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Exploring 8-hydroxy-2-deoxyguanosine as a biomarker of oxidative DNA damage in various diseases and pathological conditions: Review

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Abstract
Background: 8-Hydroxy-2-deoxyguanosine is a biomarker of oxidative stress, released from damaged DNA due to disease processes and chemical exposure. Several studies targeted the levels of this biomarker to evaluate the detrimental effects on the level of genetic material.
Materials and Methods: Keywords, such as: 8-Hydroxy-2-deoxyguanosine, 8-OHdG,oxidative stress, were searched in many search engines to review 8-Hydroxy-2-deoxyguanosine levels in most of the available studies in order to clarify the degree of DNA damage in various pathological conditions by determining the level of the above mentioned biomarker.
Results: in most of the reviewed studies, such as: neurodegenerative disorders, malignant conditions, diabetes mellitus, among other inflammatory processes, the concentrations of 8-Hydroxy-2-deoxyguanosine were higher than in control groups. Surprisingly, the few studies conducted on alcoholics showed a decline in the levels of this biomarker compared to non-alcohol drinkers.
Conclusion: 8-Hydroxy-2-deoxyguanosine is one of the vital DNA damage indicators which needs to be given more attention in terms of seeking the harmful oxidative burden on human genetic material for providing more robust measures to early detection such harms before progressing to severe and irreversible health problems.

Keywords: DNA damage, diseases and pathological conditions, 8-hydroxy-2-deoxyguanosine

Introduction

The 8-hydroxy-2-deoxyguanosine (8-OHdG) is widely used as a marker to measure the level of oxidative stress in a cell leading to the formation of so-called DNA oxidation (Chao *et al*., 2021; Gholinezhad *et al*., 2020) [21, 43].

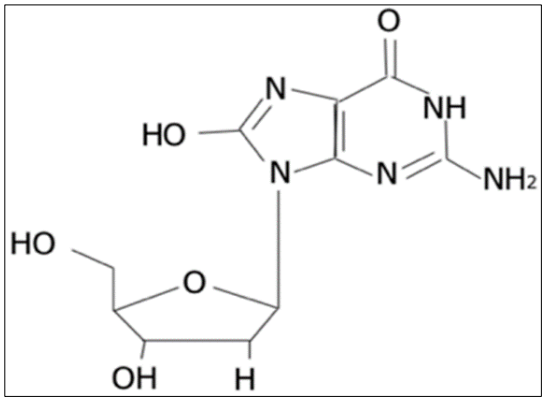

Fig 1: Structure of 8-OHdG (Graile *et al*., 2020) [50].

Oxygen radical is, in fact, a molecule named hydroxyl radical that is a major reactive oxygen species that interacts with the nucleobases of the DNA as was studied earlier by Valavanidis *et al*. (2009). The guanine of aforementioned nucleobases is the most histolyzing, leading to the generation of 8-OHdG.

Figure 1. The relation of the 8-OHdG at a higher position with chronic respiratory diseases deemed as COPD got proved **(**Di Minno *et al*., 2016; Neofytou and Tzortzaki, 2012) [29, 94]. Smoking, aging and exposure to different physical, chemical and biological factors can also lead to an augment of 8-OhdG levels (Abusoglu *et al*., 2014; Sakano *et al*., 2009) [1, 109].

The concept of oxidative stress indicates the situation when neutralizing the overabundance of ROS's by the glutathione system is less efficient than ROS formation. These the process of membrane disintegrate and initiate lipid, protein and DNA harms ends the life of the cell (Du *et al*. 2012; Khatri *et al*. 2013) [35, 69]. First of all, ROS most often occurs from oxygen, it may be the case of superoxide (O2), the hydroxide (OH) or peroxyl rad. Enzymes like (ROO), and (H_2O_2) are part of the respiratory system of the bacteria. Meantime, free radicals when getting neutralized, expel toxins and harmful molecules from your body in the form of ROSs (Herzog *et al*., 2009) [59]. Oxidative stress, also known as the enhancement of the potency of ROSs over antioxidants, takes place when antioxidants are oxidative and become weaker with age. Thus this arouses free radicals to have a windfall profit as a result, and they deprive our cells and tissues of oxygen and nutrients essential for cellular integrity (Elsaesser and Howard 2012; Fu *et al*., 2014; Djurisic *et al*., 2015) [36, 42, 34].

Oxidative stress is considered to be one of the most dramatic of all these effects and it is leading to DNA damage. The process of the modern biological detection of DNA oxidation is often done with biomarkers (Brown *et al*., 201) [13]. 8-OHdG is the most abundant nuclear predicate of oxidation of nucleic acid molecular biomarkers which makes it stand out among the bunch of other options. Graille and associates (2020a) presented the birth of 8-OHdG in 1984. Their research study showed a free radicals study.

The main focus of this review is the use of 8-OHdG, the helper factor of genetic material, to pinpoint oxidative stress state as the beginning path of illnesses like cancer, aging, and more.

Chapter One
Review of Literature
Definition of 8-Hydroxy-2-Deoxyguanosine

Oxidative product of the DNA, 8-hydroxy-2-deoxyguanosine (8-OHdG), otherwise One of the most widely studied and abundant oxidated adducts (Osaka and Nasirzadeh, 2021; Urbaniak *et al*., 2020) [98, 49] is 8-hydroxy-2-deoxyguanosine (Here GAC mutagenicity which is of the mutationly G to T is induced by it. The group of the major organic radical heterogeneous atoms listed as -OH, singlet oxygen, and peroxide and peroxynitrite which has also earlier been called 8-OHdG belong to the group of the organic radical ROS. Furthermore, Fenton chemistry also results in the creation of another free radical, the superoxide, that can further react to 8-OHdG under the influence of sunlight. 8-OHdG, produced either in nuclear or mitochondrial DNA, is the most indicative product in the determination of BP conception (Urbaniak *et al*., 2020; Omari Shekaftik and Nasirzadeh, 2021) [49, 98].

8-OHdG formation is so fast and is quite common even in low reactive oxygen species environments; on the other hand, 8-OHdG repair is slow and hardly visible under normal cellular oxidative conditions. Meanwhile, at present, most techniques for detecting 8-OHdG depend on the use of antibodies which comprise histo chemical assays, DNA isolation and quantification on 8-OHdG DNA and measurements of 8-OHdG in tissues and bodily fluids. The advent and utilization of the antibody method has not only resulted in the fastening of the research on 8-OHdG but also been useful in the identification of a variety of lesions in DNA that have been linked to 8-OHdG. Besides point mutations, 8-OHdG seems to relatively err on the side of failure to disturb the DNA helix rather than double-strand breakage and the loss of one or multiple bases. This explains why the oxidative stress markers especially 8-OHdG which are highly proliferated in non-dividing tissues like brain where they seem to be widely used in gene transcription Besides the usual products of the lipid peroxidation, the range of pro-inflammatory mediators like the cytokines, interferon and tumor necrosis factor-alpha can unblock the expression of the 8-OHdG. Studies are ongoing to establish if 8-OHdG has any disease implications. The number of studies agree that an increase in 8-OHdG immune reactivity is generally associated with cancer tissues. The variation in the 8-OHdG levels is believed to be associated with a positive or a negative prognosis of non-small cell lung carcinomas. Aside from that, the increased levels of 8-OHDG have also been determined in some genetic disorders which are hereditary (Graille *et al*., 2020; Urbaniak *et al*., 2020) [48, 49].

An average life of a radical free forms anywhere from 10ns approaches 10min. However, there have arisen persistent radicals which can linger and exert significant damage. Concentration of the free radicals has become a major issue as it leads to the reason for genesis of different type of diseases. Free radicals are used in all living cells through which they can work as antioxidants or inhibit the function the form of prooxidants. These are, however, true that we are all under siege of the "arsenal" that is free radicals but still in the end, life depends on these fighting. Oscillation species has a prominent role in the inflammation which according to what has been mentioned in the literature (Canakci *et al*., 2005) [18].

An oxidative or reductive profile is a result of action of reactive oxygen species as well as the level of antioxidants, and consequently the preservation of health is akin to a servo mechanism that controls the organism's health. Disease states usually involve an overproduction of ROS species and then they exceeding of the antioxidant defenses (The blevel of the ROS species is higher than that of the production of antioxidants) as a result of an excess of defensive mechanisms against oxidativestress (Muthuraj *et al*., 2021) [91].

And thus, in more than hundred diseases including periodontal illness which is induced by cyclic oxidant stress because oxidative stress can break down the proteins, lipids, and DNA, people are exposed to the damage **(**Çanakçi *et al*., 2009) [17].

Significance of 8-Hydroxy-2-Deoxyguanosine

In addition to cell signaling, apoptosis and gene expression other biological reactions get affected through the oxidative stress and the impacts are very much evident. The ROS system interaction is a way of antioxidant defense which helps to fight oxidation in case of higher quantity can lead to a permanent damage. Living organisms produce two primary forms of reactive oxygen species (ROS): This are going to be homolysis of O2-• form OH•. Although the

ROS, which restrict the system inside the cell wreck the existing macromolecules including proteins, membrane lipids and DNA, are the main reasons lead to cell death. Furthermore, the Haber–Bosch reaction can be carried across cellular level wherewith there exists the odds that it may lead to oxidative stress. This mechanism can be described as the catalytic interaction between H2O2 and Fe ions that ends with production of reactive ROS: i.e., O2• and OH•. The ionisation is the same, except in this case, the ferric ions are produced in the last stage by reduction of ferrous ions in the first one. This is all about the effect of not iron but is really iron. Fenton reelection is subsequent, which in turn is followed by the Fenton reagent. (as represented by Figure 1.3; McCord, 1987) [87].

