogallol into a yellow solution that can be measured at an absorbance of 420 nm [75].

Alternatively, SOD activity can be measured using indirect methods developed by Nishikimi et al. [115] & Kakkar et al. [116] or Oyanagui (1984) & Sun et al. (1988) [117, 118]. The principle of this indirect method is that superoxide radicals, generated by the NADH/D-amino acid oxidase-phenazine methosulfate (PMS) system or the xanthine-xanthine oxidase system, respectively, cause the reduction of tetrazolium salts such as 2-(4-idophenyl)-3-(4-nitrophenol) 5-phenyltetrazolium (INT), 3′,5′-dichloro-2,4-dinitrophenylamino-carbonyl]-3,4-tetrazolium-bis (4-methoxy-6-nitro)benzenesulfonic acid (XTT), or nitro blue tetrazolium (NBT), into blue formazan which can be measured spectrophotometrically at 470-560 nm. The SOD in the samples competes for the generated superoxide radicals, thereby inhibiting the reaction of tetrazolium reduction [77-79, 119-123]. In all the methods discussed above, a unit of SOD is generally defined as the amount of the enzyme which causes inhibition of the reaction (autoxidation of adrenaline, autoxidation of pyrogallol, or tetrazolium reduction).

It is worth noting that these methods can also be applied following a separation step in sample preparation to determine the different activities of the three SOD isoforms (cytosolic Cu/Zn-SOD, mitochondrial MnSOD, and extracellular EC-SOD). Due to its affinity to heparin, EC-SOD can be separated from the intracellular isoforms by passing the samples over a concanavalin A sepharose column [124]. On the other hand, applying differential centrifugation to the samples results in a mitochondrial pellet and cytosolic supernatant, which can be used to assess the separate activities of MnSOD and Cu/Zn-SOD, respectively [125, 126]. The selective measurement of MnSOD activity can also be achieved by the addition of sodium cyanide to the samples to inhibit the Cu/Zn-SOD isoform [127, 128].

(2) Catalase. Catalase is a ubiquitously expressed antioxidant enzyme that is responsible for the degradation of hydrogen peroxide into water and oxygen [129]. Numerous methods have been designed to assess the activity of this antioxidant in biological samples. A quantitative spectrophotometric method, developed by Beers and Sizer [130] and described by Nelson and Kiesow [131] or Aebi [132], follows the breakdown of hydrogen peroxide catalyzed by catalase, by observing the decrease in ultraviolet absorbance of a hydrogen peroxide solution at \( \lambda = 240 \text{ nm} \) as a function of time [67, 75, 77-79]. Another simple colorimetric assay based on the utilization of hydrogen peroxide by catalase using the K2Cr2O7/acetic acid reagent has been described by Sinha [133]. When heated in the presence of hydrogen peroxide, the dichromate in acetic acid reduces to chromic acetate, which can be measured colorimetrically at 610 nm [119]. In both these methods, the catalase activity is determined by the disappearance of hydrogen peroxide and each unit is therefore defined as the amount that degrades 1 \( \mu \text{mol} \) of hydrogen peroxide per minute. Alternatively, the activity of the catalase enzyme can be determined using another spectrophotometric assay developed by Goth [134], which measures the stable complex formation of hydrogen peroxide with ammonium molybdate at an absorbance of 405 nm [121].

In contrast to the previously discussed assays, the method developed by Johansson and Håkan Borg [135] determines the activity of catalase using its peroxidatic function of alcohol oxidation. In this method, the formaldehyde, generated by the reaction of catalase with methanol in the presence of an optimal concentration of hydrogen peroxide, is measured spectrophotometrically at \( \lambda = 550 \text{ nm} \) with purpald reagent (4-amino-3-hydrazino-5-mercapto-1,2,4-triazole) as a chromagen [123].

(3) Glutathione Peroxidase. Glutathione peroxidase (GPx) is another antioxidant enzyme that catalyzes the reduction of hydrogen peroxide and lipid peroxides to water and their corresponding lipid alcohols via the oxidation of reduced glutathione (GSH) into glutathione disulfide (GSSG) [136]. Its activity can be assessed by the method of Rotruck et al. [137], as described by Hafeman et al. [138], in which the samples are incubated with hydrogen peroxide in the presence of glutathione for a particular time period. The amount of utilized hydrogen peroxide is then determined by directly estimating GSH content using Ellman’s reagent, 5,5′-dithiobisnitrobenzoic acid (DTNB) (discussed in Section 1) [139]. Another method developed by Kokatnur and Jelling [140] and later described by Paglia and Valentine [141] and Pleban et al. [142] relies on a similar principle, with GPx catalyzing the oxidation of glutathione by cumene hydroperoxide (for selenium-independent GPx) or hydrogen peroxide
(for selenium-dependent GPx). However, in this method, the oxidized glutathione is later reduced by exogenous glutathione reductase causing the coenzyme of the reaction, NADPH, to become oxidized into NADP+. The change in the absorbance can then be read spectrophotometrically at $\lambda = 340\text{ nm}$ [67, 119, 123, 143].

(4) **Glutathione S-Transferase.** Glutathione S-transferases (GSTs) are members of the multigene family of isoenzymes that are ubiquitously expressed in humans. In addition to their catalytic role in conjugating GSH to a variety of harmful electrophilic compounds for detoxification, a number of GST isoenzymes reduce lipid hydroperoxides through their selenium-independent GPx activity and detoxify lipid peroxidation end-products such as 4-HNE [144, 145]. Their activity is most commonly determined by the method of Habig et al. [146], which is based on the ability of GST to conjugate 1-chloro-2,4-dinitrobenzene (CDNB) to reduced glutathione. The conjugation is accompanied by an increase in absorbance at 340 nm which can be measured spectrophotometrically to directly estimate the level of GST activity in clinical samples [66, 119, 123, 143].

2.3.2. Nonenzymatic Antioxidants

(1) **Glutathione.** Inside the cell, free glutathione can exist as the reduced GSH and oxidized GSSG forms, although it is primarily maintained in the former state by glutathione reductase [147]. GSH is the most abundant intracellular low-molecular-weight thiol and plays a critical role in metabolic protective functions, including hydroperoxide reduction, xenobiotic detoxification, and free radical scavenging [148]. The levels of GSH are commonly determined by the method developed by Ellman [139] and described by Beutler et al. [149], Sedlak and Lindsay [150], or Hu [151], based on the ability of the Ellman reagent, DTNB, to react with compounds containing sulfhydryl groups, yielding a mixed disulfide (GS-TNB) and 2-nitro-5-thiobenzoic acid (TNB). The levels of the latter are quantified spectrophotometrically by measuring the absorbance of the anion \((\text{TNB}^-)\) at 412 nm using a molar extinction coefficient of $14,150\text{ M}^{-1}\text{ cm}^{-1}$ [143]. This method has been modified by Tietze [152] using an enzymatic recycling procedure by glutathione reductase to enhance the sensitivity of the assay and to measure instead the total glutathione content of the biological samples. In this method, the NADPH-dependent glutathione reductase of the recycling system subsequently reduces the generated GS-TNB, releasing a second TNB molecule and recycling GSH, thereby amplifying the response. In addition, any GSSG, present in the samples or formed during the reaction, is also reduced to GSH by glutathione reductase. Therefore, the glutathione concentration of the sample measured at an absorbance of 415 nm would account for both GSH and GSSG levels [75, 153].

Alternatively, the level of GSH can be determined using the GSH-400 method, based on a two-step chemical reaction followed by a spectrophotometric detection. First, 4-chloro-7-trifluoromethylbenzopyridine reacts with all mercaptans present in the sample to form substitution products (thioethers). Then, the passage through an alkaline medium gives rise to a specific $\beta$-elimination reaction of the thioether obtained with glutathione, leading to the formation of a chromophoric thione with an absorbance of 400 nm [83, 154].

Fluorometric assays have also been developed for glutathione analysis offering high specificity and specificity. The most frequently used probe, ortho-phthalaldehyde (OPA) or its analogue 2,3-naphthalenedicarboxaldehyde, reacts with GSH to form a highly fluorescent product with Ex/Em = 340/420 nm [155–157]. Other fluorescent probes, such as monochlorobimane (MCB) and monobromobimane (MBB), used less frequently, also form stable fluorescent adducts with GSH, which can be determined at Ex/Em = 394/490 nm. In comparison with OPA, MCB and MBB have the substantial advantage of penetrating into the cell to react directly with cellular thiols, preventing possible GSH oxidation after cell lysis and allowing analysis by flow cytometry and fluorescence microscopy [158–161].

(2) **Vitamin A.** Vitamin A refers to a group of fat-soluble retinoids (retinol, retinal, and retinyl esters) and provitamin A carotenoids (most notably $\beta$-carotene) that function as important dietary antioxidants, due to their ability to scavenge and directly neutralize free radicals [162]. The levels of retinoids and carotenoids are typically measured in plasma/serum or tissue samples to assess vitamin A inadequacy using atmospheric pressure chemical ionization (APCI) liquid chromatography/mass spectrometry [80, 163] or reversed-phase HPLC [164–168].

(3) **Vitamin C.** Water-soluble vitamin C (ascorbic acid), primarily found in the cytosol and extracellular fluid, plays a protective effect in reducing oxidative damage by reacting with ROS molecules such as aqueous peroxyl radicals [14, 169]. The total ascorbic acid level is commonly estimated by the method developed by Roe and Keuther [170]. This method involves the oxidation of ascorbic acid into dehydroascorbic acid by Cu$^2+$, followed by its coupling with 2,4-dinitrophenylhydrazine (DNPH). The resulting derivative is then treated with strong acid leading to the production of an orange-red product, which can be measured spectrophotometrically at 520 nm [171]. Ascorbic acid can also be measured using the method developed by Zannoni et al. In this method, ferric iron is reduced by ascorbic acid, producing ferrous iron, which then forms a red-colored complex with 2,2′-dipyridyl, displaying an absorbance at 520 nm [172]. It is worth noting that incubation of the samples with dithiothreitol prior to performing this assay, as suggested by Masato, would reduce dehydroascorbic acid into ascorbic acid, enabling the determination of total ascorbic acid in clinical samples [173]. Alternatively, the levels of vitamin C can be determined using reversed-phase HPLC [174–177].

(4) **Vitamin E.** Vitamin E (a-tocopherol) is a lipid-soluble vitamin which acts as a lipid peroxyl radical scavenger, preventing lipid peroxidation chain reactions in the cell membranes [14, 169].
Its level can be measured by the method of Emmerie and Engel [178], later described by Hashim and Schuttertjger [179] and Baker et al. [180], and is based on the reduction of ferric ions to ferrous ions by \( \alpha \)-tocopherol. Similar to the method by Zannoni et al. (discussed in Section 3), the ferrous ions are then coupled with 2,2′-dipryidyl, which can be detected colorimetrically at 520 nm [119]. The method of Desai also involves the reduction of ferric ions by vitamin E, but the formation of a pink-colored complex is achieved with batophenanthroline orthophosphoric acid, and the absorbance is read at 536 nm [181].

Vitamin E levels in serum can also be estimated using fluorometry by the method of Hansen and Warwick [182]. Following the precipitation of serum proteins by alcohol, vitamin E can be extracted into hexane level and quantified at \( \lambda_{\text{excitation}} = 295 \text{ nm} \) and \( \lambda_{\text{emission}} = 340 \text{ nm} \) [183]. Alternatively, tocopherols can be analyzed by gas chromatography-mass spectrometry (GC-MS) on a SPB1 column using a selected ion monitoring technique [77–79] or by reversed-phase HPLC [164–166, 168].

2.3.3. Total Antioxidant Capacity. Until recently, investigating the status of antioxidants has been carried out by measuring the levels or activities of each separately. However, measurement of the overall effect of antioxidants can be quite useful in assessing the oxidative state in clinical samples due to the various interactions between the different antioxidants [184]. Several methods that are less time-consuming and labor-intensive have therefore been developed to determine the total antioxidant status (TAS) in clinical samples.

The 2,2-diphenyl-1-picryl-hydrazyl (DPPH) reduction assay is a method that uses free radical traps to assess the antioxidant capacity of the samples. DPPH is a stable free radical due to the delocalization of the spare electron over the molecule as a whole, with a deep violet color characterized by an absorption band at 520 nm. When DPPH is mixed with an antiradical compound that can neutralize it, it becomes colorless. Therefore, the decrease in optical density of DPPH radicals is monitored to evaluate the antioxidant potential of the samples [185–187].

The 2,2′-azino-bis (3-ethylbenz-thiazoline-6-sulfonic acid) (ABTS) assay, developed by Erel [188, 189], similarly uses a strongly colored stable radical compound to evaluate the antioxidant state of samples. Here, ABTS is first oxidized by metmyoglobin and hydrogen peroxide into its radical cation form (ABTS•+), a blue-green chromophore with an absorption at 750 nm. When antioxidants are added, ABTS•+ is reduced to ABTS and becomes decolorized again. Therefore, this method also follows the discoloration of the stable radical spectrophotometrically to measure the relative antioxidant ability of the samples. This assay is often referred to as Trolox equivalent antioxidant capacity (TEAC) method, because the reaction rate is commonly calibrated with a water-soluble analogue of vitamin E, Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid), as an antioxidant standard. The ABTS assay has an advantage over other techniques in that it is freely soluble in both organic and aqueous solvents so it is applicable for both hydrophilic and lipophilic antioxidants [90, 185, 190–193].

The total radical-trapping antioxidant parameter (TRAP) assay is another free radical trapping method which has been widely applied to evaluate the antioxidant capacity particularly in plasma. In this assay, thermal decomposition of the water-soluble azo compound 2,2′-azobis(2-methylpropionamide) dihydrochloride (ABAP) generates peroxyl radicals at a known steady rate, which is monitored through a linear decrease in R-phycocerythrin (R-PE) fluorescence over time using a luminescence spectrometer \( (\lambda_{\text{excitation}} = 495 \text{ nm and } \lambda_{\text{emission}} = 575 \text{ nm}) \). When the sample is added to the reaction mixture, the antioxidants provide protection for the fluorescence decay of R-PE. The length of the lag phase is therefore used to directly estimate the total antioxidant capacity [75, 185, 194, 195]. This method is relatively more complex and time-consuming than the others are.

The ferric-reducing antioxidant power (FRAP) assay is a simpler and faster method to assess the antioxidative potential of plasma; however, this method cannot detect antioxidants that act by radical quenching. The colorimetric assay is based on the ability of antioxidants to reduce the ferric tripyridyltriazine (Fe\(^{3+}\)-TPTZ) complex to the ferrous form at low pH. The end-product (Fe\(^{2+}\)-TPTZ) has an intense blue color with absorption at 593 nm which can be monitored using a diode-array spectrophotometer to estimate the antioxidant capacity of the samples [45, 185, 196].