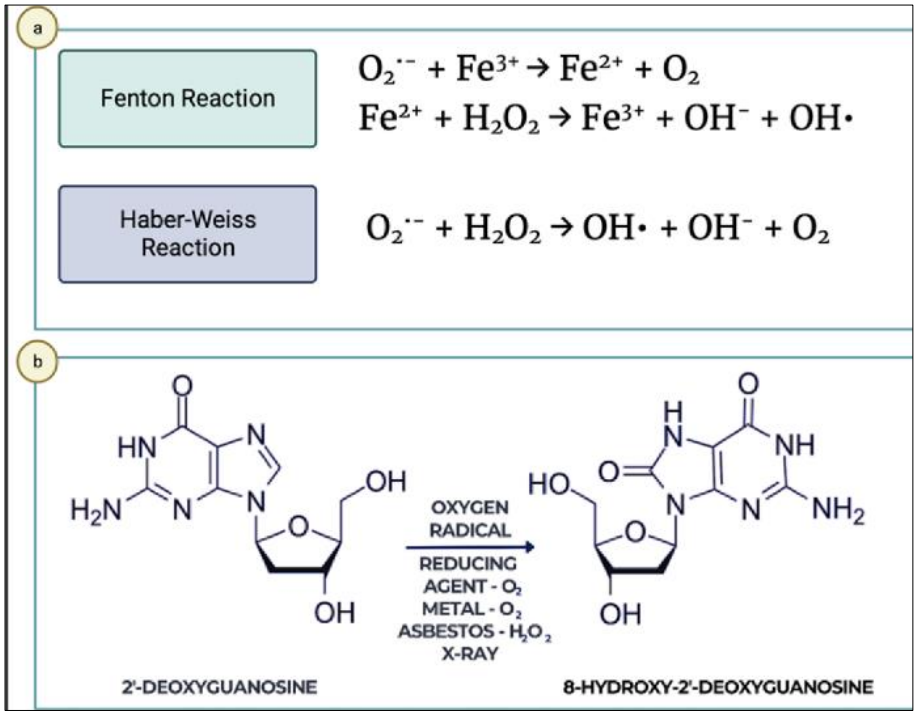

Fig 2: (a, b) "Hydroxyl radical and formation of its scavengers and their involvement in health and disease" (Goriuc *et al.*, 2024) [47].

With 8-OHdG enough can be found in human liquids, etc. There is a consideration about the reliability of the test-kit that is based on the level of oxidative DNA damage of the assay because of its precision and similarity to the original. Guanine of course, is the nitrogenous base a bit weaker again the oxidative potential equally as the other three DNA bases. Yet, that was partly prevailed by the counter reactions of the others reactive groups. Guanine oxidation causes transversions (Always fills the gap of guanine-thymine or guanine-adenine pairing) therefore gene mutation occurs as a result and dangerous outcomes arise. In this regard, guanine strands and junctions presented to such oxidative process will become the most vulnerable ones to be the targets of halide oxidation, alkylation and other violent reactions that will eventually lead to the most frequent DNA defects. Human bodies have 24 hours cycle which means that they have high and low time, and during the low period of time, bodies are more vulnerable to any irregularities which might appear in different organs that may cause their malfunction, resulting in severe consequences that humans may die from (Jena and Mishra, 2012) [67].

The human mitochondrial DNA is made up of 16569 base pairs formed if two stranded DNA. MtDNA dispersed nucleic acid and the number of copies per mitochondrion is different each time from 2 to 10. The construction of this 13-genes is borrowed from the genome that encodes oxidative phosphorylation mitochondrial respiration. In addition, this gene includes two ribosomal RNA genes and the number tRNA genes is required for the mitochondrial DNA transcription. In addition, you need to be aware that this mitochondrion are all over the cell and are ranging from a couple of hundred and a couple of thousands. ROS conglomerate a sequence of reactions consecutively and these reactions are generated at a particular place near inner mitochondrial membranes. Human mtDNA (mitochondrial DNA) wrapping blockade of the histone molecule and features a direct DNA-membrane interface. So, mtDNA is the exact idea that shows the rate of the replication is faster than any of the nuclear DNA since there is no DNA repair systems nor any DNA correction mechanisms that are functionally properly.

However, as a result of recent research the mtDNA abnormalities are shown to originate at molecular level and may be seen at DNA deletions or point mutations stage resulting into wide spectrum of pathological disorders such as degenerative diseases or aging. It is an example when "5 bp delection" has a tendency to recur again and again among various organs like that of aged people (Çanakçi *et al.*, 2009; Mustafa *et al.*, 2020) [17, 90].

Hydroxy-2-Deoxyguanosine in Pathology

Nowadays 8-OHdG which is a relative important indicator proposing the DNA bulldozing process is highly linked with the cases of cancers, neurological diseases, poor periodontal conditions and inflammatory chronic conditions. Apart from this, excessive oxidative stress has been reported in many disorders like inflammatory bowel disease and T2DM, and it is a creating or contributing factor for ascription of inflammation (Çanakçi *et al.*, 2009; Chapple and Mathews, 2007; Takane *et al.*, 2005; Rai *et al.*, 2008) [17, 22, 135, 101].

Principally, (Elucidating this) meta-analysis study has projected that CVD patients (Particularly) have higher 8-

OHdG levels than the control group. A study has also shown that the concentration of the 8-OHdG did not depend upon any of the CVD risk factors like diabetes, hyperlipidemia, or body mass index (Di Minno *et al*., 2016) [29]. Recent studies have documented that 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels rise as endpoint of clinical outcomes of stroke. Besides the participation with these 8-OHdG level which is the indicator of the plaque that has a relationship with the stroke relapse in patients is also observed (Korkmaz *et al*., 2018) [73]. It is usually a consequence of both oxidation and inflammation are found together in CKD. Occasionally, these two diseases coexisting each other can be an extra detrimental factor to a kidney. Mortality Risk Index does not work probably since it does not depend on glomerular filtration rate estimation. One of the most important advantages is that it is not necessary to check the inflammatory component here (Dai *et al.*, 2019) [27].

In terms of neurodegenerative disorders, 8-OHdG show a potency for the purpose of diagnosing Alzheimer disease via serum. Such uniqueness of this factor is ideal for differentiating people on the basis of the treatment choices they make because it revealed the same increasing trend (Korkmaz *et al*., 2018) [73].

Besides, the HD affected have a high 8-OHdG level in dorsolateral prefrontal cortex as well as blood and white blood cell fractions (Long *et al*., 2012) [81].

Many investigations have shown that there is a larger concentration of 8-OHdG in the substantia nigra in cases of PD patients than healthy subjects have did. It was also noted that more peripheral regions such as the caudate nucleus and others also registered a higher level of this type of DNA damage. The dendritic cells have been noticed to be a main contributor as to how different types of neuro degeneration occur under different circumstances while it has also been noted that the lymphyc users and other organs may also play significant roles in the progression of this disease. In brief, those cells could undergo upturned 8-OHdG synthase activities (Gmitterová *et al*., 2009) [45].

In addition to that, there is established an undebated connection between high 8-OHdG concentration and genetic defects, the phenotype of which is the signs of carcinogenesis. The set link among the oxidative DNA damage products, the 8-OHdG serous ovarian cancer stage at advanced age, and insufficient intake of antioxidants at this age group to reduce the increased chances is clearly established by the meta-analytical literature. A different study says that the activation of oxidative stress is the main factor that leads to the creation of colon cancer (CRC). Due to relatively high 8-OHdG urine levels correlated with CRC risk at an earlier time, the fluid biomarker worked functionally to serve the concern detection and assessment in Indels of CRC, which partially obscured by Guo *et al.* (2016) [52] for further evaluation. This is just another evidence that 8-Ohdg even at elevated level cannot necessarily reflect a cancer because cancer cannot be defined by higher 8-OHdg. The tumour tissue antioxidant activity was lowered and it might be that the 8-OHdG is their predictors of a poor prognoses (Qing *et al.*, 2019) [100].

Hydroxy-2-Deoxyguanosine and Diabetes Mellitus

When the blood glucose levels are chronically in high levels and such health conditions can be related to the development of the oxidative stress (Szendroedi *et al*., 2011) [34]. Water itself is acted upon in the H2O2, OH•, and O2•− metabolic processes, which is one of the sources of the secondary products. Among cellular content, mitochondria (Mainly producers of reactive oxygen species or ROS), peroxisomes (involved in fatty acid breakdown), and the Cytochrome P450 system (find their use in the mixed-functional oxidation system), play a pivotal role in the oxidative stress process and are constantly growing up ROS (Halliwell and Gutteridge, 2015) [58].

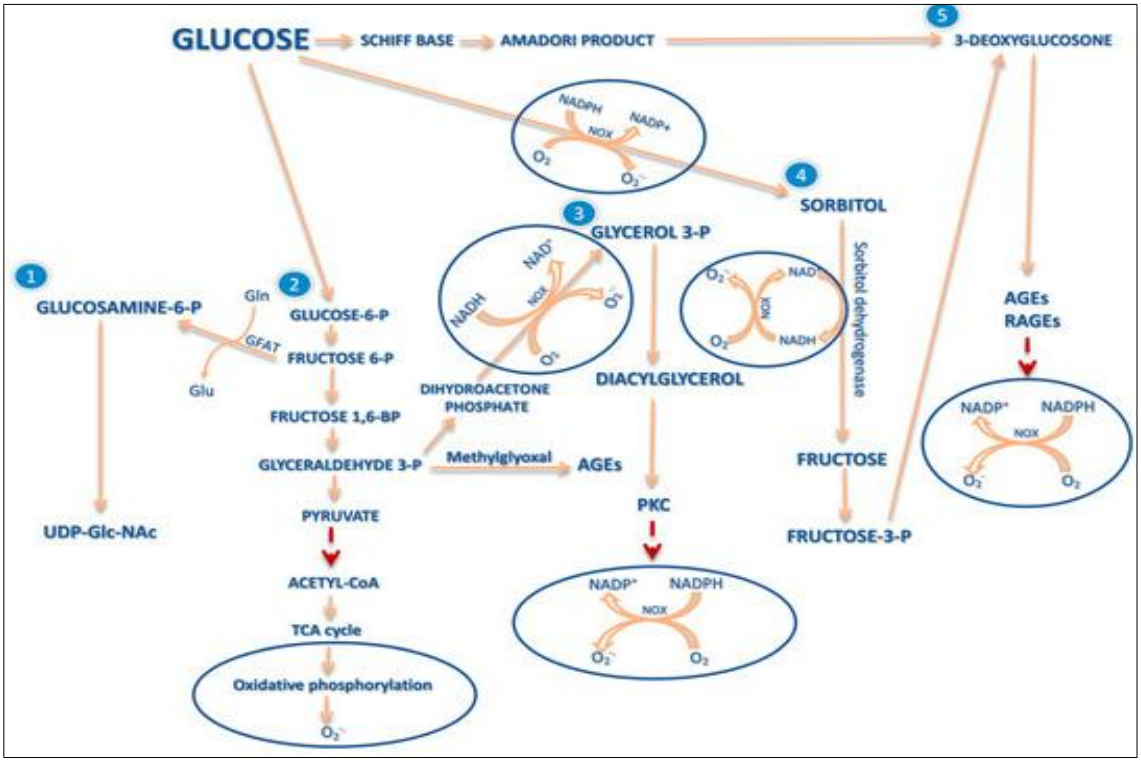

Fig 3: "Activation of alternative pathways for glucose metabolism" (Turek *et al*., 2015) [31].

Increase in hyperglycemia leads to ROS levels that significantly rise, it occurs interactions that degrade cellular balance and leads to cell lesions due to the molecular disruption **(**Canakçi *et al*., 2009) [16].

Reactive oxygen species (ROS) generation taking place in oxyhemoglobin effecting glucose transporter 4 translocation from intracellular compartments therefore increasing the blood glucose level (Ding *et al*., 2021; Leguisamo *et al*., 2012) [33, 78]. The cell loses homeostatic balance in hyperglycemia, as the overproduction of reactive oxygen species (ROS) results in the ROS-catalyzed oxidative breakdown of glucose. Such process which further continues in turn boost production of advanced glycosylation end products (AGEs) in T2D patients. The major factors contributing to the restoration of two rainforests i.e. transparency of the process and balance of water resources played remarkable roles on the global level (Kowaltowski *et al*., 2009) [74].

The other influenced program will affect the disruption of OXPHOS process as well as the decline of NADH oxidoreductase activity. It would be par for the course to mention the insulin resistance (Cojocaru *et al*., 2023) [25].

It is the oxidative damage that plays a key role and has been explored by many researches (Cai and Kang, 2001) [15]. This damage leads to diabetic complications, which result in a lot of deaths. The existence of increased DNA and protein oxidation, together with lipid, provides the correlated data which could be translated into the living humans with the observation of consequence of oxidative stress and its involving with diabetes induced problems.

Concerning oxidative alterations the nucleus and mitochondrial DNA are principally the region to be affected (Cooke *et al*., 2002) [26]. Guanine (Which is the main nitrogenous base commonly known as purines and pyrimidines) is highly prone to getting damaged by several types of carcinogens. Oxidative stress is nothing but product run due to introduction of hydroxyl group at eighth position of guanine base which results in the generation of 8-OHdG as the only end product. The transport of an OH adduct from 8-oxodeoxyguanosine to 8-OHdG is specifically linked to a higher frequency of indices of damage in cytomicrobial DNA degradation. With the help of the 8-OHdG and the 4977bp mtDNA deletion described by Suzuki *et al*., stress assessment is reported as more useful and meaningful for the patients with diabetes (Suzuki *et al*., 1999) [133].

The Laboratory methods for the detection of serum/urinary 8-OHdG level are various and it varies from protein-specific to enzyme-linked immunosorbent assay, greatDi drug to Immunofluorescence to other baseline protein-, peptide-based techniques such as by high-performance liquid chromatography or liquid chromatography mass spectrometry.

There is a chance for patients suffering from the complications of T2DM to show such problems as a sharp increase in 8-OHdG concentration when compared to healthy individuals without this diagnosis. Besides, 8-OH dG in urine is known to be the best local marker of the oxidative stress-related damages leading to human diseases. In Performing analysis, Negishi *et al*. found in his research, 2001 HbA1c was linearly opposed to 8-OHdG excreted in urine over a period of 24 hours. This research by Leinonen *et al*., gave the fact that the 24 hours urine excretion value among diabetics was equal to those of the control volunteers (Leinonen *et al*., 1997) [79].

8-hydroxy-2-deoxyguanosine and Smoking

Cancers caused by lungs occupy the top spot globally in terms cancer incidence for the past few years. They also carry the highest associated deaths due to the cancer-related disease worldwide (Ferlay *et al*., 2014) [40]. In cigarette smoking (CS), lung cancer (LC) may be characterized as one of its important etiologic factors (Ferlay *et al*., 2014) [40]. Notwithstanding the fact CSS affects the manner through which it contributes to the development of lung cancer is mysterious. Smoking has already become a main factor that is known to contribute to the oxidative stress, which is then followed by DNA damage and mutations of the genes implicating tumors in the line. These parameters seem to be of great significance in the onset of cancer (An *et al*., 2019) [5].

An interaction of reactive oxygen and nitrogen species causes DNA damage which nucleotide 8-hydroxy-2-deoxy guanosine (8-OHdG) is a result. The compound is a very specific biomarker for oxidative stress. In addition to the aging process, 8-OHdG level also can be positively related with some diseases such as cancer, diabetes, and hypertension (David *et al.*, 2007) [28].

It is a common knowledge that oxidative stress due to smoking plays a role in the incidence of p53 mutations (Gibbons *et al*., 2014) [44]. The restricted mutant p53 mode to facilitate DNA repair was considered to play a role in the development of cancer.

The process of accumulation of carboxyhemoglobin, which is a consequence of smoking, significantly reduces the function of hemoglobin to transport oxygen, poisons with hypoxia, which, as a result, leads to a hypoxic state. Subsequently, this is able to suppress the production of reactive oxygen species (ROS) and meanwhile decrease 8-hydroxy-2-deoxyguanosine (8- OHdG) expression (Archer *et al*., 1993) [6].

This correlation between smoking and low levels estrogens can be explained by the fact that smoking leads to antioxidant enzymes overproduction due to the oxidative stress. The smoking-ROS-8-OHdG axis of the NSCLC (Non-small cell lung cancer) is emerging as a complex modulatory system, with ROS, antioxidant enzymes status, and hypoxia of tumor microenvironment being involved (An *et al*., 2019) [5].

A study conducted by An *et al*. in 2019 proved that, among all the unhealthy habits, smoking is the prime contributing factor to high level of oxidative stress. Nevertheless, no link between the components of which smoking constitute and an up-regulation of 8-OHdG was detected in the research. This may signify that the pattern of at 8-OHdG expression in cancer is much more sophisticated and could get the functional status of antioxidant enzymes and/or the hypoxic environment of cancer into consideration. We found out that immune histochemical staining expression of p53 had some association with smoking status of patients.

In the assessment of the effects of smoking on the plasma antioxidant defenses and urinary 8-hydroxy-2-deoxyguanosine, Metta along with his colleagues conducted a study on heart disease patients with ischemic heart disease as the subjects. The study indicated the seriousness of oxidative stress through a significant negative correlation between serum 8-OHdG and TAS, which are indicative of oxidative stress. The urinary 8-OHdG being used as a super sensitive marker could in turn, help us to located damaged DNA in smokers.

8-Hydroxy-2-Deoxyguanosine and Alcohol Drinkers

The results of research have shown that ethanol is involved in oxidative stress of the liver; rats that consumed ethanol showed high level of lipid peroxidation in their liver (Koch *et al*., 1991; Uysal *et al*., 1989) [71, 50]. In this regard, cognitive impairment is among the visible symptoms reported (Rouach *et al*., 1987) [107], as are DNA segmentation in liver cells (Rajasinghe *et al*., 1990) [102], decreased vitamins A and E levels (Nordmann, 1987; Hagen *et al*., 1989) [97, 53], and low levels of glutathione observed in Further, another study from 1997 published by Thome *et al*. reported an increase in the hydroxyl radical levels in the peripheral blood of the human individuals after taking alcohol. It can be mentioned that after exposure of ethanol ROS production occurs and such mechanisms are was proposed how ROS generation happens during ethanol exposure **(**Bondy, 1992) [11]. As reactive oxygen species (ROS) have been implicated in the progression of e CHD as well as cancer, it is accordingly postulated that they have a role in escalating both conditions (Floyd, 1990) [41].

The paper by Bianchini in 2001 [9] investigated the alcohol intake and it is an indicator of 8-oxodGuo level. This comparison was carried out at the individual level, utilizing the study centre comparison, and the center level, altering comparison of mean oxidative DNA with the alcohol intake between the four study centers. The research findings revealed to be a negative association between 8-oxodGuo and the volume of overall alcohol consumption at the individual level, especially among women who reported regular alcohol intake. Furthermore, he found a parallel between the degree of DNA damages of oxidative kind, which is consequences of alcool ingestion a could be established by the amount of 8-oxodGuo in lymphocytes. Besides that, alcohol use in average scale had negative relevance with amounts of 8-oxodGuo of people can be seen in all four populations of the study. However, the curious relationship of alcohol consumption on decreasing DNA damage by free radicals does not correspond to the type of beverage that one consumes (Bianchini, 2001) [9].

8-Hydroxy-2-Deoxyguanosine in Cardiovascular Diseases

The CVD risk factors consist of a set of variables with the diabetes type 2, hypertension, smoking behavior, overweight, and dyslipidemia taking the lead role. The ROS formation, as well as its physiological correction function, and its involvement in numerous diseases like heart attacks, is an important issue (Brea *et al*., 2012) [12]. Physiologically, the ROS is being destroyed normally by the antioxidant system. Nevertheless this situation can be seen as a precarious equilibrium since the concentration of ROS exceedingly could cause oxidative damage to proteins, lipids and DNA (Sies, 1991) [131]. DNA injury is usually encountered with the removal of system as oxidation metabolites are directly excreted to the urine (Shigenaga *et al*., 1989) [114].

The diuretic effect and oxidative stress induced by the alcohol leads to increase of the urine levels of the oxidized metabolites, which causes a higher risk of development of various pathological diseases (Evans *et al*., 2004) [38]. The rise of their 8-OHdG test level was noticed in a work done by Serdar in 2012 to people understand diabetic patients. Consequently, the research by Rosello-Lleti *et al*. (2012) [105] demonstrated that hypertension patients could be at a higher risk of developing oxidative stress, since they had to deal with higher oxidative stress markers - 8-OHdG.

Unlike what already has been reported in the scientific publications that there is a substantive connection between DNA damage and atherosclerosis formation (Maria Grazia Andreassi *et al*., 2003; Ross, 1999) [85, 106], the direct cause of the damage in the development and formation of the illness remains a puzzle. Consequently, it's still necessary for more innovative and extensive research programs to discover. In 2016, a systematic review of available literature from Di Minno *et al.* was conducted to find the relation between the 8-OHdG level and cardiovascular disease. We separated the acquired data into four groups that covered four kinds of vascular diseases (Coronary artery disease, stroke, peripheral arterial disease, carotid stenosis), the method and design of studies. Data were presented in a tabular form as allegedly shown in the table 1.1

Table 1: "stratification of the analysis according to different vascular diseases (coronary artery disease, stroke, peripheral artery disease, and carotid atherosclerosis) (a), different techniques (b), and samples (c) used for 8-ohdg measurement" (Di Minno *et al.*, 2016) [29].