The biological antioxidant potential (BAP) test is another assay based on the ability of antioxidants to reduce ferric ions to ferrous ions. However, in this method, ferric ions are bound to a chromogenic thiocyanate derivative substrate, which becomes decolorized when the ferrous ions are reduced to ferrous ions by the antioxidants of the serum sample. This reduction is therefore quantified to estimate the antioxidant capacity of the sample by measuring the absorbance change at 505 nm [44, 197].

As for the method developed by Koracevic et al., a standardized solution of the Fe-EDTA complex reacts with hydrogen peroxide by a Fenton-type reaction leading to the formation of hydroxyl radicals which degrade sodium benzoate solution resulting in the release of colored TBARS. Addition of antioxidants inhibits the production of TBARS, and the inhibition of color development is detected spectrophotometrically at 532 nm to estimate the total antioxidant status in the clinical samples [198].

3. Oxidative Stress in Clinical Samples of Cancer Patients

ROS is a contributing factor in the natural process of aging as well as in various pathological diseases including cancer. Oxidative stress has been reported in almost all types of cancers, promoting many aspects of tumor development and progression [199]. During the process of carcinogenesis, an increase in ROS levels can occur due to elevated metabolic activity, oncogene activation, increased cellular receptor signaling, or mitochondrial dysfunction. Overproduction of ROS can also be induced exogenously by carcinogenic insults such
as cigarette smoke, heavy metals, ionizing radiation, and asbestos [199–202]. Alternatively, oxidative stress observed in cancer cells can arise from low levels or inactivation of antioxidant defense mechanisms as a result of mutations in tumor suppressor genes. For instance, mutant BRCA1 and p53 have been shown to attenuate the activation and function of nuclear factor (erythroid-derived 2)-like 2 (Nrf2), a transcription factor that stimulates a stress response pathway by inducing expression of ROS-detoxifying enzymes [203–205].

The free radicals, generated during oxidative stress conditions, can consequently act as secondary messengers in intracellular signaling pathways involved in cell cycle progression and proliferation, cell survival and apoptosis, cell migration and angiogenesis, tissue invasion and metastasis, and tumor stemness, thereby affecting all characters of oncogenic phenotype of cancer cells [199, 200]. In addition to these oxidative stress-mediated signaling events, high levels of ROS can also lead to nonspecific damage of macromolecules such as nucleic acids, proteins, and lipids, often creating more free radicals, and triggering a chain of destruction, to promote oncogenic transformation [206]. ROS can cause individual DNA base changes or gross chromosomal alterations, thereby inducing mutagenesis and genomic instability. The cells harboring DNA mutations typically undergo apoptosis if they are unable to completely repair these DNA lesions; however, under certain circumstances, these cells escape programmed cell death, giving rise to transformed progeny [14, 200, 207–209]. The mutagenic effects of ROS are not limited to DNA damage, but can also involve an attack of ROS molecules on proteins and lipids. For instance, oxidative damage to the cells’ lipids initiates lipid peroxidation, leading to the generation of a range of mutagenic products that could alter cellular functions and enhance cancer initiation or progression [210, 211]. On the other hand, ROS-induced protein damage to DNA repair enzymes has been suggested as an explanation for the increased susceptibility of mutations which contribute to the process of carcinogenesis [212].

Identification of oxidative stress biomarkers in clinical samples of cancer patients and defining their roles in cancer initiation and progression holds great promise in promoting the development of targeted therapeutic approaches and diagnostic strategies evaluating disease status. While literature records of direct measurement of ROS levels in clinical samples are limited, significant amount of data do exist regarding oxidative damage to the cell’s biomolecules (DNA, lipids, and proteins) as well as on enzymatic, nonenzymatic, and total antioxidant status in clinical samples of cancer patients. In the tables below, we summarize some of these findings in 10 different types of cancer. Table 1 outlines findings regarding oxidative damage to DNA, lipids, and proteins in clinical samples of cancer patients, while Tables 2, 3, and 4 summarize data related to enzymatic antioxidant activities, nonenzymatic antioxidant levels, and total antioxidant status, respectively. We have particularly selected publications that report quantitative values of the oxidant/antioxidant markers.

### 4. Conclusion

Oxidative stress is implicated in the natural process of aging as well as in a variety of disease states. A detailed understanding regarding the link between oxidative stress and pathogenesis can be exploited to assess disease status as well as to develop preventive and therapeutic strategies in humans. In this review, three approaches were suggested to assess oxidative stress in clinical samples: (1) direct measurement of ROS levels, (2) detection of the resulting oxidative damage to biomolecules (DNA, lipids, and proteins), and (3) determination of antioxidant status (enzymatic antioxidant activities, nonenzymatic antioxidant levels, or total antioxidant capacity).

Direct ROS determination is a valuable and promising oxidative stress biomarker that can reflect on disease status. However, as we noted earlier, their measurement in biological systems is a complex task given the short half-life and high reactivity of these species. On the other hand, “footprints” of oxidative stress are extremely stable and provide a more reliable approach to evaluate oxidative stress in clinical samples. While some of these modifications only reflect the local degree of oxidative stress, others have a direct effect on the function of target molecules. This functional significance or the causal role of oxidative modifications further highlights the clinical applicability of these oxidative stress markers. However, sample processing should be performed with caution to ensure their stability and to avoid the possibility that biomolecules may become oxidatively damaged during their isolation. As for the correlation of the antioxidant status to the state of oxidative stress in clinical samples, the measurement of individual antioxidant levels/activities could yield conflicting results. For instance, some papers report low antioxidant status in cancer samples, explaining it as a loss of their protective capacity due to high oxidative stress, while others interpret the findings of high levels/activities of the antioxidants as an adaptive response mechanism to detoxify oxidative stress-related harmful metabolites. To overcome such biases, it is advisable to determine the total antioxidant status by evaluating all antioxidants simultaneously without excluding their interactions with each other.

The choice of the oxidative stress biomarkers and the methods used to measure them in order to assess oxidative status in clinical samples should be decided based on the aim of the study and its design, as well as on the clinical relevance in the selected subjects. No single parameter has yet been recommended as a gold standard for defining redox status in clinical samples. Furthermore, the individual markers described above only partially reflect on oxidative status. Therefore, an integrative approach examining both pro- and antioxidant reactions has been recently suggested to obtain a comprehensive score with higher sensitivity to physiological and pathological alternations. Global redox status indexes such as OXY-SCORE or oxidative-INDEX, computed by subtracting the antioxidant capacity from ROS levels/ROS-induced damage, or oxidative stress index (OSI), which is the ratio of total oxidant status to total antioxidant status, reflect simultaneously on oxidative and antioxidant status in clinical samples and provide a better and more powerful index in the evaluation of...
| Type of cancer | DNA | Oxidative damage | Protein |
|---------------|-----|-----------------|---------|
| **Bladder cancer** | | | |
| Urinary 8-OHdG (ELISA): 8.12 ng/g creatinine compared to 4.13 ng/g in controls ($p = 0.019$) | Urinary MDA (TBARS): 9.54 μmol/g creatinine compared to 6.76 μmol/g in controls ($p = 0.024$) | Plasma PC content (DNPH): 0.5 mg/mg protein compared to 0.38 mg/mg in controls ($p < 0.001$) [Figure 3(b)] |
| Serum 8-OHdG (ELISA): 0.24 ng/mL | Serum MDA (Yoshioka’s TBARS): 13.91 ± 8.59 nmol/mL compared to 2.12 ± 0.78 nmol/mL in controls ($p < 0.001$) [183] | |
| Urinary 8-OHdG (ELISA): 12.2 ng/mL [102] | Tissue MDA (TBARS): 4.29 ± 3.2 μmol/mg protein compared to 2.3 ± 0.6 μmol/mg in controls (ns) [214] | |
| Urinary 8-OHdG (ELISA): 70.5 ± 38.2 ng/mg creatinine compared to 36.1 ± 24.5 ng/mg in controls ($p < 0.001$) [100] | Tissue MDA (Ohkawa’s TBARS): 5.92 ± 1.41 nmol/mg protein compared to 4.09 ± 1.25 nmol/mg in adjacent normal tissues ($p < 0.001$) | |
| | Tissue LOOH (FOX method): 0.57 ± 0.16 mmol/g tissue compared to 0.41 ± 0.12 mmol/g in adjacent normal tissues ($p < 0.001$) | |
| | Tissue CD (Suryanarayana Rao and Recknagel): 0.55 ± 0.17 mg/g tissue compared to 0.39 ± 0.11 in adjacent normal tissues ($p < 0.001$) | |
| | Blood (TBARS): 26.14 nmol/mL compared to 15.83 nmol/mL in controls ($p < 0.01$) [220] | |
| **Breast cancer** | | | |
| Tissue 8-OHdG (HPLC): 2.07 ± 0.95 per 10⁵ dG compared to 1.34 ± 0.46 in corresponding noncancerous tissues ($p < 0.0001$) | Serum MDA (TBARS): 6 μmol/L compared to 2 μmol/L in controls ($p < 0.05$) [Figure 1(a)] | |
| | Plasma MDA (Yagi’s TBARS): 5.07 ± 0.53 nmol/mL compared to 2.54 ± 0.38 nmol/mL in controls ($p < 0.05$) | |
| Tissue 8-OHdG (HPLC): 10.7 ± 15.5 per 10⁵ dG compared to 6.3 ± 6.8 in controls ($p = 0.035$) | Erythrocyte MDA (Donnan’s TBARS): 2.95 ± 0.76 pmol/mg Hg compared to 2.23 ± 0.47 pmol/mg in controls ($p < 0.05$) [218] | |
| Tissue 8-OHdG (IHC): 3.9 ± 7.2 signal intensity compared to 1.1 ± 1.4 in controls ($p = 0.008$) | Tissue MDA (Okawa’s TBARS): 5.92 ± 1.41 nmol/mg protein compared to 4.09 ± 1.25 nmol/mg in adjacent normal tissues ($p < 0.001$) | |
| Tissue hOGG1 (IHC): 3.34 ± 1.95 signal intensity compared to 2.27 ± 1.96 in controls ($p = 0.008$) | Tissue PC content (ELISA): 3.5 nmol/mg protein lysate compared to 2.3 nmol/mg in adjacent normal tissues ($p < 0.05$) [Figure 1(a)] | |
| **Cervical cancer** | | | |
| Cellular 8-OHdG (IHC): 64.5 ± 17.4 (low grade) and 91.8 ± 22.5 signal intensity (high grade) compared to 50.2 ± 14.2 in | Plasma MDA (Yagi’s TBARS): 6.5 nmol/mg Hg compared to 3.5 nmol/mg in controls ($p < 0.001$) [Figure 1] | |
| | Plasma PC content (Levine’s DNPH): 1.47 ± 0.54 nmol/mg compared to 0.80 ± 0.39 nmol/mg in controls ($p < 0.001$) [225] | |
| Type of cancer | DNA | Oxidative damage | Protein |
|---------------|-----|------------------|---------|
|               |     | Lipid            |         |
|               |     | Controls (p = 0.17 and p < 0.001) [222] |         |
| Urinary 8-OHdG (ELISA): 8.94 ± 1.70 ng/mg creatinine compared to 10.27 ± 2.60 ng/mg in controls (ns) [223] | | | |
| Plasma CD (Suryanarayana Rao and Recknagel): 1.75 μmol/mg Hg compared to 0.75 μmol/mg in controls (p < 0.001) [Figure 1] [224] | | | |
| Plasma MDA (Ohkawa’s TBARS): 6.2 nmol/mg Hb compared to 3.1 nmol/mg in controls (p < 0.0001) [Figure 1] [225] | | | |
| Erythrocyte MDA (Domnan’s TBARS): 5.1 nmol/mg Hg compared to 3.0 nmol/mg in controls (p < 0.0001) [Figure 5] [119] | | | |
| Plasma MDA (HPLC): 13.61 ± 0.73 nmol/mL compared to 9.85 ± 0.69 nmol/mL in controls (p < 0.05) [223] | | | |
| Plasma LOOH (FOX method): 0.84 ± 0.33 mmol/L compared to 0.36 ± 0.17 mmol/L in controls (p < 0.001) [225] | | | |
| Colorectal cancer | Tissue 8-OHdG (HPLC): 2.53 ± 0.15 per 10^7 dG compared to 1.62 ± 0.13 in corresponding surrounding tissues (p < 0.005) [94] | Tissue MDA (HPLC): 1.7 ± 0.39 (stage II), 2.25 ± 0.43 (stage III), and 4.04 ± 0.47 nmol/g tissue (stage IV) compared to 1.39 ± 0.15 in normal colon mucosa (p < 0.001) | Serum oxidized-LDL (ELISA): 39.2 U/L compared to 36.2 U/L in controls (p = 0.045) [226] |
| Tissue 8-OHdG (HPLC): 49 [range: 23-114] per 10^6 dG compared to 21 [range: 9-39] per 10^6 dG in corresponding normal mucosa (p = 0.012) [96] | Tissue 4-HNE (HPLC): 0.37 ± 0.07 (stage II), 0.45 ± 0.09 (stage III), and 0.52 ± 0.11 nmol/g tissue (stage IV) compared to 0.29 ± 0.03 in normal colon mucosa (p < 0.001) [83] | | |
| Tissue 8-OHdG lyase activity (Yamamoto): 36.16 ± 1.79% compared to 19.72 ± 1.13 in nonmalignant counterparts (p < 0.001) | Tissue MDA (Ohkawa’s TBARS): 81.1 ± 17.8 nmol/mg protein compared to 69.8 ± 12.8 in normal mucosa (p = 0.046) [109] | | |
| Tissue hOGG1 transcripts (quantitative RT-PCR): 3.05 ± 3.21 × 10^5 copies/μg RNA compared to 4.55 ± 0.54 × 10^5 copies/μg in nontumorous counterparts (p < 0.001) | Tissue MDA (Beuge and Aust’s TBARS): 0.86 ± 0.10 nmol/mg tissue compared to 0.54 ± 0.08 in normal samples (p < 0.01) [227] | | |
| Tissue 8-OHdG (IHC): 229.1 ± 20.0 staining intensity compared to 113.3 ± 7.1 in corresponding normal epithelial cells (p < 0.001) | | | |
| | | Tissue MDA (HPLC): 1.7 ± 0.39 (stage II), 2.25 ± 0.43 (stage III), and 4.04 ± 0.47 nmol/g tissue (stage IV) compared to 1.39 ± 0.15 in normal colon mucosa (p < 0.001) | | |
| | | Tissue 4-HNE (HPLC): 0.37 ± 0.07 (stage II), 0.45 ± 0.09 (stage III), and 0.52 ± 0.11 nmol/g tissue (stage IV) compared to 0.29 ± 0.03 in normal colon mucosa (p < 0.001) | | |
| | | Tissue hOGG1 transcripts (quantitative RT-PCR): 3.05 ± 3.21 × 10^5 copies/μg RNA compared to 4.55 ± 0.54 × 10^5 copies/μg in nontumorous counterparts (p < 0.001) | | |
| | | Tissue MDA (Beuge and Aust’s TBARS): 0.86 ± 0.10 nmol/mg tissue compared to 0.54 ± 0.08 in normal samples (p < 0.01) | | |
| Type of cancer | DNA | Oxidative damage | Protein |
|---------------|-----|------------------|---------|
|               | nontumorous counterparts ($p < 0.001$) [95] | **Plasma MDA (TBARS):** 0.78 ± 0.5 nmol/mL compared to 1.23 ± 1.03 in smoker controls and 1.19 ± 1.09 in nonsmoker controls (ns) [120] | **Plasma PC content (Levine’s DNPH):** $1E-05 ± 5E-06$ nmol/mg protein compared to $8E-05 ± 5E-06$ in smoker controls and $7E-06 ± 9E-06$ in nonsmoker controls ($p = 0.003$) [120] |
| Lung cancer   | *Tissue 8-OHdG (HPLC):* 2.4 ± 1.1 per $10^5$ dG compared to 1.6 ± 0.6 per $10^5$ dG in normal mucosa ($p = 0.007$) | **Plasma MDA (TBARS):** 1.01 ± 0.28 μmol/L compared to 0.97 ± 0.88 μmol/L in corresponding post-resection samples ($p < 0.05$) | **Tissue MDA (Ohkawa’s TBARS):** 0.154 ± 0.06 nmol/mg protein compared to 0.087 ± 0.038 nmol/mg in adjacent normal tissues ($p < 0.05$) [143] |
|               | *Tissue hOGG (HPLC):* 4.3 ± 1.3 pmol of OHdG released from DNA/1 h compared to 2.7 ± 1.2 in normal mucosa ($p = 0.022$) [109] | *Tissue MDA (TBARS):* 0.46 ± 0.50 μmol/g protein compared to 0.85 ± 0.42 μmol/g in adjacent normal tissues ($p < 0.05$) | *Tissue MDA (TBARS):* 0.49 nmol/mg protein compared to 0.71 nmol/mg in adjacent normal tissues ($p = 0.001$) [230] |
| Liver cancer  | *Blood 8-OHdG (HPLC):* 24 ± 11 per $10^5$ dG compared to 16 ± 6 per $10^5$ dG in normal mucosa ($p = 0.007$) | *Plasma oxidized-LDL (ELISA):* 37.64 ± 8.00 U/L compared to 33.72 ± 8.71 U/L in corresponding post-resection samples ($p < 0.05$) [90] | *Tissue MDA (TBARS):* 0.49 nmol/mg protein compared to 0.71 nmol/mg in adjacent normal tissues ($p = 0.001$) [230] |
|               | *Tissue TG (IHC):* 72 ± 8.0 and 79 ± 4.9 percent positive rate in nonlesion sites of never smokers and current smokers, respectively [44] | | |
|               | *Tissue 8-OHdG (IHC):* 8.605 staining intensity compared to 4.845 in nonalcoholic steatohepatitis controls ($p = 0.003$) [105] | | |
|               | *Tissue 8-OHdG (HPLC):* 52 fmol/μg DNA compared to 129 fmol/μg in adjacent normal tissues ($p = 0.003$) [230] | | |
| Type of cancer | DNA | Oxidative damage | Protein |
|---------------|-----|------------------|---------|
|               |     | Plasma MDA (HPLC): 3.26 ± 0.46 nmol/mL (stage I/II) and 5.83 ± 0.68 nmol/mL (stage III/IV) compared to 1.10 ± 0.23 in controls (p < 0.05) [231] | Tissue MDA (TBARS): 0.65 ± 0.09 μM compared to 0.15 μM in controls (p = 0.009) [Figure 2] [33] |
| Ovarian cancer | Serum 8-OHdG (ELISA): 198.6 ± 80.2 pg/mL [101] | Serum MDA (Buege and Aust’s TBARS): 4.18 ± 0.80 nmol/mL (stage II) and 6.23 ± 1.37 nmol/mL (stage IV) compared to 2.51 ± 0.60 in controls (p < 0.001) [236] | Tissue PC content (Mesquita’s DNPH): 18 nmol/mg total protein compared to 5.5 nmol/mg in controls (p = 0.009) [Figure 3] [33] |
|               | Serum 8-OHdG (ELISA): 3.22 ± 0.49 ng/mL [234] | Serum MDA (TBARS): 8.7 ± 3.0 nmol/L compared to 6.7 ± 2.7 nmol/L in controls (p = 0.002) [237] | Tissue PC content (Levine’s DNPH): 10-14 nmol/mg protein compared to 4 nmol/mg in normal surrounding samples (p < 0.05) [Figure 1] [56] |
|               | Tissue 8-OHdG (ELISA): 27.8 ± 8.98 per 10⁶ dG compared to 18.8 ± 5.2 per 10⁶ dG in adjacent normal tissues (p = 0.02) [235] | Erythrocytes MDA (TBARS): 5.9 ± 0.6 nmol/g Hb compared to 5.3 ± 0.3 nmol/g in controls (p = 0.001) [238] |
| Prostate cancer | Urinary 8-OHdG (ELISA): 58.8 ± 43.4 ng/mg creatinine compared to 36.1 ± 24.5 ng/mg in controls (p = 0.021) [100] | Plasma MDA (TBARS): 10.5 ± 6.5 nmol/mL compared to 7.5 ± 1.9 nmol/mL in controls (p < 0.05) [Figure 1(a)] [171] | Serum PC (Levine’s DNPH): 1.06 nmol/mg protein compared to 0.88 nmol/mg in controls (p < 0.05) [Figure 1(b)] [171] |
|               | Urinary 8-OHdG (ELISA): 20.8 ± 8.9 ng/mg creatinine compared to 16.1 ± 7.8 ng/mg in controls (p < 0.05) [239] | Serum MDA (Yoshioka’s TBARS): 16.98 ± 6.66 nmol/mL compared to 4.45 ± 1.65 nmol/mL in controls (p < 0.005) [240] | |
|               | Plasma MDA (TBARS): 44.6 ± 19.7 × 10⁻² nmol/mL compared to 28.5 ± 8.8 × 10⁻² nmol/mL in controls (p < 0.001) | Erythrocytes MDA (TBARS): 43.0 ± 19.7 nmol/g Hb compared to 24.1 ± 8.8 nmol/g in controls (p < 0.001) |
| Skin cancer   | Urinary 8-OHdG (ELISA): 110.08 ± 30.09 ng/mg creatinine compared to 61.92 ± 17.35 ng/mg in controls (p < 0.001) | Plasma MDA (TBARS): 2.367 μM compared to 1.860 μM in controls (p < 0.0001) [241] | Cellular PUFAs (GC-MS): 11.8 ± 4.1% arachidonic acid/total fatty acids compared |
|               |     | Cellular PUFAs (LC-MS): 51.8 ± 12.3% arachidonic acid/total fatty acids compared |