	No. of studies	No. of patients	Effect size	Test for subgroup differences
(A) Different types of cardiovascular disease				
Coronary artery disease	7	351 Cases 404 Controls	SMD: 1.24; 95% CI: 0.47 to 2.01, $p < 0.002$, I^2: 95%, $p < 0.00001$	χ^2: 0.75, p = 0.39
Noncoronary artery diseases[a]	7	459 Cases 702 controls	SMD: 0.83; 95% CI: 0.33 to 1.34, p = 0.001, I^2: 91%, $p \leq 0.0001$	
(B) Different techniques for 8-OHdG measurement				
ELISA	11	545 Cases 909 Controls	SMD: 1.09; 95% CI: 0.60 to 1.58, $p < 0.0001$, I^2: 93%, $p < 0.00001$	χ^2: 0.16, p = 0.69
GC/LC-MS	3	265 Cases 197 Controls	SMD: 0.86; 95% CI: −0.15 to 1.87, p = 0.09, I^2: 95%, $p < 0.00001$	GC/LC-MS
(C) Different study design				
Case–control studies	5	325 Cases 360 Controls	SMD: 1.00; 95% CI: −0.30 to 1.71, p = 0.005, I^2: 94%, $p < 0.00001$	χ^2: 0.02, p = 0.90
Prospective studies	9	485 Cases 746 Controls	SMD: 1.06; 95% CI: 0.48 to 1.65, p = 0.0004, I^2: 94%, $p < 0.00001$	

Including three studies on stroke, two on carotid atherosclerosis, and two on peripheral artery disease. 95% CI, 95% confidence interval; SMD, standard mean difference.

8-Hydroxy-2′-deoxyguanosine and Primary Open-Angle Glaucoma: Glaucoma is a kind of degenerative disorder among the nervous systems and always leads to permanent loss of ageing. It results from the process of receding and dying of retinal ganglian cells (RMCs) and damaging the optic nerve. Glaucoma is a multifactorial problem that has different causes like high IOP (Intraocular pressure) and other functions of the eye. Oxidative stress which is induced via free radicals could be amongst the pathways that start

the intrinsic apoptotic death track (Nita and Grzybowski, 2016) [96]. Based on the existing knowledge, oxidative stress is regarded as the main culprit of the molecular damage at the anterior segment of the eye which is also known as the anterior chamber. Through the destruction of the tissues, this leads to an increased intraocular pressure (IOP) which could lead to the development of glaucoma (Nita and Grzybowski, 2016) [96].

Primary open-angle glaucoma (POAG) is an age-related disease, which manifests in the form of the TM disorder. The TM's malfunctioning is of a critical role in the development of POAG. Carried out researches on lives organisms such as human creatures showed noticeably high ratio of oxidative DNA damage in TM cells of patients who have been diagnosed with glaucoma (Izzotti *et al*., 2003) [62]. Furthermore, there was a considerable co-relation between the rise in the intraocular pressure (IOP) and visual field impairment which was directly subjective to the extent of oxidative DNA damage observed in the trabecular meshwork network (TM) cells (Saccà, 2005) [108].

Kondkar *et al*., 2020 [72] performed a case-control study to determine whether system oxidative stress and DNA damage that play a role in primary open-angle glaucoma (POAG) was the reason for the disease. We investigated the relationship between 8-OHdG levels from plasma, a sign of oxidative DNA damage, and the POAG or its association clinical features. In order to quantify the risk for POAG with different markers of oxidative stress levels (8-OHdG), the cases and controls that were not divided into the quartiles were grouped in the same way. This division allowed for the identification of two specific values: The beadplate (0.0118 ng/mL) which is at least 25% of the population (lower 25th percentile); and the boss bead (0.2660 ng/ml), which is at the most 75% of the population (upper 75th percentile). The participants were placed into various groups (I, II, and III) according to the application of aforementioned threshold values (1.10 ng/mg and 1.75 ng/mg). The distribution study indicated that the worse picture got as the 8-OHdG elevation was getting higher ($\chi 2 = 8.58$, df = Moreover, an individual with levels below the first quartile (=below 11. 18 ng/mL), within the interquartile range (25th–75th percentile), or above the third quartile (75th percentile) had a considerably elevated risk of primary open-angle glaucoma (POAG).

Table 2: "Plasma levels of 8-hydroxy-2′-deoxyguanosine and the risk of primary open-angle glaucoma (Kondkar *et al*., 2020) [72].

8-OHdG cutoff ng/mL	Controls no. (%)	POAG no. (%)	Odds ratio (95% confidence interval)	*P*< value[a]
By quartiles				
<11.18	17 (33.3)	6 (12.0)	Reference	–
11.18–26.60	19 (26.6)	30 (60.0)	4.47 (1.49 – 13.35)	0.005
>26.60	9 (40.0)	14 (28.0)	4.40 (1.26 – 15.41)	0.017
By ROC curve				
<14.80	24 (53.3)	11 (22.0)	Reference	
≥14.80	21 (46.6)	39 (78.0)	4.05 (1.66 – 9.86)	0.002

Note. [a]Pearson's Chi^2 test; first quartile (<25th percentile); interquartile (25th–75th percentile); third quartile (>75th percentile). Overall Chi^2 = 8.58, df = 2, 8-OHdG, 8-hydroxy-2′-deoxyguanosine; POAG, primary open-angle glaucoma; ROC, receiver operator characteristic.

8-Hydroxy-2'-Deoxyguanosine and Mental Illnesses

During the last few years, approximately 970 million people have been touched by mental health worldwide **(**James *et al*., 2018) [64]. The true number of severe mental disorders cases reported is 282 for schizophrenia, 594 for bipolar disorder, and 3,627 in a hundred of thousands for depression (According to Rehm and Shield, 2019) [103].

The disease conditions, which appear to be significant causes of disability burden were schizophrenia, accounting for 2. Bipolar disorder constitutes 8%, while schizophrenia is stipulated as 1. 4% suicide, of which 11% is attributable to depression. 8%.

Nevertheless, that applying the scientific techniques to study psychiatric conditions is like rediscovering a black box for the majority of us, who have not yet found the answers to how these disorders work. A somehow alarming number of new data are being produced suggesting that the arousal of excessive oxidation is one of the major mechanisms that in the end lead to mental disorders. The brain is the lipid-rich organ that consumes the most oxygen compared to the other organs in the body. While the brain is too rich in NAD (P) H, only a small amount of oxygen in the brain is used to produce approximately 4.5 times more NADPH than in the other organs in the body, thus, making it vulnerable to glutathione metabolism via producing ROS. Besides, the brain which contains of certain level of antioxidant ability by the side of iron and copper is also known for making reducing agents thus same as the neurotransmitter which function at a lower level of antioxidant (Halliwell, 2006; Ng *et al.*, 2008; Smaga *et al.*, 2015) [58, 95, 132].

In the pathogenesis of mental disorders, a failure of the antioxidative protection system is assumed, which is accompanied by decreased levels of antioxidants and an antioxidant enzyme deficit (Salim, 2014) [110]. Furthermore, an increase of the oxidative stress parameters markers found in cases of mental illnesses enhances the role oxidative stress plays in the mental illnesses onset (Brown *et al*., 2014; Liu *et al*., 2015) [13, 80]. A study done in 2014 showed that the level of oxidant in the brain and the periphery tissues of a patient were significantly higher than that of an antioxidant during cerebral ischemia/reperfusion. To a long extent, oxidative damage is associated with mental illness. the defects in the DNA repair have family history also share the responsibility with environment clues. The outcome of these induced errors is a gradual accumulation of DNA damage eventually leading to neurons malfunctions both in the structure as well as in the functions.

As well, Christensen *et al*. (2018) [24] revealed a significant link between the levels of 8-oxodG in the urine and the cerebrospinal fluid of the dead who had severe mental disorders. This indicates that the type of oxidative DNA damage was the most predominant form of oxidative damage in these individuals.

8-Hydroxy-2-Deoxyguanosine in Cancer

MDA levels, 8-OHdG and also antioxidant defense enzymes can be easily monitored, and thus have great diagnostic

significance in the cancerology. Oxidative stress and low antioxidant levels, which are often found already before anticancer treatment begins, are known to be typical characteristics of many cancer patients (Sharma *et al*., in 2007) [113]. On the other hand, the redox state also plays a fundamental role in predicting of cancer therapy and risk and can be a great deal favorable intervention to patients through proper treatment procedure. Current main treatment modalities depends on the development of medications that increase the release of reactive oxygen species (ROS) and cause the cell death of the cancer cells. Total harmless in this method was very often caused the development of some side effects in these healthy tissues. However, the authors of the paper by Ivanova, *et al* (2014) [61], contrast this state with the cancer cells, which display constantly undervalued ROS and high reductive neutralization potential. This polarity of redox states is what the scientists exploit to create powerful drugs and anti-canceric therapies leading to the regulation of redox signaling (Jelic *et al.*, 2021) [65].

Mechanisms of carcinogenesis caused by reactive Oxygen species

Protracted inflammation may initiate oxidative damage leading to the preneoplastic condition (Guina *et al*., 2015) [51]. Suppressing inappropriate cycling of ROS/reactive nitrogen species (RNS) in cells with chronic inflammation positively affects the removal of the activated immunes cells, resulting in the abortion of the escalation of the dysregulated processes, and finally, in the bankruptcy of the preneoplastic state. In the event of ROS/RNS production that surpasses the antioxidant capacity of the human body's defense system, cellular damage may become irreversible and lead to stimulation of lipids, nucleic acids, and proteins. Data can be on the level of the DNA, and if this damage happens, it may cause genetic or/and epigenetic modifications that disrupt the oncogenes and tumor suppressor genes. The causal link between oxidative stress and chronic inflammation is high, and if these mechanisms are not removed, it could start the changes to the genes/epigenetic that will be ranked as the disease inducing pathology (Murata *et al*., 2012) [89]. However, there are many studies that can be referred to, so that it has been clearly demonstrated that oxidative stress affects many signaling pathways linked to cell growth (Klaunig *et al*., 2009) [70].