Note: The values are reported as mean ± standard deviation unless stated otherwise.
| Type of cancer                  | DNA       | Oxidative damage | Protein                          |
|--------------------------------|-----------|------------------|----------------------------------|
|                                | Tissue 8-OHdG (IHC): 2.88 ± 0.30 IRS compared to 2.30 ± 0.67 in controls and 2.27 ± 0.72 in adjacent epidermis (p < 0.001) | to 4.67 ± 0.9% in normal melanocytes (p < 0.001) [79] |                                |
|                                | Tissue hOGG1 (IHC): 1.77 ± 0.40 IRS compared to 2.56 ± 0.47 in controls and 2.53 ± 0.47 in adjacent epidermis (p < 0.001) [107] | Plasma MDA (HPLC): 281.2 ± 17.36 nM (T1/T2) and 377.9 ± 36.15 nM (T3/T4) compared to 191.7 ± 15.01 nM in controls (p < 0.0001) [75] |                                |
| Thyroid cancer                 | Serum 8-OHdG (ELISA): 4.98 ± 2.56 ng/mL compared to 3.72 ± 1.17 in controls (p < 0.001) [243] | Serum MDA (TBARS): 65 μmol/L compared to 52 μMol/L in controls (p < 0.001) [79] |                                |
|                                | Erythrocytes MDA (Donnan’s TBARS): 6.63 ± 0.6 pmol/mg Hb compared to 3.20 ± 0.32 pmol/mg in controls (p < 0.001) [247] |                                |                                |
|                                | Blood MDA (Uchiyama and Mihara’s TBARS): 233 ± 36 nM/g tissue (follicular carcinoma) and 239 ± 29 nmol/g (papillary carcinoma) compared to 141 ± 17 nmol/g in controls (p < 0.05) [244] |                                |                                |
|                                | Tissue MDA (Uchiyama and Mihara’s TBARS): 127.00 ± 2.82 nmol/g tissue compared to 87.75 ± 4.71 nmol/g in adjacent tissue (p = 0.01) [245] |                                |                                |
|                                | Blood MDA (Uchiyama and Mihara’s TBARS): 3.59 ± 0.1 nmol/mL compared to 1.23 ± 0.1 nmol/mL in controls (p < 0.05) |                                |                                |
|                                | Blood LOOH (FOX method): 4.94 ± 0.83 μM/mL compared to 1.7 ± 0.25 μM/mL in controls (p < 0.05) [246] |                                |                                |
|                                | Serum LOOH (FOX method): 14.71 ± 8.68 μmol/L compared to 6.51 ± 3.01 μmol/L in controls (p < 0.001) [243] |                                |                                |
|                                | Plasma MDA (Yagi’s TBARS): 6.57 ± 0.7 nmol/mL compared to 2.89 ± 0.30 nmol/mL in controls (p < 0.001) |                                |                                |
|                                | Erythrocytes MDA (Donnan’s TBARS): 6.63 ± 0.6 pmol/mg Hb compared to 3.20 ± 0.32 pmol/mg in controls (p < 0.001) [247] |                                |                                |
|                                | Blood AOPP (Witko-Sarsat): 271.14 ± 16.40 μmol/mL compared to 61.59 ± 16.42 in controls (p < 0.05) [246] |                                |                                |
|                                | Blood PC content (Levine’s DNPH): 6.21 ± 0.63 nmol/mg compared to 4.32 ± 0.24 in controls (p < 0.05) [248] |                                |                                |
| Type of cancer | Enzymatic antioxidant activities | GST |
|---------------|---------------------------------|-----|
| Bladder cancer | SOD: 194 ± 28 U/mg protein compared to 194 ± 28 U/mg in controls (p < 0.001) [251] |     |
|                | Catalase: 28 ± 0.14 U/mL in controls compared to 28 ± 0.14 U/mL in controls (p < 0.001) [183] |     |
|                | GPx: 500 U/g protein compared to 750 U/g protein in controls (p < 0.001) [218] |     |
|                | GST: 8.0 ± 0.12 U/min/mg Hb compared to 20.0 ± 0.12 U/min/mg Hb in controls (p < 0.001) [220] |     |
| Breast cancer  | SOD: 14.66 ± 4.11 U/mL Hg compared to 0.73 ± 0.31 U/mL Hg in controls (p < 0.001) [219] |     |
|                | Catalase: 2.05 ± 0.57 U/mL Hg compared to 3.22 ± 0.55 U/mL Hg in controls (p < 0.05) [218] |     |
|                | GPx: 550 U/g protein compared to 750 U/g protein in controls (p < 0.001) [217] |     |
|                | GST: 0.72 U/min/mg Hg compared to 2.2 U/min/mg Hg in controls (p < 0.001) [220] |     |
| Cervical cancer| SOD: 0.9 U/min/mg Hb compared to 0.9 U/min/mg Hb in controls (p < 0.001) [224] |     |
|                | Catalase: 0.1 U/min/mg Hb compared to 0.1 U/min/mg Hb in controls (p < 0.001) [220] |     |
|                | GPx: 2.9 U/min/mg Hb compared to 3.5 U/min/mg Hb in controls (p < 0.05) [223] |     |
|                | GST: 0.0 U/min/mg Hb compared to 0.0 U/min/mg Hb in controls (p < 0.001) [220] |     |