The epidermal growth factor receptor signaling route is, however, one of the relevant pathways negatively affected by oxidative "stress." Three of the key signaling proteins, Ford factor 2 related nuclear origin, RAS/RAF kinases, the mitogen activated protein kinases ERK1/2, and MEK are inhibited by the oxidative stress. Furthermore, a variety of signaling proteins including phosphatidylinositol 3 kinase, phospholipase and protein kinase C are also impaired by oxid (Huo *et al*., 2014; J Korbecki *et al*., 2013) [60, 63].

Moreover, ROS govern the down-regulation of p53 suppressor gene that is effective in the process of apoptosis. Oxidative stress that is induced by the organizm's cells change the genes, proliferation, and cells life. It is one of the fundamental issues that has not only the potential for formation of tumors, but also the progress of cancer (Matsuzawa and Ichijo, 2008; Barrera, 2012) [86, 8].

8-hidroxy-2-deoxyguanosine in different types of cancer

There will be a marked increase of 8 OHdG levels in pagents of cancer of gastric as a result. The 8-OHdG levels of CAG patients and GC patients were analyzed and then we used the control group to compare. From the biomarker data, it was observable that the levels were high in both CAG and GC patients as well as in the control groups. In the next place, the transcription level of MnSOD was also evidently elevated in the GC group compared to the tole group. Measurement of ESR/SOD and 8 hydroxy-2-deoxyguanosine for this effect in the increased levels of patients with CAG will be done.

A study showed that 8OHdG could be used as a predictive marker in epithelial ovarian cancer. Among such individuals, higher concentrations of 8 OHdG were directly consistent with a lower survival rate for ovarian cancer patients that are commonly associated with traditional markers of a poor prognosis and those with a serous histology. The level of 8 OHdG which was a marker of oxidative damage rose significantly in the Stages III and IV group of cancers as compared to the group in which the ovarian tumour was still localised. That 8 OHdG were seen in areas of high grade papillary serous carcinomas is indeed very impressive, however, they were not found in any low grade papillary serous carcinomas or cystadenoma. Therefore, it follows a particularly poorer optimal outcome with regard to overall survival and progression free survival.

Oxidative stress is associated with colorectal cancer as such evaluation of oxidative stress and antioxidants is pertinent to the therapeutic and preventive management of colorectal cancer (Chang *et al.*, 2008) [20].

Another experimental data indicated, the patients group had higher concentration of 8 OHdG in comparison with control group, but the oxidative defense enzymes such as SOD, CAT, and GSH-Px was most remarkably down-regulated. Also, the research done by Marakala *et al*. (2012) [84] points out the smaller amount of 8 OHdG and the higher activity of GPx was found in both cancer of the stomach and colon. However, the activity of SOD was more than control group in case of both cancers. Besides that, the increased superoxide dismutase (SOD) activity was positively correlated with the concentration of cancer antigen 15 3 (CA 15 3). This is a common marker that presents predictive values for the group of gastric cancer patients' prognosis. The DNA damage due to ROS is regarded as a carcinogenic factor. Therefore, the finding of lower 8-OHdG level and antioxidant activity suggests that patients with stomach and colon cancer have impaired pathway to repair the damage (Dincer *et al.*, 2007) [32].

Since the average level of 8 OHdG has been measured in three cohorts of persons suffering from colorectal cancer, here are the adenoma, early-stage cancer, and advanced-stage cancer. It was noted that 8 OHdG level was significantly higher in adenoma and early-stage cancer which suggests that this marker is a possible risk factor for colorectal adenoma and early cancer. Researching advanced cancer patients did not show the increased content of 8 OHdG; this might be because such patients have not fully met their caloric intake need or had nutritional problems at this stage of the disease (Sato *et al.*, 2010) [111].

A mismatch in redox was seen in the patients suffering from head and neck cancer. The enhancement of ROS and 8-OHdG levels, as well as the decreased TAC and GSH level, proves that their involvement in the development of HNC/ throat cancer cannot be underestimated (Khandelwal *et al*., 2012) [68].

The purpose of the study was to evaluate the usefulness of 8 OHdG as a biomarker for oxidative stress in cancer of the

oesophagus. The 8 OHdG concentration in tumorous areas was considerably greater than in normal epithelial tissue (Kubo *et al.*, 2013) [76].

8-Hydroxy-2-Deoxyguanosine in Other Diseases

Alongside the 3 major diseases of the cancer, neurodegenerative and cardiovascular type, the 8-OHdG is also linked to the diabetes mellitus, the inflammatory and the autoimmune diseases. In their paper, Shibutani and group (2010) reported that 8-OHdG levels in blood of patients with diabetes were markedly higher than those without the disease. Moreover they were difficult also performed immunohistochemistry to mark 8-OHdG in their kidney biopsies aspirations (Graille *et al*., 2020; Urbaniak *et al*., 2020) [48, 49].

The expression of 8-OHdG in the glomerulus of diabetic patients turned out to be much higher than in non-diabetic individuals. Moreover, the depth of the 8-OHdG staining was quite linearly related to the clinical data of the patients. The obtained data suggest that the measured 8-OHdG may play a useful role in evaluating the severity and progress of diabetes mellitus as well as its complications, among which diabetic nephropathy is probably the most recent one. Furthermore, 8-OHdG has also been linked to the inflammatory conditions including Crohn's disease.

In his studies of Bizzaro, it was observed that 8-OHdG blood plasma levels in Crohn's disease patients were significantly higher compared with those of rheumatoid arthritis patients and ones with no such health problem (Krzystek-Korpacka *et al*., 2020) [75]. The subject of the study are the oxidative DNA damage caused by the precarious oxygen species, which are suspected of the disease expansion. Similarly, they implied that the 8-OHdG levels determination might be a good tool for assessing the extent of inflammation this persistent disorder may have on a patient`s health. Additionally, 8-OHdG has demonstrated potential as an autoantigen in two significant systemic autoimmune diseases: lupus erythematosus of the systemic lupus (SLE) and the systemic sclerosis (SSc).

According to Luo *et al*. (2008) research it was suggested that serum from patients having lupus or scleroderma could differently bind to the 8-OHdG complex. Despair of antigen-antibody complexes ensured that the Ku 86, Ku 70, and PARP-1 proteins other than 8-OHdG were also manipulated. However, it may also trigger an immunological reaction because of which some of the identical autoantibodies can originate among those patients affected by this condition. Furthermore, this clears our perceptions concerning the route carrying oxidative DNA damage in autoimmune problems, and opens doors for additional intervention or treatment measures

Conclusion

8-OHdG has now become very useful by showing its multiple roles as a diagnostic marker of oxidative DNA damage that is associated with many ailments including neurodegenerative disorders, cancers, diabetes as well as inflammatory processes or periodontal diseases. Oxidative stress biomarkers like 8-hydroxy-2′-deoxyguanosine [(8-OHdG)] which is produced when DNA gets damaged by reactive oxygen and nitrogen species. 8-OHdG is the biomarker that attaches humans aging and a range of diseases, e.g., cancer, diabetes, and hypertension.

While the tests collectively demonstrate how the oxidative stress, biomarkers, and complications of diabetes are likely to be related, they offer a peek into future possible diagnostic and treatment options. When the blood glucose is in a state of high level in T2DM, the result is oxidative stress, and as the ROS gets produced, it causes cellular disruption. It is this oxidative damage which, occurring in the vast majority of tissues, is regarded as diabetes complication’s cause.

We are able to state that in the meantime oxidative DNA damage was rather a common thing in schizophrenic and bipolar subjects but in depressive disorder it did not show any significant effect. An especially great coincidence of deoxyguanosine and mental illness implied the prospect of using this biosignal 8-OHdG or 8-oxodG as biomarker in measurements of oxidation of DNA and oxidative stress.

Furthermore, there was a diminished relationship between level of alcohol intake and the oxidative DNA damage, where 8-oxodGuo was used as a marker of oxidative DNA damage in lymphocytes. Amazingly, the low-level intake in alcoholics was associated with alleviation of oxidative DNA damage independently of beverage classified in either the wine "type" or "others".

Also on the basis of the studies mentioned in this review, it would appear that 8-OHdG levels in DNA from leukocytes should not be regarded as a sensitive marker of exposure to tobacco smoking.

Assessment of oxidative stress and augmentation of the antioxidant defense system may be important for the treatment and prevention of carcinogenesis. In general, levels of antioxidative enzymes are mostly lower in cancer patients, while 8-OHdG and MDA are higher.

References

1. Abusoglu S, Celik HT, Tutkun E, Yilmaz H, Serdar MA, Bal CD, *et al*. 8-hydroxydeoxyguanosine as a useful marker for determining the severity of trichloroethylene exposure. Arch Environ Occup Health. 2014;69:180-186. Available from: HTML.com
2. Emam AN, Girgis E, Khalil WKB, Mohamed MB. Toxicity of Plasmonic Nanomaterials and Their Hybrid Nanocomposites. Adv Mol Toxicol. 2014;173-202. Available from: Sciencedirect.com
3. Ajileye AB, Akinbo FO. Oxidative DNA damage estimated by urinary 8-Hydroxy-2'–Deoxyguanosine (8-OHdG) and 8-Oxoguanine DNA Glycosylase (OGG1) in cigarette and non-cigarette. J Cell Biotechnol. Available from: HTML
4. Al-Taie A, Sancar M, Izzettin FV. 8-Hydroxydeoxyguanosine: A valuable predictor of oxidative DNA damage in cancer and diabetes mellitus. Cancer; c2021. Available from: HTML
5. An AR, Kim KM, Park HS, Jang KY, Moon WS, Kang MJ, *et al*. Association between Expression of 8-OHdG and Cigarette Smoking in Non-small Cell Lung Cancer. J Pathol Transl Med. 2019;53(4):217-224. Available from: PubMed.com
6. Archer SL, Huang J, Henry T, Peterson D, Weir EK. A redox-based O_2 sensor in rat pulmonary vasculature. Circ Res. 1993;73:1100-12. Available from: Google Scholar
7. Atef S, Abd El-Alim BA, Galal REE, Rashed LA, Hassan MM. Diagnostic Implications Of Urine 8-Hydroxy-2-Deoxyguanosine (8-OHdG) As A Sensitive

Biomarker For Early Prediction Of Diabetic Kidney Disease Among Adolescents With Type 1 Diabetes Mellitus. J Pharm Negative Results. 2023;185-195. Available from: pnrjournal.com
8. Barrera G. Oxidative Stress and Lipid Peroxidation Products in Cancer Progression and Therapy. ISRN Oncol. 2012;2012:1-21. Available from: Hindawi.com
9. Bianchini F. Inverse correlation between alcohol consumption and lymphocyte levels of 8-hydroxydeoxyguanosine in humans. Carcinogenesis. 2001;22(6):885-890. Available from: HTML
10. Bláhová L, Janoš T, Mustieles V, Rodríguez-Carrillo A, Fernández MF, Bláha L. Rapid extraction and analysis of oxidative stress and DNA damage biomarker 8-hydroxy-2′-deoxyguanosine (8-OHdG) in urine: Application to a study with pregnant women. Int J Hyg Environ Health. 2023;250:114175. Available from: Sciencedirect.com
11. Bondy SC. Ethanol toxicity and oxidative stress. Toxicol Lett. 1992;63:231-41.
12. Brea D, Roquer J, Serena J, Segura T, Castillo J. Oxidative stress markers are associated to vascular recurrence in non-cardioembolic stroke patients non-treated with statins. BMC Neurol. 2012;12:65. Available from: Google Scholar
13. Brown NC, Andreazza AC, Young LT. An updated meta-analysis of oxidative stress markers in bipolar disorder. Psychiatry Res. 2014;218:61-68.
14. Brown TA, Lee JW, Holian A, Porter V, Fredriksen H, Kim M, *et al*. Alterations in DNA Methylation Corresponding with Lung Inflammation and as a Biomarker for Disease Development after MWCNT Exposure. Nanotoxicology. 2016;10(4):453-461. Available from: HTML.com
15. Cai L, Kang YJ. Oxidative Stress and Diabetic Cardiomyopathy: A Brief Review. Cardiovasc Toxicol. 2001;1:181-193. Available from: Google Scholar
16. Canakçi CF, Canakçi V, Tatar A, Eltas A, Sezer U, Çiçek Y, *et al*. Increased Salivary Level of 8-Hydroxydeoxyguanosine Is a Marker of Premature Oxidative Mitochondrial DNA Damage in Gingival Tissue of Patients with Periodontitis. Arch Immunol Ther Exp (Warsz). 2009;57:205-211. Available from: Google Scholar
17. Çanakçi CF, Çanakçi V, Tatar A, Eltas A, Sezer U, Çiçek Y, *et al*. Increased salivary level of 8-hydroxydeoxyguanosine is a marker of premature oxidative mitochondrial DNA damage in gingival tissue of patients with periodontitis. Arch Immunol Ther Exp (Warsz). 2009;57(3):205-211. Available from: Google Scholar
18. Canakci CF, Cicek Y, Canakci V. Reactive Oxygen Species and Human Inflammatory Periodontal Diseases. Biochem (Mosc). 2005;70(6):619-628. Available from: Google Scholar
19. Çelik HEA, Tuna G, Ceylan D, Küçükgöncü S. A comparative meta-analysis of peripheral 8-hydroxy-2′-deoxyguanosine (8-OHdG) or 8-oxo-7, 8-dihydro-2′-deoxyguanosine (8-oxo-dG) levels across mood episodes in bipolar disorder. Psychoneuroendocrinology. 2023;151:106078. Available from: HTML
20. Chang D, Wang F, Zhao YS, Pan HZ. Evaluation of Oxidative Stress in Colorectal Cancer Patients. Biomed Environ Sci. 2008;21(4):286-289. Available from: PubMed.com
21. Chao MR, Evans MD, Hu CW, Ji Y, Møller P, Rossner P, *et al*. Biomarkers of nucleic acid oxidation–A summary state-of-the-art. Redox Biol. 2021;42:101872. Available from: Sciencedirect.com
22. Chapple ILC, Matthews JB. The Role of Reactive Oxygen and Antioxidant Species in Periodontal Tissue Destruction. Periodontol 2000. 2007;43:160-232. Available from: Google Scholar
23. Chen PY, Chen CW, Su YJ, Chang WH, Kao WF, Yang CC, *et al*. Associations between levels of urinary oxidative stress of 8-OHdG and risk of atopic diseases in children. Int J Environ Res Public Health. 2020;17(21):8207. Available from: mdpi.com
24. Christensen MR, Poulsen HE, Henriksen T, Weimann A, Ellervik C, Lynnerup N, *et al*. Elevated levels of 8-oxoGuo and 8-oxodG in individuals with severe mental illness - An autopsy-based study. Free Radic Biol Med. 2018;126:372-378.
25. Cojocaru KA, Luchian I, Goriuc A, Antoci LM, Ciobanu CG, Popescu R, *et al*. Mitochondrial Dysfunction, Oxidative Stress, and Therapeutic Strategies in Diabetes, Obesity, and Cardiovascular Disease. Antioxidants (Basel). 2023;12:658. Available from: Google Scholar
26. Cooke MS, Lunec J, Evans MD. Progress in the analysis of urinary oxidative DNA damage. Free Radic Biol Med. 2002;33:1601–1614.
27. Dai L, Watanabe M, Qureshi AR, Mukai H, Machowska A, Heimbürger O, *et al*. Serum 8-hydroxydeoxyguanosine, a marker of oxidative DNA damage, is associated with mortality independent of inflammation in chronic kidney disease. Eur J Intern Med. 2019;68:60–65.
28. David SS, O'Shea VL, Kundu S. Base-excision repair of oxidative DNA damage. Nature. 2007;447:941–50.
29. Di Minno A, Turnu L, Porro B, Squellerio I, Cavalca V, Tremoli E, *et al*. 8-hydroxy-2-deoxyguanosine levels and cardiovascular disease: a systematic review and meta-analysis of the literature. Antioxid Redox Signal. 2016;24:548–555.
30. Tugasworo D, Prasetyo A, Kurnianto A, *et al*. Malondialdehyde (MDA) and 8-hydroxy-2′-deoxyguanosine (8-OHdG) in ischemic stroke: A systematic review. Egypt J Neurol Psychiatry Neurosurg. 2023;59(1):87.
31. Turek IA, Wozniak LA, Cypryk K, Wojcik M. Hyperglycaemia-induced oxidative stress in gestational diabetes mellitus (GDM). Diabetol Prakt. 2015;4:189–198. Google Scholar.
32. Dincer Y, Himmetoglu S, Akcay T, Ey E, Gunes KN, Tortum O. Prognostic significances of oxidative DNA damage evaluated by 8-hydroxy-deoxyguanosine and antioxidant enzymes in patients undergoing resection of gastric and colon carcinoma. Clin Chem Lab Med. 2007;54(2):131–136.
33. Ding XW, Robinson M, Li R, Aldhowayan H, Geetha T, Babu JR. Mitochondrial dysfunction and beneficial effects of mitochondria-targeted small peptide SS-31 in diabetes mellitus and Alzheimer's disease. Pharmacol Res. 2021;171:105783.
34. Djurisic AB, Leung YH, Ng AMC, Xu XY, Lee PKH, Degger N, *et al*. Toxicity of metal oxide nanoparticles:

mechanisms, characterization, and avoiding experimental artefacts. Small. 2015;11(1):26–44.
35. Du H, Zhu X, Fan C, Xu S, Wang Y, Zhou Y. Oxidative damage and OGG1 expression induced by a combined effect of titanium dioxide nanoparticles and lead acetate in human hepatocytes. Environ Toxicol. 2012;27(10):590-597.
36. Elsaesser A, Howard CV. Toxicology of nanoparticles. Adv Drug Deliv Rev. 2012;64(2):129-137.
37. Endah D, Budiawan B, Dani IC. Confirmation DNA damage through *in vitro* study of formation DNA adduct 8-OHdG as biomarker caused by acrylamide exposure. AIP Conf Proc; c2023.
38. Evans MD, Dizdaroglu M, Cooke MS. Oxidative DNA damage and disease: Induction, repair and significance. Mutat Res. 2004;567:1-61.
39. Fan H, Tian H, Jin F, Zhang X, Su S, Liu Y, *et al*. CypD induced ROS output promotes intracranial aneurysm formation and rupture by 8-OHdG/NLRP3/MMP9 pathway. Redox Biol. 2023;67:102887.
40. Ferlay J, Soerjomataram I, Ervik M, *et al*. Cancer incidence and mortality worldwide: IARC CancerBase No. 11. Lyon: International Agency for Research on Cancer; c2014.
41. Floyd RA. Role of oxygen free radicals in carcinogenesis and brain ischemia. FASEB J. 1990;4:2587-97.
42. Fu PP, Xia Q, Hwang HM, Ray PC, Yu H. Mechanisms of nanotoxicity: Generation of reactive oxygen species. J Food Drug Anal. 2014;22(1):64-75.
43. Gholinezhad M, Aliarab A, Abbaszadeh-Goudarzi G, Yousefnia-Pasha Y, Samadaian N, Rasolpour-Roshan K, *et al*. Nitric oxide, 8-hydroxydeoxyguanosine, and total antioxidant capacity in human seminal plasma of infertile men and their relationship with sperm parameters. Clin Exp Reprod Med. 2020;47(1):54.
44. Gibbons DL, Byers LA, Kurie JM. Smoking, p^{53} mutation, and lung cancer. Mol Cancer Res. 2014;12:3-13.
45. Gmitterová K, Heinemann U, Gawinecka J, Varges D, Ciesielczyk B, Valkovic P, *et al*. 8-OHdG in cerebrospinal fluid as a marker of oxidative stress in various neurodegenerative diseases. Neurodegener Dis. 2009;6:263-269.
46. Goh XX, Tang PY, Tee SF. 8-hydroxy-2'-deoxyguanosine and reactive oxygen species as biomarkers of oxidative stress in mental illnesses: A meta-analysis. Psychiatry Investig. 2021;18(1):54-62.
47. Goriuc A, Cojocaru KA, Luchian I, Ursu RG, Butnaru O, Foia L. Using 8-hydroxy-2′-deoxyguanosine (8-OHdG) as a reliable biomarker for assessing periodontal disease associated with diabetes. Int. J Mol Sci. 2024;25(3):1425.
48. Graille M, Wild P, Sauvain JJ, Hemmendinger M, Guseva Canu I, Hopf NB. Urinary 8-OHdG as a biomarker for oxidative stress: a systematic literature review and meta-analysis. Int. J Mol Sci. 2020;21(11):3743.
49. Urbaniak SK, Boguszewska K, Szewczuk M, Kaźmierczak-Barańska J, Karwowski BT. 8-Oxo-7, 8-dihydro-2′-deoxyguanosine (8-oxodG) and 8-hydroxy-2′-deoxyguanosine (8-OHdG) as a potential biomarker for gestational diabetes mellitus (GDM) development. Molecules. 2020;25(1):202.
50. Uysal M, Ozdemirler G, Kutalp G, Oz H. Mitochondrial and microsomal lipid peroxidation in rat liver after acute acetaldehyde and ethanol intoxication. J Appl Toxicol. 1989;9:155-8.
51. Guina T, Biasi F, Calfapietra S, Nano M, Poli G. Inflammatory and redox reactions in colorectal carcinogenesis. Ann N Y Acad Sci. 2015;1340(1):95-103. Available from: PubMed.
52. Guo C, Li X, Wang R, Yu J, Ye M, Mao L, *et al*. Association between oxidative DNA damage and risk of colorectal cancer: Sensitive determination of urinary 8-hydroxy-2′-deoxyguanosine by UPLC-MS/MS analysis. Sci Rep. 2016;6:32581. Available from: Google Scholar.
53. Hagen BF, Bjorneboe A, Bjorneboe GE, Drevon CA. Effect of chronic ethanol consumption on the content of alpha-tocopherol in subcellular fractions of rat liver. Alcohol Clin Exp Res. 1989;13:246-51.
54. Hainsworth DP, Gangula A, Ghoshdastidar S, Kannan R, Upendran A. Diabetic retinopathy screening using a gold nanoparticle–based paper strip assay for the at-home detection of the urinary biomarker 8-hydroxy-2′-deoxyguanosine. Am J Ophthalmol. 2020;213:306-319. Available from: ajo.com.
55. Halczuk K, Boguszewska K, Urbaniak SK, Szewczuk M, Karwowski BT. 8-oxo-7, 8-dihydro-2′-deoxyguanosine (8-oxodG) and 8-hydroxy-2′-deoxyguanosine (8-OHdG) as a cause of autoimmune thyroid diseases (AITD) during pregnancy? Yale J Biol Med. 2020, 93(4). Available from: lodz.pl.
56. Halczuk KM, Boguszewska K, Urbaniak SK, Szewczuk M, Karwowski BT. Focus: Sex & Reproduction: 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxodG) and 8-hydroxy-2′-deoxyguanosine (8-OHdG) as a cause of autoimmune thyroid diseases (AITD) during pregnancy? Yale J Biol Med. 2020;93(4):501. Available from: NIH.
57. Halliwell B. Oxidative stress and neurodegeneration: where are we now? J Neurochem. 2006;97:1634-58. Available from: PubMed.
58. Halliwell B, Gutteridge JMC. Free Radicals in Biology and Medicine. Oxford: Oxford University Press; c2015. ISBN: 978-0-19-180213-3. Available from: Google Scholar.
59. Herzog E, Byrne HJ, Davoren M, Casey A, Duschl A, Oostingh GJ. Dispersion medium modulates oxidative stress response of human lung epithelial cells upon exposure to carbon nanomaterial samples. Toxicol Appl Pharmacol. 2009;236(3):276-81. Available from: ScienceDirect.
60. Huo L, Li CW, Huang TH, Lam YC, Xia W, Tu C, *et al*. Activation of Keap1/Nrf2 signaling pathway by nuclear epidermal growth factor receptor in cancer cells. PubMed. 2014;6(6):649-63. Available from: NIH.
61. Ivanova D, Bakalova R, Lazarova D, Gadjeva V, Zhelev Z. The impact of reactive oxygen species on anticancer therapeutic strategies. PubMed. 2014;22(6):899-908.
62. Izzotti A, Cartiglia C, De Flora S, Saccà SC. Methodology for evaluating oxidative DNA damage and metabolic genotypes in human trabecular