Table 2: Enzymatic antioxidant activities in clinical samples of cancer patients.
| Type of cancer     | SOD   | Enzymatic antioxidant activities                                  | GPx                                      | GST                                      |
|-------------------|-------|------------------------------------------------------------------|------------------------------------------|------------------------------------------|
|                   |       |                                                                  |                                          |                                          |
| Colorectal cancer |       |                                                                  |                                          |                                          |
|                   | 0.11 U/mg Hb compared to 1.84 ± 0.09 U/mg in controls (p < 0.05) | [Figure 6] [119]: 9.16 ± 0.46 mU/mg Hb compared to 6.06 ± 0.52 mU/mg in controls (p < 0.05) [223] |
|                   |       | In tissue (Cu/Zn-SOD—Misra and Fridovich): 237 ± 42 (stage I), 289 ± 47 (stage II), and 421 ± 58 U/g tissue (stage III) compared to 117 ± 25 in normal colon mucosa (p < 0.001) [83] | In tissue (Paglia and Valentine): 1854 ± 552 (stage I), 1987 ± 699 (stage II), and 2467 ± 368 U/g tissue (stage III) compared to 1723 ± 189 in normal colon mucosa (p < 0.001) [83] | In tissue (Habig's CDNB): 31.0 ± 22.11 U/g protein compared to 42.5 ± 23.45 U/g in corresponding distal margin (p = 0.021) [123] |
|                   |       | In tissue (Misra and Fridovich): 4.9 ± 2.2 U/mg protein compared to 7.5 ± 2.6 U/mg in normal mucosa (p = 0.002) [109] | In tissue (Paglia and Valentine): 76 ± 14 (stage I), 57 ± 16 (stage II), and 33 ± 18 U/g tissue (stage III) compared to 84 ± 17 U/g in normal colon mucosa (p < 0.001) [83] | In erythrocytes (Habig's CDNB): 3.61 ± 0.99 U/g Hb compared to 0.82 ± 0.08 U/g in controls (p < 0.05) [253] |
|                   |       | In tissue (Oyanagui/Sun et al.): 88.9 ± 40.69 U/g protein compared to 58.4 ± 29.23 U/g in corresponding distal margin (p < 0.0001) [123] | In tissue (Beers and Sizer): 19.3 ± 7.4 U/mg protein compared to 24.8 ± 6.2 U/mg in normal mucosa (p = 0.004) [109] | In tissue (Habig's CDNB): 31.0 ± 22.11 U/g protein compared to 42.5 ± 23.45 U/g in corresponding distal margin (p = 0.021) [123] |
|                   |       |                                                                  | In tissue (Johansson and Borg): 114.2 ± 63.48 U/g protein compared to 103.4 ± 53.13 U/g in corresponding distal margin (ns) [123] | In erythrocytes (Pleban et al.): 7.46 ± 8.80 U/g Hb compared to 12.80 ± 8.88 U/g in controls (p < 0.05) [253] |
|                   |       |                                                                  | In tissue (Beers and Sizer): 6.58 ± 1.5 U/g tissue compared to 3.94 ± 1.1 U/g in normal samples (p < 0.01) [123] |                                                                  |
|                   |       |                                                                  | In tissue (Oyanagui/Sun et al.): 1.60 U/mL compared to 1.91 U/mL (p < 0.01) [227] |                                                                  |
| Lung cancer        |       |                                                                  | In tissue (Goth): 33.53 ± 6.09 U/mg protein compared to 71.33 ± 14.38 U/mg in adjacent normal tissues (p < 0.01) [121] | In tissue (Habig's CDNB): 19.94 ± 0.73 IU/L compared to 3.64 ± 0.17 in controls (p < 0.001) [256] |
|                   |       |                                                                  | In serum (Johansson and Borg): 31.1 nmol/min/mL compared to 39.73 nmol/min/mL (ns) [254] | In tissue (Habig's CDNB): 1.72 ± 0.89 U/mg protein compared to 1.12 ± 0.43 U/mg in adjacent normal tissue (p = 0.0002) [257] |
|                   |       |                                                                  | In serum (GPX3 - ELISA): 10.1 ± 5.0 μg/mL compared to 13.0 ± 5.8 μg/mL in controls (p < 0.001) [255] |                                                                  |
| Liver cancer       | 119.8 U/mL compared to 153.0 U/mL (HBV positive controls) and 172.7 U/mL (healthy controls) (p < 0.001) [258] | In blood (Aebi): 16.094 ± 1.774 EU/g Hb (primary) and 13.599 ± 0.516 EU/g (metastatic) compared to 61.480 ± 0.210 in controls | In plasma (Paglia and Valentine): 125.60 ± 85.79 nmol/mL/min compared to 148.84 ± 92.77 in corresponding post-resection samples (ns) | In plasma (Habig's et al.): 47.65 ± 22.51 nmol/mL/min compared to 38.85 ± 16.27 nmol/mL/min in corresponding post-resection samples |
| Type of cancer          | SOD                                      | Catalase                                 | GPx                                      | GST                                      |
|------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|
| **In plasma (Oyanagi/Sun et al.):** | 13.5 ± 0.23 U/mL (stage I/II) and 10.7 ± 0.56 U/mL (stage III/IV) compared to 17.8 ± 0.14 in controls (p < 0.05) [231] | (p < 0.005) [259] | In tissue (Paglia and Valentine): 41.43 ± 17.10 nmol/min/mg protein compared to 31.07 ± 10.95 nmol/min/mg in adjacent normal tissues (p < 0.05) [90] | (p < 0.05) |
| **In plasma (Johansson and Borg):** | 8.26 ± 0.25 (stage I/II) and 5.07 ± 0.37 U/mL (stage III/IV) compared to 11.1 ± 0.32 in controls (p < 0.05) [231] |                                | In tissue (Paglia and Valentine): Se-GPx: 0.021 ± 0.009 μmol/min/mg protein compared to 0.031 ± 0.015 μmol/min/mg in adjacent normal tissues (p < 0.05) Non-Se-GPx: 0.045 ± 0.021 μmol/min/mg protein compared to 0.062 ± 0.02 μmol/min/mg in adjacent normal tissues (p < 0.05) [143] |
| **In tissue (Paglia and Valentine):** | 41.43 ± 17.10 nmol/min/mg protein compared to 31.07 ± 10.95 nmol/min/mg in adjacent normal tissues (p < 0.05) [90] |                                | In tissue (Paglia and Valentine): Se-GPx: 0.021 ± 0.009 μmol/min/mg protein compared to 0.031 ± 0.015 μmol/min/mg in adjacent normal tissues (p < 0.05) Non-Se-GPx: 0.045 ± 0.021 μmol/min/mg protein compared to 0.062 ± 0.02 μmol/min/mg in adjacent normal tissues (p < 0.05) [143] |
| **In tissue (IHC):** | 1.24 ± 0.51 IRS compared |                                | In tissue (IHCH): 1.24 ± 0.51 IRS compared |
| **Ovarian cancer**     | In serum (Goth): 28.2 ± 15.5 nmol/L/min compared to 36.1 ± 14.6 nmol/L/min in controls (p = 0.019) [237] |                                | In serum (GPX3—ELISA): 22.4 ng/mL compared to 27.8 in controls (p = 0.01) [260] |                                |
|                        | In serum (Habig et al.): 13.2 ± 0.6 μmol/dL compared to 9.2 ± 0.9 μmol/dL in controls (p < 0.001) [238] |                                | In erythrocytes (Paglia and Valentine): 50.3 ± 1.2 U/g Hb compared to 48.7 ± 1.1 U/g in controls (p < 0.001) [238] |                                |
| **Skin cancer**        | In whole blood (McCord and Fridovich): 1292.7 ± 534.6 U/g Hb compared to 1017.9 ± 253.5 in controls (ns) [67] |                                | In whole blood (Nekon and Kiesow): 139282.81 U/g Hb compared to 11451.35 U/g in controls (p < 0.0001) [241] |                                |
|                        | In cells (Roth and Gilbert): 1846.925 U/g Hb compared to 4547.013 U/g in controls (p < 0.00001) [241] |                                | In plasma (Paglia and Valentine): 0.42 ± 0.13 ng/ml Hb compared to 0.77 ± 0.20 ng/ml in controls (p < 0.001) |                                |
|                        |                                |                                | In plasma (Paglia and Valentine): 0.42 ± 0.13 ng/ml Hb compared to 0.77 ± 0.20 ng/ml in controls (p < 0.001) |                                |
|                        | In erythrocytes (Habig et al.): 1.815 ± 0.883 U/g Hb compared to 2.002 ± 0.529 U/g in controls (ns) [261] |                                |                                |                                |
| Type of cancer | SOD | Catalase | GPx | GST |
|---------------|-----|----------|-----|-----|
| Thyroid cancer | 63 ± 11 (follicular carcinoma) and 65 ± 10 U/g tissue (papillary carcinoma) compared to 58 ± 9 in controls (p < 0.05) [244] | In cells (Beers and Sizer): 586 ± 35 (follicular carcinoma) and 559 ± 31 U/g tissue (papillary carcinoma) compared to 564 ± 29 in controls (p < 0.05 and ns) [244] | In tissue (Rotruck et al.): 22.6 ± 5.5 (follicular carcinoma) and 20.4 ± 3.9 U/min/g tissue × 10³ (papillary carcinoma) compared to 18.6 ± 3.2 in controls (p < 0.05) [244] | In leukocytes (Habig et al.): 0.713 ± 0.065 U/mg protein compared to 0.497 ± 0.063 U/mg in controls (p < 0.001) [262] |

In erythrocytes (Sinha): 4.42 ± 0.38 U/mg Hb compared to 5.86 ± 0.58 U/mg in controls (p < 0.001) [247] | In erythrocytes (Kakkar): 1.64 ± 0.16 U/mg Hb compared to 2.14 ± 0.24 U/mg in controls (p < 0.001) [247] | | |

In erythrocytes (Rotruck et al.): 26.6 ± 2.48 U/g Hb compared to 34.06 ± 3.5 U/g in controls (p < 0.001) [247] | | | |

In tissue (Rotruck et al.): 22.6 ± 5.5 (follicular carcinoma) and 20.4 ± 3.9 U/min/g tissue × 10³ (papillary carcinoma) compared to 18.6 ± 3.2 in controls (p < 0.05) [244] | In tissue (Paglia and Valentine): 0.61 ± 0.07 U/mg protein compared to 0.97 ± 0.02 U/mg in adjacent tissues (p = 0.001) [244] | | |

In plasma (Rotruck et al.): 186.13 ± 8.44 U/L compared to 222.68 ± 28.8 U/L in controls (p < 0.001) [247] | In plasma (Rotruck et al.): 186.13 ± 8.44 U/L compared to 222.68 ± 28.8 U/L in controls (p < 0.001) [247] | | |

In plasma (Rotruck et al.): 27.7 ± 1.3 U/mg protein compared to 30.5 ± 1.2 U/mg in controls (p < 0.001) [247] | In plasma (Rotruck et al.): 27.7 ± 1.3 U/mg protein compared to 30.5 ± 1.2 U/mg in controls (p < 0.001) [247] | | |

In plasma (Rotruck et al.): 27.7 ± 1.3 U/mg protein compared to 30.5 ± 1.2 U/mg in controls (p < 0.001) [247] | In plasma (Rotruck et al.): 27.7 ± 1.3 U/mg protein compared to 30.5 ± 1.2 U/mg in controls (p < 0.001) [247] | | |

In plasma (Rotruck et al.): 27.7 ± 1.3 U/mg protein compared to 30.5 ± 1.2 U/mg in controls (p < 0.001) [247] | In plasma (Rotruck et al.): 27.7 ± 1.3 U/mg protein compared to 30.5 ± 1.2 U/mg in controls (p < 0.001) [247] | | |

In plasma (Rotruck et al.): 27.7 ± 1.3 U/mg protein compared to 30.5 ± 1.2 U/mg in controls (p < 0.001) [247] | In plasma (Rotruck et al.): 27.7 ± 1.3 U/mg protein compared to 30.5 ± 1.2 U/mg in controls (p < 0.001) [247] | | |
Table 3: Nonenzymatic antioxidant levels in clinical samples of cancer patients.

| Type of cancer | Glutathione | Nonenzymatic antioxidant levels | Vitamin E (α-tocopherol) |
|---------------|-------------|---------------------------------|--------------------------|
| **Bladder cancer** | In tissue (Ellman): 7.11 ± 3.3 μg/mg protein compared to 14.45 ± 4.11 μg/mg in controls (p < 0.001) [214] | In plasma (HPLC): 1.41 μg retinol/mL compared to 1.53 μg/mL in controls (p < 0.001) [264] | In serum (fluorometry): 0.71 ± 0.19 mg/dL compared to 1.43 ± 0.09 mg/dL in controls (p < 0.001) [183] |
|                | In plasma (Ellman): 5.14 ± 2.02 μM compared to 6.04 ± 2.05 μM in controls (p = 0.047) [263] | In plasma (Roe and Keuther): 0.19 ± 0.08 mg/dL compared to 0.51 ± 0.09 mg/dL in controls (p < 0.001) [183] | In plasma (HPLC): 23.93 μg/mL compared to 27.48 μg/mL in controls (p < 0.001) [264] |
| **Breast cancer** | In tissue (Tietze): 18.89 ± 4.21 mg/100 g tissue compared to 9.49 ± 3.23 mg/100 g in adjacent normal tissues (p < 0.001) [219] | In plasma (HPLC): 248.5 ng β-carotene/mL compared to 226.0 ng/mL in controls (p = 0.02) | In plasma (Baker et al.): 0.72 ± 0.19 mg/dL compared to 1.12 ± 0.11 mg/dL in controls (p < 0.05) [218] |
|                | In plasma (Ellman): 27.58 ± 1.75 mg/dL compared to 32.11 ± 2.29 mg/dL in controls (p < 0.05) [218] | In plasma (Roe and Keuther): 0.63 ± 0.2 mg/dL compared to 1.1 ± 0.1 mg/dL in controls (p < 0.05) [218] | In plasma (Hashim and Schuttlinger): 0.92 ± 0.68 mg/dL compared to 1.73 ± 0.78 mg/dL in controls (p < 0.05) [266] |
| **Cervical cancer** | In plasma (Ellman): 37 mg/dL. compared to 21 mg/dL in controls (p < 0.001) [Figure 2] [224] | In serum (HPLC): 2.04 μmol retinol/L compared to 2.14 μmol/L in controls (p < 0.001) [Figure 4] | In plasma (Baker et al.): 0.8 mg/dL compared to 2.3 mg/dL in controls (p < 0.001) [Figure 2] [224] |
|                | In plasma (Ellman): 1.5 mg/dL compared to 2 mg/dL in controls (p < 0.0001) [Figure 6] [219] | In plasma (Roe and Keuther): 0.3 mg/dL compared to 1.1 mg/dL in controls (p < 0.001) [Figure 4] [224] | In plasma (Baker et al.): 1 mg/dL compared to 2.3 mg/dL in controls (p < 0.0001) [Figure 3] [119] |
|                | In erythrocytes (Ellman): 35 mg/dL in controls (p < 0.0001) [267] | In plasma (Roe and Keuther): 0.7 mg/dL compared to 1.3 mg/dL in controls (p < 0.0001) [Figure 3] [119] | In serum (HPLC): 17.1 μmol/L compared to 17.3 μmol/L in controls (ns) [267] |
|                | In plasma (Hu): 269.66 ± 82.48 μmol/mL compared to 316.18 ± 74.09 μmol/mL in controls (p < 0.001) [225] | In plasma (Baker et al.): 458 ± 88 (stage I), 399 ± 90 (stage II) and 325 ± 92 nmol/g tissue (stage III) compared to 513 ± 64 in normal colon mucosa (p < 0.001) [83] | In serum (HPLC): 21.87 μmol/L compared to 21.69 μmol/L in controls (ns) [226] |
| **Colorectal cancer** | In tissue (GSH-400 method): 174 ± 36 (stage I), 156 ± 39 (stage II), and 150 ± 48 nmol/g tissue (stage III) compared to 167 ± 15 in normal colon mucosa (p < 0.05) [83] | In tissue (HPLC): 0.62 ± 0.1 μg retinol/mL compared to 0.6 ± 0.2 μg/mL in controls (ns) [268] | In tissue (HPLC): 33.1 ± 9.1 (stage I), 29.1 ± 9.4 (stage II), and 13.3 ± 10.3 nmol/g tissue (stage III) compared to 37.5 ± 5.2 in normal colon mucosa (p < 0.001) [83] |
|                | In erythrocytes (Beutler et al.): 7.05 ± 1.61 nmol/g Hb compared to 11.20 ± 1.1 nmol/g in controls (p < 0.05) [253] | In tissue (HPLC): 348.7 ± 86 (stage I), 399 ± 90 (stage II) and 325 ± 92 nmol/g tissue (stage III) compared to 513 ± 64 in normal colon mucosa (p < 0.001) [83] | In serum (HPLC): 18.4 ± 11.2 μg/mL compared to 16.6 ± 7.6 in controls (ns) [268] |
|                | | In plasma (HPLC): 29.457 ± 27.414 μM compared to 49.76 ± 29.24 μM in controls (p = 0.0006) [174] | In plasma (HPLC): 18.87 ± 14.5 μM compared to 24.69 ± 14.55 μM in controls (p = 0.049) [174] |

Oxidative Medicine and Cellular Longevity
| Type of cancer | Glutathione | Nonenzymatic antioxidant levels | Vitamin E (α-tocopherol) |
|---------------|-------------|---------------------------------|--------------------------|
| **Lung cancer** | *In tissue (Ellman)*: 24.1 ± 12.0 nmol/mg compared to 13.6 ± 6.5 in adjacent normal tissue (*p* = 0.0004) [257] | *In serum (HPLC)*: 1.362 μM retinol compared to 2.496 μM in controls (*p* < 0.001) | *In serum (HPLC)*: 14.07 μM compared to 24.458 μM in controls (*p* < 0.001) [269] |
| **Liver cancer** | *In plasma (Tietze)*: 38.86 ± 26.15 μmol/L compared to 48.66 ± 30.17 μmol/L in corresponding post-resection samples (*p* < 0.05) | *In serum (HPLC)*: 32.5 μg retinol/dL compared to 41.8 μg/dL in controls (*p* < 0.001) | *In plasma (HPLC): 22.8 ± 3.4 (stage I/II) and 24.1 ± 2.7 μmol/L (stage III/IV) compared to 19.2 ± 2.8 in controls (*p* < 0.05) [231] |
| **Ovarian cancer** | *In erythrocytes (Beutler et al.): 11.7 ± 2.9 mg/g Hb compared to 18.7 ± 2.7 mg/g in controls (p < 0.001) [238] | *In plasma (HPLC): 59.8 μg retinol/dL compared to 68.6 μg/dL in controls (p = 0.0183) 13.6 μg β-carotene/dL compared to 21.5 μg/dL in controls (p < 0.0001) [272] | *In erythrocytes (Baker et al.): 0.93 ± 0.18 mg % (stage II) and 0.72 ± 0.12 (stage IV) compared to 1.10 ± 0.15 in controls (p < 0.01 and p < 0.001) [236] |
| **Prostate cancer** | *In plasma (Ellman): 1.87 μmol/mL* compared to 1.45 μmol/mL in controls (p < 0.05) [Figure 2(a)] | *In plasma (HPLC): 580.3 ng retinol/mL compared to 565.6 ng/mL in controls (p = 0.02) [273] | *In serum (Hansen and Warwick): 12 μmol/mL compared to 16 μmol/mL in controls (p < 0.05) [Figure 2(d)] [171] |
| Type of cancer | Glutathione | Nonenzymatic antioxidant levels | Vitamin E (α-tocopherol) |
|---------------|-------------|-------------------------------|--------------------------|
| Skin cancer   | compared to 1.37 μmol/mL in controls *(p < 0.05)* [Figure 2(b)] [171] | *In plasma (HPLC):* 725.3 ng retinol/mL compared to 722.9 ng/mL in controls (ns) [273] | *In plasma (HPLC):* 10809 ng/mL compared to 11068 ng/mL in controls (ns) [273] |
|               | *In blood (Beutler et al.):* 36.75 ± 3.9 mg % compared to 42.73 ± 3.3 mg % in controls *(p < 0.001)* [240] | *In plasma (HPLC):* 10809 ng/mL compared to 11068 ng/mL in controls (ns) [273] | |
|               | *In plasma (Ellman):* 0.321 ± 0.123 nmol/L compared to 0.447 ± 0.094 nmol/L in controls *(p < 0.0001)* [261] | *In plasma (HPLC):* 0.00939 ± 0.00219 nmol β-carotene/mg tissue compared to 0.00941 ± 0.00266 nmol/mg in adjacent tissue *(p = 0.022)* [175] | |
|               | *In tissue (HPLC):* 0.67473 ± 0.19749 nmol/mg tissue compared to 0.82778 ± 0.2214 in adjacent tissue *(p = 0.022)* [175] | *In plasma (HPLC):* 0.00939 ± 0.00219 nmol β-carotene/mg tissue compared to 0.00941 ± 0.00266 nmol/mg in adjacent tissue *(p = 0.022)* [175] | |
| Thyroid cancer| *In tissue (Beutler et al.):* 2.8 ± 0.1 (follicular carcinoma) and 3.4 ± 0.4 μM/g tissue (papillary carcinoma) compared to 2.9 ± 0.5 in controls (ns and p < 0.05) [244] | *In plasma (Roe and Keuther):* 0.64 ± 0.06 mg/dL compared to 1.56 ± 0.15 mg/dL in controls *(p < 0.001)* [247] | *In cells (GC-MS):* 5.83 ± 0.25 ng/10⁶ cells compared to 3.38 ± 0.5 in normal melanocytes *(p < 0.005)* [79] |
|               | *In serum (Ellman):* 244.34 ± 27.0 μmol/L compared to 377.87 ± 37.39 in controls *(p < 0.05)* [248] | *In plasma (Roe and Keuther):* 0.64 ± 0.06 mg/dL compared to 1.56 ± 0.15 mg/dL in controls *(p < 0.001)* [247] | *In plasma (HPLC):* 59.95 μM (stage I), 58.85 μM (stage II), 57.27 μM (stage III), and 47.16 μM (stage IV) compared to 64.86 μM in controls *(ns for stages I-III; p < 0.0001 for stage IV)* [177] |
|               | *In plasma (Beutler et al.):* 38.2 ± 3.02 mg/dL compared to 48.7 ± 3.76 in controls *(p < 0.001)* [248] | *In plasma (Roe and Keuther):* 0.64 ± 0.06 mg/dL compared to 1.56 ± 0.15 mg/dL in controls *(p < 0.001)* [247] | *In plasma (HPLC):* 59.95 μM (stage I), 58.85 μM (stage II), 57.27 μM (stage III), and 47.16 μM (stage IV) compared to 64.86 μM in controls *(ns for stages I-III; p < 0.0001 for stage IV)* [177] |
|               | *In plasma (Beutler et al.):* 39.3 ± 2.6 mg/dL compared to 52.6 ± 4.1 in controls *(p < 0.001)* [247] | *In plasma (Roe and Keuther):* 0.64 ± 0.06 mg/dL compared to 1.56 ± 0.15 mg/dL in controls *(p < 0.001)* [247] | *In plasma (HPLC):* 59.95 μM (stage I), 58.85 μM (stage II), 57.27 μM (stage III), and 47.16 μM (stage IV) compared to 64.86 μM in controls *(ns for stages I-III; p < 0.0001 for stage IV)* [177] |
|               | *In plasma (Desai):* 1.8 ± 0.15 mg/dL compared to 3.35 ± 0.5 in controls *(p < 0.001)* [247] | *In plasma (Roe and Keuther):* 0.64 ± 0.06 mg/dL compared to 1.56 ± 0.15 mg/dL in controls *(p < 0.001)* [247] | *In plasma (HPLC):* 59.95 μM (stage I), 58.85 μM (stage II), 57.27 μM (stage III), and 47.16 μM (stage IV) compared to 64.86 μM in controls *(ns for stages I-III; p < 0.0001 for stage IV)* [177] |
|               | *In plasma (Desai):* 1.58 ± 0.14 μg/mg protein compared to 2.08 ± 0.19 in controls *(p < 0.001)* [247] | *In plasma (Roe and Keuther):* 0.64 ± 0.06 mg/dL compared to 1.56 ± 0.15 mg/dL in controls *(p < 0.001)* [247] | *In plasma (HPLC):* 59.95 μM (stage I), 58.85 μM (stage II), 57.27 μM (stage III), and 47.16 μM (stage IV) compared to 64.86 μM in controls *(ns for stages I-III; p < 0.0001 for stage IV)* [177] |
overall oxidative stress in clinical samples and the establishment of a definitive relationship between oxidative stress and disease status [280–283].

As a final note, to our knowledge, no adequate comparison has yet been performed between different biomarkers and the methodologies used to measure them, making it difficult if not impossible to make a reliable comparison of findings from different groups. A critical evaluation and adaptation of proposed methodologies available in the literature should therefore be undertaken prior to carrying out a proposed study, so as to enable the investigators to choose the most suitable procedure for each chosen biomarker. In addition, such a comparison will enable careful meta-analysis of multiple scientific studies related to oxidative stress.

### Conflicts of Interest

The authors declare no conflict of interest.

### Acknowledgments

We would like to thank our colleagues, Sonia Whang and Catherine Ho, for their editorial suggestions.

### References

[1] W. Dröge, “Free radicals in the physiological control of cell function,” Physiological Reviews, vol. 82, no. 1, pp. 47–95, 2002.

[2] M. Genestra, “Oxyl radicals, redox-sensitive signalling cascades and antioxidants,” Cellular Signalling, vol. 19, no. 9, pp. 1807–1819, 2007.

[3] G. Pizzino, N. Irrera, M. Cucinotta et al., “Oxidative stress: harms and benefits for human health,” Oxidative Medicine and Cellular Longevity, vol. 2017, Article ID 8416763, 13 pages, 2017.

[4] P. Rajendran, N. Nandakumar, T. Rengarajan et al., “Antioxidants and human diseases,” Clinica Chimica Acta, vol. 436, pp. 332–347, 2014.

[5] M. Valko, D. Leibfritz, J. Moncol, M. Mazur, and J. Telser, “Free radicals and antioxidants in normal physiological functions and human disease,” The International Journal of Biochemistry & Cell Biology, vol. 39, no. 1, pp. 44–84, 2007.

[6] T. P. Devasagayam, J. C. Tilak, K. K. Boloor, K. S. Sane, S. S. Ghaskadbi, and R. D. Lele, “Free radicals and antioxidants in human health: current status and future prospects,” The Journal of the Association of Physicians of India, vol. 52, pp. 794–804, 2004.

[7] T. Finkel, “Signal transduction by reactive oxygen species,” The Journal of Cell Biology, vol. 194, no. 1, pp. 7–15, 2011.

[8] B. Halliwell, “Antioxidants in human health and disease,” Annual Review of Nutrition, vol. 16, no. 1, pp. 33–50, 1996.

[9] V. Lobo, A. Patil, A. Phatak, and N. Chandra, “Free radicals, antioxidants and functional foods: impact on human health,” Pharmacognosy Reviews, vol. 4, no. 8, pp. 118–126, 2010.

[10] A. Phaniendra, D. B. Jestadi, and L. Periyasamy, “Free radicals: properties, sources, targets, and their implication in various diseases,” Indian Journal of Clinical Biochemistry, vol. 30, no. 1, pp. 11–26, 2015.
Oxidative Medicine and Cellular Longevity

[11] P. D. Ray, B.-W. Huang, and Y. Tsuji, "Reactive oxygen species (ROS) homeostasis and redox regulation in cellular signaling," *Cellular Signalling*, vol. 24, no. 5, pp. 981–990, 2012.

[12] J. M. McCord, "The evolution of free radicals and oxidative stress," *American Journal of Medicine*, vol. 108, no. 8, pp. 652–659, 2000.

[13] P. Theron, "Oxidative stress and damages to biomolecules (lipids, proteins, DNA)," *Annales Pharmaceutiques Françaises*, vol. 64, no. 6, pp. 383–389, 2006.

[14] E. Birben, U. M. Sahiner, C. Sackesen, S. Erzurum, and O. Kalyani, "Oxidative stress and antioxidant defense," *The World Allergy Organization Journal*, vol. 5, no. 1, pp. 9–19, 2012.

[15] N. S. Dhalla, R. M. Temsah, and T. Netticidan, "Role of oxidative stress in cardiovascular diseases," *Journal of Hypertension*, vol. 18, no. 6, pp. 655–673, 2000.

[16] K. A. Gelderman, M. Hultqvist, L. M. Olsson et al., "Rheumatoid arthritis: the role of reactive oxygen species in disease development and therapeutic strategies," *Antioxidants & Redox Signaling*, vol. 9, no. 10, pp. 1541–1568, 2007.

[17] O. Hwang, "Role of oxidative stress in Parkinson’s disease," *Experimental Neurobiology*, vol. 22, no. 1, pp. 11–17, 2013.

[18] A. T. Y. Lau, Y. Wang, and J.-F. Chiu, "Reactive oxygen species: current knowledge and applications in cancer research and therapeutic," *Journal of Cellular Biochemistry*, vol. 104, no. 2, pp. 657–667, 2008.

[19] L. Lyras, N. J. Cairns, A. Jenner, P. Jenner, and B. Halliwell, "An assessment of oxidative damage to proteins, lipids, and DNA in brain from patients with Alzheimer’s disease," *Journal of Neurochemistry*, vol. 68, no. 5, pp. 2061–2069, 1997.

[20] L. Sayre, M. Smith, and G. Perry, "Chemistry and biochemistry of oxidative stress in neurodegenerative disease," *Current Medicinal Chemistry*, vol. 8, no. 7, pp. 721–738, 2001.

[21] V. Sosa, T. Moliné, R. Somoza, R. Pauciucci, H. Kondoh, and M. E. Lleonart, "Oxidative stress and cancer: an overview," *Ageing Research Reviews*, vol. 12, no. 1, pp. 376–390, 2013.

[22] P. K. Toshniwal and E. J. Zarling, "Evidence for increased lipid peroxidation in multiple sclerosis," *Neurochemical Research*, vol. 17, no. 2, pp. 205–207, 1992.

[23] L. H. Kushi, A. R. Folsom, R. J. Prineas, P. J. Mink, Y. Wu, and R. M. Bostick, "Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women," *New England Journal of Medicine*, vol. 334, no. 18, pp. 1156–1162, 1996.

[24] E. E. Devore, F. Grodstein, F. J. A. van Rooij et al., "Dietary antioxidants and long-term risk of dementia," *Archives of Neurology*, vol. 67, no. 7, pp. 819–825, 2010.

[25] M. J. Engelhart, M. I. Geerlings, A. Ruitenberg et al., "Dietary intake of antioxidants and risk of Alzheimer disease," *JAMA*, vol. 287, no. 24, pp. 3223–3229, 2002.