meshwork. Toxicol Mech Methods. 2003;13(3):161-8. Available from: Google Scholar.
63. Korbecki J, Baranowska-Bosiacka I, Gutowska I, Chlubek D. The effect of reactive oxygen species on the synthesis of prostanoids from arachidonic acid. PubMed. 2013;64(4):409-21. Available from: PubMed.
64. James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, *et al*. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-1858. Available from: PubMed.
65. Jelic M, Mandic A, Maricic S, Srdjenovic B. Oxidative stress and its role in cancer. J Cancer Res Ther. 2021;17:22-8.
66. Jelic MD, Mandic AD, Maricic SM, Srdjenovic BU. Oxidative stress and its role in cancer. J Cancer Res Ther. 2021;17(1):22-8. Available from: LWW.
67. Jena NR, Mishra PC. Formation of ring-opened and rearranged products of guanine: Mechanisms and biological significance. Free Radic Biol Med. 2012;53:81-94. Available from: Google Scholar.
68. Khandelwal S, Kumar A, Pant M, Singh H. Determinants of oxidative stress and DNA damage (8-OhdG) in squamous cell carcinoma of head and neck. Indian J Cancer. 2012;49(3):309. Available from: PubMed.
69. Khatri M, Bello D, Gaines P, Martin J, Pal AK, Gore R, *et al*. Nanoparticles from photocopiers induce oxidative stress and upper respiratory tract inflammation in healthy volunteers. Nanotoxicology. 2013;7(5):1014-27. Available from: HTML.
70. Klaunig JE, Kamendulis LM, Hocevar BA. Oxidative stress and oxidative damage in carcinogenesis. Toxicol Pathol. 2009;38(1):96-109. Available from: PubMed.
71. Koch OR, Galeotti T, Bartoli GM, Boveris A. Alcohol-induced oxidative stress in rat liver. Xenobiotica. 1991;21:1077-84.
72. Kondkar AA, Azad TA, Sultan T, Osman EA, Almobarak FA, Al-Obeidan SA. Elevated plasma level of 8-hydroxy-2′-deoxyguanosine is associated with primary open-angle glaucoma. J Ophthalmol. 2020;2020:1-8. Available from: Hindawi.
73. Korkmaz KS, Butuner BD, Roggenbuck D. Detection of 8-OHdG as a diagnostic biomarker. J Lab Precis Med. 2018;3:95. Available from: Google Scholar.
74. Kowaltowski AJ, de Souza-Pinto NC, Castilho RF, Vercesi AE. Mitochondria and reactive oxygen species. Free Radic Biol Med. 2009;47:333-43. Available from: Google Scholar.
75. Krzystek-Korpacka M, Kempiński R, Bromke MA, Neubauer K. Oxidative stress markers in inflammatory bowel diseases: systematic review. Diagnostics. 2020;10(8):601. Available from: MDPI.
76. Kubo N, Morita M, Nakashima Y, Kitao H, Egashira A, Saeki H, *et al*. Oxidative DNA damage in human esophageal cancer: clinicopathological analysis of 8-hydroxydeoxyguanosine and its repair enzyme. Dis Esophagus. 2013;27(3):285-93. Available from: PubMed
77. Lee JY, Kim M, Oh SB, Kim HY, Kim C, Kim TY, *et al*. Superoxide dismutase 3 prevents early stage diabetic retinopathy in streptozotocin-induced diabetic rat model. PLoS One. 2022;17(1):e0262396. Available from: PLoS
78. Leguisamo NM, Lehnen AM, Machado UF, Okamoto MM, Markoski MM, Pinto GH, *et al*. GLUT4 content decreases along with insulin resistance and high levels of inflammatory markers in rats with metabolic syndrome. Cardiovasc Diabetol. 2012;11:100. Available from: Google Scholar
79. Leinonen J, Lehtimäki T, Toyokuni S, Okada K, Tanaka T, Hiai H, *et al*. New biomarker evidence of oxidative DNA damage in patients with non-insulin-dependent diabetes mellitus. FEBS Lett. 1997;417:150–2. Available from: Google Scholar
80. Liu T, Zhong S, Liao X, Chen J, He T, Lai S, *et al*. A meta-analysis of oxidative stress markers in depression. PLoS One. 2015;10:e0138904.
81. Long JD, Matson WR, Juhl AR, Leavitt BR, Paulsen JS; The PREDICT-HD Investigators and Coordinators of the Huntington Study Group. 8OHdG as a marker for Huntington disease progression. Neurobiol Dis. 2012;46:625. Available from: Google Scholar
82. Ma Y, Meng X, Sowanou A, Wang J, Li H, Li A, *et al*. Effect of fluoride on the expression of 8-hydroxy-2′-deoxyguanosine in the blood, kidney, liver, and brain of rats. Biol Trace Elem Res. 2023;201(6):2904-16. Available from: HTML
83. Ma Y, Zhang L, Rong S, Qu H, Zhang Y, Chang D, *et al*. Relation between gastric cancer and protein oxidation, DNA damage, and lipid peroxidation. Oxid Med Cell Longev. 2013;2013:1–6. Available from: Hindawi
84. Marakala V, Malathi M, Shivashankara AR. Lipid peroxidation and antioxidant vitamin status in oral cavity and oropharyngeal cancer patients. Asian Pac J Cancer Prev. 2012;13(11):5763–5. Available from: PubMed
85. Andreassi MG, Botto N, Cocci F, Battaglia D, Antonioli E, Masetti S, *et al*. Methylenetetrahydrofolate reductase gene C677T polymorphism, homocysteine, vitamin B12, and DNA damage in coronary artery disease. Clin Chem. 2003;49(6):171–7. Available from: Google Scholar
86. Matsuzawa A, Ichijo H. Redox control of cell fate by MAP kinase: physiological roles of ASK1-MAP kinase pathway in stress signaling. Biochim Biophys Acta. 2008;1780(11):1325–36. Available from: PubMed
87. McCord JM. Oxygen-derived radicals: A link between reperfusion injury and inflammation. Fed Proc. 1987;46:2402–6. Available from: Google Scholar
88. Metta S, Satyanarayana U, Kumar MA, Dharwadkar AA. Impact of smoking on plasma antioxidant defenses and urinary 8-hydroxy-2-deoxyguanosine in ischemic heart diseases. Natl J Physiol Pharm Pharmacol. 2021;11(2):1-1. Available from: HTML
89. Murata M, Thanan R, Ma N, Kawanishi S. Role of nitrative and oxidative DNA damage in inflammation-related carcinogenesis. J Biomed Biotechnol. 2012;2012:1-11. Available from: PubMed
90. Mustafa MF, Fakurazi S, Abdullah MA, Maniam S. Pathogenic mitochondria DNA mutations: Current detection tools and interventions. Genes. 2020;11:192. Available from: Google Scholar
91. Muthuraj M, Janakiram S, Chithresan K. Is 8-OHdG a reliable marker in periodontitis-the sixth complication