[26] M. Grundman, "Vitamin E and Alzheimer disease: the basis for additional clinical trials," *The American Journal of Clinical Nutrition*, vol. 71, no. 2, pp. 630S–636S, 2000.

[27] F. Yang, A. Wolk, N. Häkansson, N. L. Pedersen, and K. Wirdefeldt, "Dietary antioxidants and risk of Parkinson's disease in two population-based cohorts," *Movement Disorders*, vol. 32, no. 11, pp. 1631–1636, 2017.

[28] L. Colarussso, M. Serafini, Y. T. Lagerros et al., "Dietary antioxidant capacity and risk for stroke in a prospective cohort study of Swedish men and women," *Nutrition*, vol. 33, pp. 234–239, 2017.

[29] M. Hariri, Z. Maghsoudi, L. Darvishi et al., "B vitamins and antioxidants intake is negatively correlated with risk of stroke in Iran," *International Journal of Preventive Medicine*, vol. 4, Supplement 2, pp. S284–S289, 2013.

[30] S. Uesugi, J. Ishihara, H. Iso et al., "Dietary intake of antioxidant vitamins and risk of stroke: the Japan Public Health Center–based Prospective Study," *European Journal of Clinical Nutrition*, vol. 71, no. 10, pp. 1179–1185, 2017.

[31] Z. Voko, M. Hollander, A. Hofman, P. J. Koudstaal, and M. M. B. Breteler, "Dietary antioxidants and the risk of ischemic stroke: the Rotterdam Study," *Neurology*, vol. 61, no. 9, pp. 1273–1275, 2003.

[32] S. Allen, J. R. Britton, and J. A. Leonardi-Bee, "Association between antioxidant vitamins and asthma outcome measures: systematic review and meta-analysis," *Thorax*, vol. 64, no. 7, pp. 610–619, 2009.

[33] S. Cohen, S. Mehrabi, X. Yao, S. Millingen, and F. O. Aïkhnionbare, "Reactive oxygen species and serious epithelial ovarian adenocarcinoma," *Cancer Research Journal*, vol. 4, no. 6, pp. 106–114, 2016.

[34] H. M. Peshavariya, J. G. Dusting, and S. Selemidis, "Analysis of dihydroethidium fluorescence for the detection of intracellular and extracellular superoxide produced by NADPH oxidase," *Free Radical Research*, vol. 41, no. 6, pp. 699–712, 2009.

[35] Y. Chen Wongworawat, M. Filippova, V. M. Williams, V. Filippov, and P. J. Duerksen-Hughes, "Chronic oxidative stress increases the integration frequency of foreign DNA and human papillomavirus 16 in human keratinocytes," *American Journal of Cancer Research*, vol. 6, no. 4, pp. 764–780, 2016.

[36] V. M. Williams, M. Filippova, V. Filippov, K. J. Payne, and P. Duerksen-Hughes, "Human papillomavirus type 16 E6 induces oxidative stress and DNA damage," *Journal of Virology*, vol. 88, no. 12, pp. 6751–6761, 2014.

[37] F. L. Mveyskens Jr., S. E. McNulty, J. A. Buckmeier et al., "Aberrant redox regulation in human metastatic melanoma cells compared to normal melanocytes," *Free Radical Biology and Medicine*, vol. 31, no. 6, pp. 799–808, 2001.

[38] L. Benov, L. Sztejnberg, and I. Fridovich, "Critical evaluation of the use of hydroethidine as a measure of superoxide anion radical," *Free Radical Biology & Medicine*, vol. 25, no. 7, pp. 826–831, 1998.

[39] P. Ubezio and F. Civiolo, "Flow cytometric detection of hydrogen peroxide production induced by doxorubicin in cancer cells," *Free Radical Biology & Medicine*, vol. 16, no. 4, pp. 509–516, 1994.

[40] D. Andrés, N. Sanz, A. Zaragoza, A. M. Alvarez, and Maria Cascales, "Changes in antioxidant defence systems induced by cyclosporine A in cultures of hepatocytes from 2- and 12-month-old rats," *Biochemical Pharmacology*, vol. 59, no. 9, pp. 1091–1100, 2000.

[41] N. S. Chandel, W. C. Trzyna, D. S. McClintock, and P. T. Schumacker, "Role of oxidants in NF-kappa B activation and TNF-alpha gene transcription induced by hypoxia and endotoxin," *The Journal of Immunology*, vol. 165, no. 2, pp. 1013–1021, 2000.

[42] R. Trotti, M. Carratelli, and M. Barbieri, "Performance and clinical application of a new, fast method for the detection of lipid peroxidation in multiple sclerosis," *Neurochemical Research*, vol. 8, no. 7, pp. 721–728, 2003.

[43] S. L. Colarusso, L. Serafini, Y. T. Lagers et al., "Dietary antioxidant capacity and risk for stroke in a prospective cohort study of Swedish men and women," *Nutrition*, vol. 33, pp. 234–239, 2017.
of hydroperoxides in serum,” Panminerva Medica, vol. 44, no. 1, pp. 37–40, 2002.

A. Alberti, L. Bolognini, D. Macciantelli, and M. Caratelli, “The radical cation of N,N-diethyl-para-phenylenediamine: a possible indicator of oxidative stress in biological samples,” Research on Chemical Intermediates, vol. 26, no. 3, pp. 253–267, 2000.

K. Ito, T. Yano, Y. Morodomi et al., “Serum antioxidant capacity and oxidative injury to pulmonary DNA in never-smokers with primary lung cancer,” Anticancer Research, vol. 32, no. 3, pp. 1063–1067, 2012.

A. M. Leufkens, F. J. B. van Duijnhoven, S. H. S. Woudt et al., “Biomarkers of oxidative stress and risk of developing colorectal cancer: a cohort-nested case-control study in the European Prospective Investigation Into Cancer and Nutrition,” American Journal of Epidemiology, vol. 175, no. 7, pp. 653–663, 2012.

W. A. Pryor, “Oxy-radicals and related species: their formation, lifetimes, and reactions,” Annual Review of Physiology, vol. 48, no. 1, pp. 657–667, 1986.

R. W. Redmond and I. E. Kochevar, “Spatially resolved cellular responses to singlet oxygen,” Photochemistry and Photobiology, vol. 82, no. 5, pp. 1178–1186, 2006.

S. Gaspár, “Detection of superoxide and hydrogen peroxide from living cells using electrochemical sensors,” in Oxidative Stress: Diagnosis, Prevention, and Therapy, pp. 289–309, American Chemical Society, 2011.

L. J. Marnett, “Peroxyl free radicals: potential mediators of tumor initiation and promotion,” Carcinogenesis, vol. 8, no. 10, pp. 1365–1373, 1987.

B. S. Berlett and E. R. Stadtman, “Protein oxidation in aging, disease, and oxidative stress,” Journal of Biological Chemistry, vol. 272, no. 33, pp. 20313–20316, 1997.

R. L. Levine, D. Garland, C. N. Oliver et al., “Determination of carbonyl content in oxidatively modified proteins,” Methods in Enzymology, vol. 186, pp. 464–478, 1990.

C. S. Mesquita, R. Oliveira, F. Bento, D. Geraldo, J. V. Rodrigues, and J. C. Marcos, “Simplified 2, 4-dinitrophenylhydrazine spectrophotometric assay for quantification of carboxyls in oxidized proteins,” Analytical Biochemistry, vol. 458, pp. 69–71, 2014.

V. Kolgiri and V. W. Patil, “Protein carbonyl content: a novel biomarker for aging in HIV/AIDS patients,” The Brazilian Journal of Infectious Diseases, vol. 21, no. 1, pp. 35–41, 2017.

M. Rajesh, K. N. Sulochana, K. Coral et al., “Determination of carbonyl group content in plasma proteins as a useful marker to assess impairment in antioxidant defense in patients with Eales’ disease,” Indian Journal of Ophthalmology, vol. 52, no. 2, pp. 139–144, 2004.

F. de Marco, E. Bucai, C. Foppoli et al., “Oxidative stress in HPV-driven viral carcinogenesis: redox proteomics analysis of HPV-16 dysplastic and neoplastic tissues,” PLoS One, vol. 7, no. 3, article e34366, 2012.

S. Mehrabi, E. E. Partridge, W. Seffins, X. Yao, and F. O. Aikhionbare, “Oxidatively modified proteins in the serous subtype of ovarian carcinoma,” BioMed Research International, vol. 2014, Article ID 585083, 7 pages, 2014.

D. A. Butterfield, V. Galvan, M. B. Lange et al., “In vivo oxidative stress in brain of Alzheimer disease transgenic mice: requirement for methionine 35 in amyloid beta-peptide of APP,” Free Radical Biology & Medicine, vol. 48, no. 1, pp. 136–144, 2010.

D. A. Butterfield and E. R. Stadtman, “Chapter 7 protein oxidation processes in aging brain,” in Advances in Cell Aging and Gerontology, P. S. Timiras and E. E. Bittar, Eds., pp. 161–191, Elsevier, 1997.

V. Witko-Sarsat, M. Friedlander, C. Capeillère-Blandin et al., “Advanced oxidation protein products as a novel marker of oxidative stress in uremia,” Kidney International, vol. 49, no. 5, pp. 1304–1313, 1996.

C. J. J. Alderman, S. Shah, J. C. Foreman, B. M. Chain, and D. R. Katz, “The role of advanced oxidation protein products in regulation of dendritic cell function,” Free Radical Biology & Medicine, vol. 32, no. 5, pp. 377–385, 2002.

B. Halliwell and J. M. C. Gutteridge, “Oxygen free radicals and iron in relation to biology and medicine: some problems and concepts,” Archives of Biochemistry and Biophysics, vol. 246, no. 2, pp. 501–514, 1986.

H. Esterbauer and K. H. Cheeseman, “Determination of aldehyde lipid peroxidation products: malonaldehyde and 4-hydroxynonenal,” Methods in Enzymology, vol. 186, pp. 407–421, 1990.

A. Hirayama, S. Nagase, M. Gotoh et al., “Hemodialysis does not influence the peroxidative state already present in uremia,” Nephron, vol. 86, no. 4, pp. 436–440, 2000.

D. Lapenna, G. Ciofani, S. D. Pierdomenico, M. A. Giamberardino, and F. Cucurullo, “Reaction conditions affecting the relationship between thiobarbituric acid reactivity and lipid peroxides in human plasma,” Free Radical Biology and Medicine, vol. 31, no. 3, pp. 331–335, 2001.

P. J. Marshall, M. A. Warso, and W. E. M. Lands, “Selective microdetermination of lipid hydroperoxides,” Analytical Biochemistry, vol. 145, no. 1, pp. 192–199, 1985.

M. R. Nogués, M. Giralt, I. Cervelló et al., “Parameters related to oxygen free radicals in human skin: a study comparing healthy epidermis and skin cancer tissue,” The Journal of Investigative Dermatology, vol. 119, no. 3, pp. 645–652, 2002.

A. Woźniak, R. Masiak, M. Szpinda et al., “Oxidative stress markers in prostate cancer patients after HDR brachytherapy combined with external beam radiation,” Oxidative Medicine and Cellular Longevity, vol. 2012, Article ID 789870, 5 pages, 2012.

S. K. Donnan, “The thiobarbituric acid test applied to tissues from rats treated in various ways,” Journal of Biological Chemistry, vol. 182, no. 1, pp. 415–420, 1950.

K. Yagi, “Lipid peroxides and human diseases,” Chemistry and Physics of Lipids, vol. 45, no. 2-4, pp. 337–351, 1987.

M. Mihara and M. Uchiyama, “Determination of malonaldehyde precursor in tissues by thiobarbituric acid test,” Analytical Biochemistry, vol. 86, no. 1, pp. 271–278, 1978.

J. A. Buege and S. D. Aust, “Micromolar lipid peroxidation,” Methods in Enzymology, vol. 52, pp. 302–310, 1978.

H. Ohkawa, N. Ohishi, and K. Yagi, “Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction,” Analytical Biochemistry, vol. 95, no. 2, pp. 351–358, 1979.

T. Yoshioka, K. Kawada, T. Shimada, and M. Mori, “Lipid peroxidation in maternal and cord blood and protective mechanism against activated-oxygen toxicity in the blood,” American Journal of Obstetrics and Gynecology, vol. 135, no. 3, pp. 372–376, 1979.
poor prognosis in epithelial ovarian cancer,” Anticancer Research, vol. 31, no. 4, pp. 1411–1415, 2011.

[102] Y. Soini, K. M. Haapasari, M. H. Vaarala, T. Turpeenniemi-Hujanen, V. Kärjä, and P. Karitahla, “8-Hydroxydeoxyguanosine and nitrosytroisine are prognostic factors in urinary bladder carcinoma,” International Journal of Clinical and Experimental Pathology, vol. 4, no. 3, pp. 267–275, 2011.

[103] P. Karitahla, Y. Soini, L. Vaskivuo, R. Bloigu, and U. Puistola, “DNA adduct 8-hydroxydeoxyguanosine, a novel putative marker of prognostic significance in ovarian carcinoma,” International Journal of Gynecological Cancer, vol. 19, no. 6, pp. 1047–1051, 2009.

[104] N. Nishida, T. Arizumi, M. Takita et al., “Reactive oxygen species induce epigenetic instability through the formation of 8-hydroxydeoxyguanosine in human hepatocarcinogenesis,” Digestive Diseases, vol. 31, no. 5–6, pp. 459–466, 2013.

[105] S. Tanaka, K. Miyanishi, M. Kobune et al., “Increased hepatic oxidative DNA damage in patients with nonalcoholic steato-hepatitis who develop hepatocellular carcinoma,” Journal of Gastroenterology, vol. 48, no. 11, pp. 1249–1258, 2013.

[106] M. Dizdaroglu, “Quantitative determination of oxidative base damage in DNA by stable isotope-dilution mass spectrometry,” FEBS Letters, vol. 315, no. 1, pp. 1–6, 1993.

[107] L. Chaisrirwong, R. Wanitphakdeeveda, P. Sithinamsuwan et al., “A case-control study of involvement of oxidative DNA damage and alteration of antioxidant defense system in patients with basal cell carcinoma: modulation by tumor removal,” Oxidative Medicine and Cellular Longevity, vol. 2016, Article ID 5934024, 12 pages, 2016.

[108] D. Li, W. Zhang, J. Zhu et al., “Oxidative DNA damage and 8-hydroxy-2-deoxyguanosine DNA glycosylase/apurinic lyase in human breast cancer,” Molecular Carcinogenesis, vol. 31, no. 4, pp. 214–223, 2001.

[109] Y. J. Park, E. Y. Choi, J. Y. Choi, J. G. Park, H. J. You, and M. H. Chung, “Genetic changes of hOGG1 and the activity of oh8Gua glycosylase in colon cancer,” European Journal of Cancer, vol. 37, no. 3, pp. 340–346, 2001.

[110] F. Yamamoto, H. Kasai, T. Bessho et al., “Ubiquitous presence in mammalian cells of enzymatic activity specifically cleaving 8-hydroxyguanine-containing DNA,” Japanese Journal of Cancer Research, vol. 83, no. 4, pp. 351–357, 1992.

[111] J. M. McCord and I. Fridovich, “Superoxide dismutase: an enzymic function for erythrocuprein (hemocuprein),” Journal of Biological Chemistry, vol. 244, no. 22, pp. 6049–6055, 1969.

[112] H. P. Misra and I. Fridovich, “The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase,” The Journal of Biological Chemistry, vol. 247, no. 10, pp. 3170–3175, 1972.

[113] S. Marklund and G. Marklund, “Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase,” European Journal of Biochemistry, vol. 47, no. 3, pp. 469–474, 1974.

[114] E. F. Roth Jr. and H. S. Gilbert, “The pyrogallol assay for superoxide dismutase: absence of a glutathione artifact,” Analytical Biochemistry, vol. 137, no. 1, pp. 50–53, 1984.

[115] M. Nishikimi, N. Appai Rao, and K. Yagi, “The occurrence of superoxide anion in the reaction of reduced phenazine methosulfate and molecular oxygen,” Biochemical and Biophysical Research Communications, vol. 46, no. 2, pp. 849–854, 1972.

[116] P. Kakkar, B. Das, and P. N. Viswanathan, “A modified spectrophotometric assay of superoxide dismutase,” Indian Journal of Biochemistry & Biophysics, vol. 21, no. 2, pp. 130–132, 1984.

[117] Y. Oyanagui, “Reevaluation of assay methods and establishment of kit for superoxide dismutase activity,” Analytical Biochemistry, vol. 142, no. 2, pp. 290–296, 1984.

[118] Y. Sun, L. W. Oberley, and Y. Li, “A simple method for clinical assay of superoxide dismutase,” Clinical Chemistry, vol. 34, no. 3, pp. 497–500, 1988.

[119] J. Grace Nirmala and R. T. Narendhirakannan, “Detection and genotyping of high-risk HPV and evaluation of anti-oxidant status in cervical carcinoma patients in Tamil Nadu State, India—a case control study,” Asian Pacific Journal of Cancer Prevention, vol. 12, no. 10, pp. 2689–2695, 2011.

[120] A. I. Margaret, E. Syahruddin, and S. I. Wanandi, “Low activity of manganese superoxide dismutase (MnSOD) in blood of lung cancer patients with smoking history: relationship to oxidative stress,” Asian Pacific Journal of Cancer Prevention, vol. 12, no. 11, pp. 3049–3053, 2011.

[121] G. Güner, H. İşlekel, Ö. Oto, E. Hazan, and Ü. Açikel, “Evaluation of some antioxidant enzymes in lung carcinoma tissue,” Cancer Letters, vol. 103, no. 2, pp. 233–239, 1996.

[122] P. Jaruga, T. H. Zastawny, J. Skokowski, M. Dizdaroglu, and R. Olinski, “Oxidative DNA base damage and antioxidant enzyme activities in human lung cancer,” FEBS Letters, vol. 341, no. 1, pp. 59–64, 1994.

[123] J. K. Strzelscy, T. Wielkoszyński, L. Krakowczyk et al., “The activity of antioxidant enzymes in colorectal adenocarcinoma and corresponding normal mucosa,” Acta Biochimica Polonica, vol. 59, no. 4, pp. 549–556, 2012.

[124] S. L. Marklund, “Analysis of extracellular superoxide dismutase in tissue homogenates and extracellular fluids,” Methods in Enzymology, vol. 186, pp. 260–265, 1990.

[125] S. L. Marklund, “Superoxide dismutase isoenzymes in tissues and plasma from New Zealand black mice, nude mice and normal BALB/c mice,” Mutation Research, vol. 148, no. 1-2, pp. 129–134, 1985.

[126] M. Mattiazzi, M. D’Aurelio, C. D. Gajewski et al., “Mutated human SOD1 causes dysfunction of oxidative phosphorylation in mitochondria of transgenic mice,” The Journal of Biological Chemistry, vol. 277, no. 33, pp. 29626–29633, 2002.

[127] S. Dieterich, U. Bieligrk, K. Beulich, G. Hasenfuss, and J. Prestle, “Gene expression of antioxidative enzymes in the human heart: increased expression of catalase in the end-stage failing heart,” Circulation, vol. 101, no. 1, pp. 33–39, 2000.

[128] J. Iqbal and P. Whitney, “Use of cyanide and diethyldithiocarbamate in the assay of superoxide dismutases,” Free Radical Biology & Medicine, vol. 10, no. 1, pp. 69–77, 1991.

[129] V. B. Djordjevic, “Free radicals in cell biology,” International Review of Cytology, vol. 237, pp. 57–89, 2004.

[130] R. F. Beers Jr. and I. W. Sizer, “A spectrophotometric method for measuring the breakdown of hydrogen peroxide by catalase,” The Journal of Biological Chemistry, vol. 195, no. 1, pp. 133–140, 1952.

[131] D. P. Nelson and L. A. Kiesow, “Enthalpy of decomposition of hydrogen peroxide by catalase at 25°C (with molar extinction coefficients of H2O2 solutions in the UV),” Analytical Biochemistry, vol. 49, no. 2, pp. 474–478, 1972.
H. Aebi, "Catalase in vitro," Methods in Enzymology, vol. 105, pp. 121–126, 1984.

A. K. Sinha, "Colorimetric assay of catalase," Analytical Biochemistry, vol. 47, no. 2, pp. 389–394, 1972.

L. Goth, "A simple method for determination of serum catalase activity and revision of reference range," Clinica Chimica Acta, vol. 196, no. 2–3, pp. 143–151, 1991.

L. H. Johansson and L. A. Häkan Borg, "A spectrophotometric method for determination of catalase activity in small tissue samples," Analytical Biochemistry, vol. 174, no. 1, pp. 331–336, 1988.

J. R. Arthur, "The glutathione peroxidases," Cellular and Molecular Life Sciences, vol. 57, no. 13-14, pp. 1825–1835, 2000.

J. T. Rotruck, A. L. Pope, H. E. Ganther, A. B. Swanson, D. G. Hafeman, and W. G. Hoekstra, "Selenium: biochemical role as a component of glutathione peroxidase," Science, vol. 179, no. 4073, pp. 588–590, 1973.

D. G. Hafeman, R. A. Sunde, and W. G. Hoekstra, "Effect of dietary selenium on erythrocyte and liver glutathione peroxidase in the rat," The Journal of Nutrition, vol. 104, no. 5, pp. 580–587, 1974.

G. L. Ellman, "Tissue sulfhydryl groups," Archives of Biochemistry and Biophysics, vol. 82, no. 1, pp. 70–77, 1959.

V. R. Kokatnur and M. Jelling, "Catalase in vitro," Methods in Enzymology, vol. 28, no. 2, pp. 311–316, 1982.

H. Czeczot, D. Scibior, M. Skrzycki, and M. Podsiad, "Gluathione and GSH-dependent enzymes in patients with liver cirrhosis and hepatocellular carcinoma," Acta Biochimica Polonica, vol. 53, no. 1, pp. 237–242, 2006.

I. Hubatsch, M. Ridderstrom, and B. Mannervik, "Human glutathione transferase A4-4: an alpha class enzyme with high catalytic efficiency in the conjugation of 4-hydroxynonenal and other genotoxic products of lipid peroxidation," The Biochemical Journal, vol. 330, no. 1, pp. 175–179, 1998.

L. F. Chasseaud, "The role of glutathione and glutathione S-transferases in the metabolism of chemical carcinogens and other electrophilic agents," Advances in Cancer Research, vol. 29, pp. 175–274, 1979.

W. H. Habig, M. J. Pabst, and W. B. Jakoby, "Glutathione S-transferases. The first enzymatic step in mercapturic acid formation," Journal of Biological Chemistry, vol. 249, no. 22, pp. 7130–7139, 1974.

S. C. Lu, "Regulation of glutathione synthesis," Molecular Aspects of Medicine, vol. 30, no. 1-2, pp. 42–59, 2009.

G. Wu, Y. Z. Fang, S. Yang, J. R. Lupton, and N. D. Turner, "Glutathione metabolism and its implications for health," The Journal of Nutrition, vol. 134, no. 3, pp. 489–492, 2004.

E. Beutler, O. Duron, and B. M. Kelly, "Improved method for the determination of blood glutathione," The Journal of Laboratory and Clinical Medicine, vol. 61, pp. 882–888, 1963.
atherosclerosis,” *Free Radical Biology and Medicine*, vol. 31, no. 4, pp. 542–547, 2001.

[165] L. A. Kaplan, J. A. Miller, E. A. Stein, and M. J. Stampfer, “Simultaneous, high-performance liquid chromatographic analysis of retinol, tocopherols, lycopene, and \( \alpha \) and \( \beta \)-carotene in serum and plasma,” in *Methods in Enzymology*, pp. 155–167, Academic Press, 1990.

[166] K. W. Miller, N. A. Lorr, and C. S. Yang, “Simultaneous determination of plasma retinol, \( \alpha \)-tocopherol, lycopene, \( \alpha \)-carotene, and \( \beta \)-carotene by high-performance liquid chromatography,” *Analytical Biochemistry*, vol. 138, no. 2, pp. 340–345, 1984.

[167] H. J. C. F. Nelis and A. P. De Leenheer, “Isocratic nonaqueous reversed-phase liquid chromatography of carotenoids,” *Analytical Chemistry*, vol. 55, no. 2, pp. 270–275, 2002.

[168] G. Taibi and C. M. A. Nicotra, “Development and validation of a fast and sensitive chromatographic assay for all-trans-retinol and tocopherols in human serum and plasma using liquid–liquid extraction,” *Journal of Chromatography B*, vol. 780, no. 2, pp. 261–267, 2002.

[169] Z. E. Suntres, “Liposomal antioxidants for protection against oxidant-induced damage,” *Journal of Toxicology*, vol. 2011, Article ID 152474, 16 pages, 2011.

[170] J. H. Roe and C. A. Kuether, “The determination of ascorbic acid in whole blood and urine through the 2, 4-dinitrophenylhydrazine derivative of dehydroascorbic acid,” *Journal of Biological Chemistry*, vol. 147, no. 2, pp. 399–407, 1943.

[171] V. Battisti, L. D. K. Maders, M. D. Bagatini et al., “Oxidative stress and antioxidant status in prostate cancer patients: relation to Gleason score, treatment and bone metastasis,” *Biomedicine & Pharmacotherapy*, vol. 65, no. 7, pp. 516–524, 2011.

[172] V. Zannoni, M. Lynch, S. Goldstein, and P. Sato, “A rapid micromethod for the determination of ascorbic acid in plasma and tissues,” *Biochemical Medicine*, vol. 11, no. 1, pp. 41–48, 1974.

[173] O. Masato, “An improved method for determination of l-ascorbic acid and l-dehydroascorbic acid in blood plasma,” *Clinica Chimica Acta*, vol. 103, no. 3, pp. 259–268, 1980.

[174] D. Gackowski, Z. Banaszkiewicz, R. F. Rozalski, A. Jawien, and R. Olinski, “Persistent oxidative stress in colorectal carcinoma patients,” *International Journal of Cancer*, vol. 101, no. 4, pp. 395–397, 2002.

[175] K. Grammenandi, M. Kyriazi, A. Katsarou-Katsari et al., “Low-molecular-weight hydrophilic and lipophilic antioxidants in nonmelanoma skin carcinomas and adjacent normal-looking skin,” *Skin Pharmacology and Physiology*, vol. 29, no. 6, pp. 324–331, 2017.

[176] D. Ivanović, A. Popović, D. Rudulović, and M. Medenica, “Reversed-phase ion-pair HPLC determination of some water-soluble vitamins in pharmaceuticals,” *Journal of Pharmaceutical and Biomedical Analysis*, vol. 18, no. 6, pp. 999–1004, 1999.

[177] T. Schleich, S. Rodemeister, S. Venturelli, T. Sinnberg, C. Garbe, and C. Busch, “Decreased plasma ascorbate levels in stage IV melanoma patients,” *Metabolism and Nutrition in Oncology*, vol. 1, no. 1, pp. e2–e6, 2015.

[178] A. Emmerie and C. Engel, “Colorimetric determination of \( \alpha \)-tocopherol (vitamin E),” *Reueil des Travaux Chimiques des Pays-Bas*, vol. 57, no. 12, pp. 1351–1355, 1938.

[179] S. A. Hashim and G. R. Schuttringer, “Rapid determination of tocopherol in macro- and microquantities of plasma. Results obtained in various nutrition and metabolic studies,” *American Journal of Clinical Nutrition*, vol. 19, no. 2, pp. 137–145, 1966.

[180] H. Baker, O. Frank, B. DeAngelis, and S. Feingold, “Plasma tocopherol in man at various times after ingesting free or acetylated tocopherol,” *Nutrition Reports International*, vol. 21, no. 4, pp. 531–536, 1980.

[181] I. D. Desai, “Vitamin E analysis methods for animal tissues,” *Methods in Enzymology*, vol. 105, pp. 138–147, 1984.

[182] L. G. Hansen and W. J. Warwick, “A fluorometric micro-method for serum vitamin A,” *American Journal of Clinical Pathology*, vol. 50, no. 4, pp. 525–529, 1968.

[183] N. Badjatia, A. Satyam, P. Singh, A. Seth, and A. Sharma, “Altered antioxidant status and lipid peroxidation in Indian patients with urothelial bladder carcinoma,” *Urologic Oncology*, vol. 28, no. 4, pp. 360–367, 2010.

[184] G. Cao and R. L. Prior, “Comparison of different analytical methods for assessing total antioxidant capacity of human serum,” *Clinical Chemistry*, vol. 44, 6, Part 1, pp. 1309–1315, 1998.

[185] M. N. Alam, N. J. Bristi, and M. Rafiquzzaman, “Review on in vivo and in vitro methods evaluation of antioxidant activity,” *Saudi Pharmaceutical Journal*, vol. 21, no. 2, pp. 143–152, 2013.

[186] G. Bartosz, “Total antioxidant capacity,” *Advances in Clinical Chemistry*, vol. 37, pp. 219–292, 2003.

[187] M. S. Blois, “Antioxidant determinations by the use of a stable free radical,” *Nature*, vol. 181, pp. 4617, pp. 1199–1200, 1958.