of diabetes mellitus? Clin Dent. 2021;15:12. Available from: Google Scholar
92. Nandakumar A, Nataraj P, James A, Krishnan R, Mahesh KM. Estimation of salivary 8-hydroxydeoxyguanosine (8-OHdG) as a potential biomarker in assessing progression towards malignancy: A case-control study. Asian Pac J Cancer Prev. 2020;21(8):2325. Available from: PubMed
93. Negishi H, Ikeda K, Kuga S, Noguchi T, Kanda T, Njelekela M, *et al*. The relation of oxidative DNA damage to hypertension and other cardiovascular risk factors in Tanzania. J Hypertens. 2001;19:529-33. Available from: Google Scholar
94. Neofytou E, Tzortzaki EG, Chatziantoniou A, Siafakas NM. DNA damage due to oxidative stress in chronic obstructive pulmonary disease (COPD). Int J Mol Sci. 2012;13:16853-64. Available from: MDPI
95. Ng F, Berk M, Dean O, Bush AI. Oxidative stress in psychiatric disorders: evidence base and therapeutic implications. Int J Neuropsychopharmacol. 2008;11:851–76. Available from: PubMed
96. Nita M, Grzybowski A. The role of the reactive oxygen species and oxidative stress in the pathomechanism of the age-related ocular diseases and other pathologies of the anterior and posterior eye segments in adults. Oxid Med Cell Longev. 2016;2016:1-23. Available from: Google Scholar
97. Nordmann R. Oxidative stress from alcohol in the brain. Alcohol Alcohol Suppl. 1987;1:75-82.
98. Shekaftik SO, Nasirzadeh N. 8-Hydroxy-2′-deoxyguanosine (8-OHdG) as a biomarker of oxidative DNA damage induced by occupational exposure to nanomaterials: A systematic review. Nanotoxicology. 2021;15(6):850–64. Available from: HTML
99. Peng P, He M, Fang W, Lai M, Xiao F, He W, *et al*. Plasma 8-OHdG act as a biomarker for steroid-induced osteonecrosis of the femoral head. BMC Musculoskelet Disord. 2023;24(1):808. Available from: Springer
100. Qing X, Shi D, Lv X, Wang B, Chen S, Shao Z. Prognostic significance of 8-hydroxy-2′-deoxyguanosine in solid tumors: A meta-analysis. BMC Cancer. 2019;19:997. Available from: Google Scholar
101. Rai B, Kharb S, Jain R, Anand SC. Biomarkers of Periodontitis in Oral Fluids. J Oral Sci. 2008;50:53-6. Available from: PubMed.
102. Rajasinghe H, Jayatilleke E, Shaw S. DNA cleavage during ethanol metabolism: role of superoxide radicals and catalytic iron. Life Sci. 1990;47:807-14.
103. Rehm J, Shield KD. Global Burden of Disease and the Impact of Mental and Addictive Disorders. Curr Psychiatry Rep. 2019, 21(2). Available from: PubMed.com.
104. Rizkita AD, Handayani S, Dani IC. *In vivo* study of 8-OHdG as a biomarker DNA damage by combining the exposure of nonyl phenol and copper using ELISA technique. In: IOP Conference Series: Materials Science and Engineering. 2020;902(1):012054. IOP Publishing. Available from: iop.org.
105. Rosello-Lleti E, Burgos FG de, Morillas P, Cortes R, Martinez-Dolz L, Almenar L, *et al*. Impact of Cardiovascular Risk Factors and Inflammatory Status on Urinary 8-OHdG in Essential Hypertension. Am J Hypertens. 2012;25(2):236-42. Available from: PubMed.
106. Ross R. Atherosclerosis - An Inflammatory Disease. N Engl J Med. 1999;340(2):115-26. Available from: Google Scholar.
107. Rouach H, Park MK, Orfanelli MT, Janvier B, Nordmann R. Ethanol-induced oxidative stress in the rat cerebellum. Alcohol Alcohol Suppl. 1987;1:207–11.
108. Saccà SC. Oxidative DNA Damage in the Human Trabecular Meshwork. Arch Ophthalmol. 2005;123(4):458. Available from: Google Scholar.
109. Sakano N, Wang DH, Takahashi N, Wang B, Sauriasari R, Kanbara S, *et al*. Oxidative stress biomarkers and lifestyles in Japanese healthy people. J Clin Biochem Nutr. 2009;44:185–95. Available from: HTML.com.
110. Salim S. Oxidative stress and psychological disorders. Curr Neuropharmacol. 2014;12:140–7.
111. Sato T, Takeda H, Otake S, Yokozawa J, Nishise S, Fujishima S, *et al*. Increased Plasma Levels of 8-Hydroxydeoxyguanosine Are Associated with Development of Colorectal Tumors. J Clin Biochem Nutr. 2010;47(1):59–63. Available from: PubMed.com.
112. Serdar M, Erdim Sertoglu M, Uyanik M, Tapan S, Akin KO, Bilgi C, *et al*. Comparison of 8-hydroxy-2′-deoxyguanosine (8-OHdG) levels using mass spectrometer and urine albumin creatinine ratio as a predictor of development of diabetic nephropathy. Free Radic Res. 2012;46(10):1291–5. Available from: PubMed.
113. Sharma A, Rajappa M, Saxena A, Sharma M. Antioxidant status in advanced cervical cancer patients undergoing neoadjuvant chemoradiation. Br J Biomed Sci. 2007;64(1):23–7.
114. Shigenaga MK, Gimeno CJ, Ames BN. Urinary 8-hydroxy-2'-deoxyguanosine as a biological marker of *in vivo* oxidative DNA damage. Proc Natl Acad Sci U S A. 1989;86(24):9697–701. Available from: PubMed.
115. Shukla S, Srivastava JK, Shankar E, Kanwal R, Nawab A, Sharma H, *et al*. Oxidative stress and antioxidant status in high-risk prostate cancer subjects. Diagnostics (Basel). 2020;10(3):126.mdpi.com
116. Rai B, Kharb S, Jain R, Anand SC. Biomarkers of Periodontitis in Oral Fluids. J Oral Sci. 2008;50:53–56. PubMed.
117. Rajasinghe H, Jayatilleke E, Shaw S. DNA cleavage during ethanol metabolism: role of superoxide radicals and catalytic iron. Life Sci. 1990;47:807–14.
118. Rehm J, Shield KD. Global Burden of Disease and the Impact of Mental and Addictive Disorders. Curr Psychiatry Rep. 2019, 21(2). PubMed.
119. Rizkita AD, Handayani S, Dani IC. *In vivo* study of 8-OHdG as a biomarker DNA damage by combining the exposure of nonyl phenol and copper using ELISA technique. In: IOP Conference Series: Materials Science and Engineering. IOP Publishing. 2020;902(1):012054.
120. Rosello-Lleti E, Burgos FG d, Morillas P, *et al*. Impact of Cardiovascular Risk Factors and Inflammatory Status on Urinary 8-OHdG in Essential Hypertension. Am J Hypertens. 2012;25(2):236-242. PubMed.
121. Ross R. Atherosclerosis - An Inflammatory Disease. N Engl J Med. 1999;340(2):115-126. Google Scholar.
122. Rouach H, Park MK, Orfanelli MT, Janvier B, Nordmann R. Ethanol-induced oxidative stress in the rat cerebellum. Alcohol Alcohol Suppl. 1987;(1):207-11.

123. Saccà SC. Oxidative DNA Damage in the Human Trabecular Meshwork. Arch Ophthalmol. 2005;123(4):458. Google Scholar.
124. Sakano N, Wang DH, Takahashi N, *et al*. Oxidative stress biomarkers and lifestyles in japanese healthy people. J Clin Biochem Nutr. 2009;44:185–195. HTML.
125. Salim S. Oxidative stress and psychological disorders. Curr Neuropharmacol. 2014;12:140-147.
126. Sato T, Takeda H, Otake S, *et al*. Increased Plasma Levels of 8-Hydroxydeoxyguanosine Are Associated with Development of Colorectal Tumors. J Clin Biochem Nutr. 2010;47(1):59-63. PubMed.
127. Serdar M, Erdim Sertoglu, Metin Uyanik, *et al*. Comparison of 8-hydroxy-2′-deoxyguanosine (8-OHdG) levels using mass spectrometer and urine albumin creatinine ratio as a predictor of development of diabetic nephropathy. Free Radic Res. 2012;46(10):1291-1295. PubMed.
128. Sharma A, Rajappa M, Saxena A, Sharma M. Antioxidant status in advanced cervical cancer patients undergoing neoadjuvant chemoradiation. Br J Biomed Sci. 2007;64(1):23-27.
129. Shigenaga MK, Gimeno CJ, Ames BN. Urinary 8-hydroxy-2'-deoxyguanosine as a biological marker of *in vivo* oxidative DNA damage. Proc Natl Acad Sci. 1989;86(24):9697–9701. PubMed.
130. Shukla S, Srivastava JK, Shankar E, *et al*. Oxidative stress and antioxidant status in high-risk prostate cancer subjects. Diagnostics. 2020;10(3):126.
131. Sies H. Oxidative stress: From basic research to clinical application. Am J Med. 1991;91(3):S31–S38. Google Scholar.
132. Smaga I, Niedzielska E, Gawlik M, *et al*. Oxidative stress as an etiological factor and a potential treatment target of psychiatric disorders. Part 2. Depression, anxiety, schizophrenia and autism. Pharmacol Rep. 2015;67:569-580. PubMed.
133. Suzuki S, Hinokio Y, Komatu K, *et al*. Oxidative Damage to Mitochondrial DNA and Its Relationship to Diabetic Complications. Diabetes Res Clin Pract. 1999;45:161–168. Google Scholar.
134. Szendroedi J, Phielix E, Roden M. The Role of Mitochondria in Insulin Resistance and Type 2 Diabetes Mellitus. Nat Rev Endocrinol. 2011;8:92–103. Google Scholar.
135. Takane M, Sugano N, Ezawa T, Uchiyama T, Ito K. A Marker of Oxidative Stress in Saliva: Association with Periodontally-Involved Teeth of a Hopeless Prognosis. J Oral Sci. 2005;47:53–57. Google Scholar.
136. Thome J, Zhang J, Davids E, *et al*. Evidence for increased oxidative stress in alcohol-dependent patients provided by quantification of *in vivo* salicylate hydroxylation products. Alcohol Clin Exp Res. 1997;21:82-5.