[188] O. Erel, “A new automated colorimetric method for measuring total antioxidant status,” *Clinical Biochemistry*, vol. 38, no. 12, pp. 1103–1111, 2005.

[189] O. Erel, “A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation,” *Clinical Biochemistry*, vol. 37, no. 4, pp. 277–285, 2004.

[190] M. B. Arnao, A. Cano, J. Hernández-Ruiz, F. García-Cánovas, and M. Acosta, “Inhibition by L-ascorbic acid and other antioxidants of the 2′,3′-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) oxidation catalyzed by peroxidase: a new approach for determining total antioxidant status of foods,” *Analytical Biochemistry*, vol. 236, no. 2, pp. 255–261, 1996.

[191] N. J. Miller and C. A. Rice-Evans, *Spectrophotometric determination of antioxidant activity*, Redox *Report*, vol. 2, no. 3, pp. 161–171, 2016.

[192] D. Wang, J. F. Feng, P. Zeng, Y. H. Yang, J. Luo, and Y. W. Yang, “Total oxidant/antioxidant status in sera of patients with thyroid cancers,” *Endocrine-Related Cancer*, vol. 18, no. 6, pp. 773–782, 2011.

[193] F. Be, L. L. de Castro, J. R. Aguiar et al., “Antioxidant capacity as a tool to assess redox status: critical view and experimental data,” *Free Radical Biology & Medicine*, vol. 47, no. 1, pp. 1682–1688, 2015.

[194] A. Ghiselli, M. Serafini, F. Natella, and C. Scaccini, “Total antioxidant capacity as a tool to assess redox status: critical view and experimental data,” *Free Radical Biology & Medicine*, vol. 29, no. 11, pp. 1106–1114, 2000.

[195] D. D. M. Wayner, G. W. Burton, K. U. Ingold, and S. Locke, “Quantitative measurement of the total, peroxyl radical-trapping antioxidant capability of human blood
plasma by controlled peroxidation. The important contribution made by plasma proteins," FEBS Letters, vol. 187, no. 1, pp. 33–37, 1985.

[196] I. F. Benzie and J. J. Strain, "Ferric reducing/antioxidant power assay: direct measurement of total antioxidant activity of biological fluids and modified version for simultaneous measurement of total antioxidant power and ascorbic acid concentration," Methods in Enzymology, vol. 299, pp. 15–27, 1999.

[197] K. Dohi, K. Satoh, H. Ohtaki et al., "Elevated plasma levels of bilirubin in patients with neurotrauma reflect its pathophysiological role in free radical scavenging," In Vivo, vol. 19, no. 5, pp. 855–860, 2005.

[198] D. Koracevic, G. Koracevic, V. Djordjevic, S. Andrejevic, and K. Dohi, K. Satoh, H. Ohtaki et al., "Oxidative stress and lipid peroxidation products in cancer development and therapy," Frontiers in Genetics, vol. 6, p. 157, 2015.

[199] G.-Y. Liou and P. Storz, "Free radical Research," FEBS Letters, vol. 710, 2010.

[200] P. Storz, "Reactive oxygen species in tumor progression," Frontiers in Bioscience, vol. 10, no. 1-3, pp. 1881–1896, 2005.

[201] G. Waris and H. Ahsan, "Reactive oxygen species: role in the development of cancer and various chronic conditions," Journal of Cancerogenenesis, vol. 5, no. 1, pp. 14–14, 2006.

[202] S. Reuter, S. C. Gupta, M. M. Chaturvedi, and B. B. Aggarwal, "Oxidative stress, inflammation, and cancer: how are they linked?", Free Radical Biology & Medicine, vol. 49, no. 11, pp. 1603–1616, 2010.

[203] A. Sznarkowska, A. Kostecka, K. Meller, and K. P. Bielawski, "G.-Y. Liou and P. Storz, "Free radical Research," FEBS Letters, vol. 710, 2010.

[204] G.-Y. Liou and P. Storz, "Reactive oxygen species in cancer," Free Radical Research, vol. 44, no. 5, pp. 479–496, 2010.

[205] P. Storz, "Reactive oxygen species in tumor progression," Frontiers in Bioscience, vol. 10, no. 1-3, pp. 1881–1896, 2005.

[206] G. Waris and H. Ahsan, "Reactive oxygen species: role in the development of cancer and various chronic conditions," Journal of Cancerogenenesis, vol. 5, no. 1, pp. 14–14, 2006.

[207] S. Reuter, S. C. Gupta, M. M. Chaturvedi, and B. B. Aggarwal, "Oxidative stress, inflammation, and cancer: how are they linked?", Free Radical Biology & Medicine, vol. 49, no. 11, pp. 1603–1616, 2010.

[208] A. Sznarkowska, A. Kostecka, K. Meller, and K. P. Bielawski, "G.-Y. Liou and P. Storz, "Free radical Research," FEBS Letters, vol. 710, 2010.

[209] G. Waris and H. Ahsan, "Reactive oxygen species: role in the development of cancer and various chronic conditions," Journal of Cancerogenenesis, vol. 5, no. 1, pp. 14–14, 2006.

[210] S. Reuter, S. C. Gupta, M. M. Chaturvedi, and B. B. Aggarwal, "Oxidative stress, inflammation, and cancer: how are they linked?", Free Radical Biology & Medicine, vol. 49, no. 11, pp. 1603–1616, 2010.

[211] G. Waris and H. Ahsan, "Reactive oxygen species: role in the development of cancer and various chronic conditions," Journal of Cancerogenenesis, vol. 5, no. 1, pp. 14–14, 2006.

[212] E. McAdam, R. Brem, and P. Karran, "Oxidative stress-induced protein damage inhibits DNA repair and determines mutation rate and therapeutic efficacy," Molecular Cancer Research, vol. 14, no. 7, pp. 612–622, 2016.

[213] J. Opanuraks, C. Boonla, C. Saelim et al., "Elevated urinary total sialic acid and increased oxidative stress in patients with bladder cancer," Asian Biomedicine, vol. 4, no. 5, pp. 703–710, 2010.

[214] H. Sönmez, Z. Ozturk, H. Ekmecki, H. Baloglu, and E. Kökoglu, "TBARS, carnitine, and reduced glutathione levels in human bladder carcinoma," Biochemistry, vol. 68, no. 3, pp. 346–348, 2003.

[215] M. Patchsung, C. Boonla, P. Amnattrakul, T. Dissayabutra, A. Mutirangura, and P. Tosukhowong, "Long interspersed nuclear element-1 hypomethylation and oxidative stress: correlation and bladder cancer diagnostic potential," PLoS One, vol. 7, no. 5, article e37009, 2012.

[216] A. Matsui, T. Ikeda, K. Enomoto et al., "Increased formation of oxidative DNA damage, 8-hydroxy-2′-deoxyguanosine, in human breast cancer tissue and its relationship to GSTP1 and COMT genotypes," Cancer Letters, vol. 151, no. 1, pp. 87–95, 2000.

[217] R. K. Gupta, A. K. Patel, R. Kumari et al., "Interactions between oxidative stress, lipid profile and antioxidants in breast cancer: a case control study," Asian Pacific Journal of Cancer Prevention, vol. 13, no. 12, pp. 6295–6298, 2012.

[218] R. Kumaraguruparan, R. Subapriya, J. Kabalimuthy, and S. Naging, "Antioxidant profile in the circulation of patients with fibroadenoma and adenocarcinoma of the breast," Clinical Biochemistry, vol. 35, no. 4, pp. 275–279, 2002.

[219] R. Kumaraguruparan, J. Kabalimuthy, and S. Naging, "Correlation of tissue lipid peroxidation and antioxidants with clinical stage and menopausal status in patients with adenocarcinoma of the breast," Clinical Biochemistry, vol. 38, no. 2, pp. 154–158, 2005.

[220] J. Bhattacharjee, S. Jogdand, R. K. Shinde, and S. Goswami, "Assessment of oxidative stress in breast cancer patients: a hospital based study," International Journal of Basic & Clinical Pharmacology, vol. 7, no. 5, p. 966, 2018.

[221] B. Aryal and V. A. Rao, "Specific protein carbonylation in human breast cancer tissue compared to adjacent healthy epithelial tissue," PLoS One, vol. 13, no. 3, article e0194164, 2018.

[222] G. Romano, A. Sgambato, R. Mancini et al., "8-Hydroxy-2′-deoxyguanosine in cervical cells: correlation with grade of dysplasia and human papillomavirus infection," Carcinogenesis, vol. 21, no. 6, pp. 1143–1147, 2000.

[223] M. L. Looi, A. Z. H. Mohd Dali, S. A. Md Ali, W. Z. Wan Ngah, and Y. A. Mohd Yusof, "Oxidative damage and antioxidant status in patients with cervical intraepithelial neoplasia and carcinoma of the cervix," European Journal of Cancer Prevention, vol. 17, no. 6, pp. 555–560, 2008.

[224] V. Manju, J. Kalaivani Sailaja, and N. Nalini, "Circulating lipid peroxidation and antioxidant status in cervical cancer patients: a case-control study," Clinical Biochemistry, vol. 35, no. 8, pp. 621–625, 2002.

[225] S. Gautham, M. L. B. Bhatt, S. Mehrrota et al., "Implication of therapeutic intervention on putative oxidative stress markers in cervical cancer," Journal of Dental and Medical Sciences, vol. 16, no. 2, pp. 86–89, 2017.
[226] K. Suzuki, Y. Ito, K. Wakai et al., “Serum oxidized low-density lipoprotein levels and risk of colorectal cancer: a case-control study nested in the Japan Collaborative Cohort Study,” Cancer Epidemiology Biomarkers & Prevention, vol. 13, no. 11, p. 1781, 2004.

[227] T. Rainis, I. Maor, A. Lanir, S. Shnizer, and A. Lavy, “Enhanced oxidative stress and leucocyte activation in neoplastic tissues of the colon,” Digestive Diseases and Sciences, vol. 52, no. 2, pp. 526–530, 2007.

[228] C.-C. Yeh, C. Y. Lai, L. L. Hsieh, R. Tang, F. Y. Wu, and F. C. C. Jüngst, B. Cheng, R. Gehrke et al., S. Bandebuch, “Oxidative stress and antioxidant status in patients with ovarian cancer,” Journal of Clinical Biochemistry, vol. 20, no. 2, pp. 162–165, 2005.

[229] V. Gadjeva, A. Dimov, and N. Georgieva, “Influence of therapy on the antioxidant status in patients with melanoma,” Journal of Clinical Pharmacy and Therapeutics, vol. 33, no. 2, pp. 179–185, 2008.

[230] J. P. Bisec, M. Djuic, I. Stanojevic et al., “Association between oxidative stress and melanoma progression,” Journal of Medical Biochemistry, vol. 37, no. 1, pp. 12–20, 2018.

[231] S. Tabur, Ş. N. Aksoy, H. Korkmaz, M. Ozkaya, N. Aksoy, and E. Akarsu, “Investigation of the role of 8-OHdG and oxidative stress in papillary thyroid carcinoma,” Tumor Biology, vol. 36, no. 4, pp. 2667–2674, 2015.

[232] M. RaqKhan and S. Sellappa, “Serum malondialdehyde levels in lung cancer patients,” Journal of Applied Biology & Biotechnology, vol. 1, no. 4, pp. 32–34, 2013.

[233] C. Jüngst, B. Cheng, R. Gehrke et al., “Oxidative damage is increased in human liver tissue adjacent to hepatocellular carcinoma,” Hepatology, vol. 39, no. 6, pp. 1663–1672, 2004.

[234] C. C. Lin and M. C. Yin, “B vitamins deficiency and decreased antioxidant state in patients with liver cancer,” European Journal of Nutrition, vol. 46, no. 5, pp. 293–299, 2007.

[235] J. M. Yuan, M. Grouls, S. G. Carmella et al., “Prediagnostic levels of urinary 8-epi-prostaglandin E2α and prostaglandin E2 metabolite, biomarkers of oxidative damage and inflammation, and risk of hepatocellular carcinoma,” Carcinogenesis, no. article bgy180, 2019.

[236] P. Poungpairoj, P. Whongsiri, S. Suwannasin, A. Khlaiphuengsin, P. Tangkijvanich, and C. Boonla, “Increased oxidative stress and RUNX3 hypermethylation in patients with hepatitis B virus-associated hepatocellular carcinoma (HCC) and induction of RUNX3 hypermethylation by reactive oxygen species in HCC cells,” Asian Pacific Journal of Cancer Prevention, vol. 16, no. 13, pp. 5343–5348, 2015.

[237] M. Pylvas-Eerola, P. Karihtala, and U. Puistola, “Preoperative serum 8-hydroxydeoxyguanosine is associated with chemoresistance and is a powerful prognostic factor in endometrioid-type epithelial ovarian cancer,” BMC Cancer, vol. 15, no. 1, p. 493, 2015.

[238] X. Xu, Y. Wang, W. Guo et al., “The significance of the alteration of 8-OHdG in serous ovarian carcinoma,” Journal of Ovarian Research, vol. 6, no. 1, p. 74, 2013.

[239] S. Bandebuch, “Oxidative stress and antioxidant status in patients of ovarian cancer,” Biomedical Research, vol. 22, no. 2, 2011.

[240] J. Didziapetrienë, J. Bublevi, G. Smalýtė, B. Kazharienë, and R. Stukas, “Significance of blood serum catalase activity and malondialdehyde level for survival prognosis of ovarian cancer patients,” Medicina, vol. 50, no. 4, pp. 204–208, 2014.

[241] S. K. Mohan and V. Priya, “Changes in lipid peroxidation, glutathione, ascorbic acid, vitamin E and antioxidant enzymes in patients with ovarian cancer,” Acta Medica Academica, vol. 38, no. 1, p. 5, 2008.

[242] H. Miyake, I. Har, S. Kamidono, and H. Eto, “Oxidative DNA damage in patients with prostate cancer and its response to treatment,” The Journal of Urology, vol. 171, no. 4, pp. 1533–1536, 2004.

[243] D. S. L. Srivastava and R. D. Mittal, “Free radical injury and antioxidant status in patients with benign prostate hyperplasia and prostate cancer,” Indian Journal of Clinical Biochemistry, vol. 20, no. 2, pp. 162–165, 2005.

[244] C. J. M. Yuan, M. Grouls, S. G. Carmella et al., “Prediagnostic levels of urinary 8-epi-prostaglandin E2α and prostaglandin E2 metabolite, biomarkers of oxidative damage and inflammation, and risk of hepatocellular carcinoma,” Carcinogenesis, no. article bgy180, 2019.
