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Salivary Oxidative Stress Biomarker among Domestic Painters Exposed to Volatile Organic Compounds

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Abstract

Domestic painters are frequently exposed to volatile organic compounds (VOCs) found in paints, thinners, and related materials, which are known to induce oxidative stress. Oxidative stress results from an imbalance between reactive oxygen species (ROS) production and the body's antioxidant defenses, potentially leading to various health issues. This study aims to evaluate the levels of oxidative stress in domestic painters exposed to VOCs by measuring specific biomarkers in saliva. The study involved a group of domestic painters and a control group with no significant exposure to VOCs. Saliva samples were collected from all participants. VOC exposure levels were assessed using workplace and personal air samplers. Salivary biomarkers, including malondialdehyde (MDA), 8-hydroxydeoxyguanosine (8-OHdG), total antioxidant capacity (TAC), superoxide dismutase (SOD), and glutathione peroxidase (GPx), were quantified using standardized assays. Health data were collected via questionnaires to assess respiratory symptoms, skin conditions, and overall health. Domestic painters exhibited significantly higher levels of MDA and 8-OHdG in their saliva compared to the control group, indicating increased lipid peroxidation and oxidative DNA damage. Alterations in TAC, SOD, and GPx levels were observed, reflecting a compensatory response to increased oxidative stress. A positive correlation was found between VOC exposure levels and oxidative stress biomarkers.

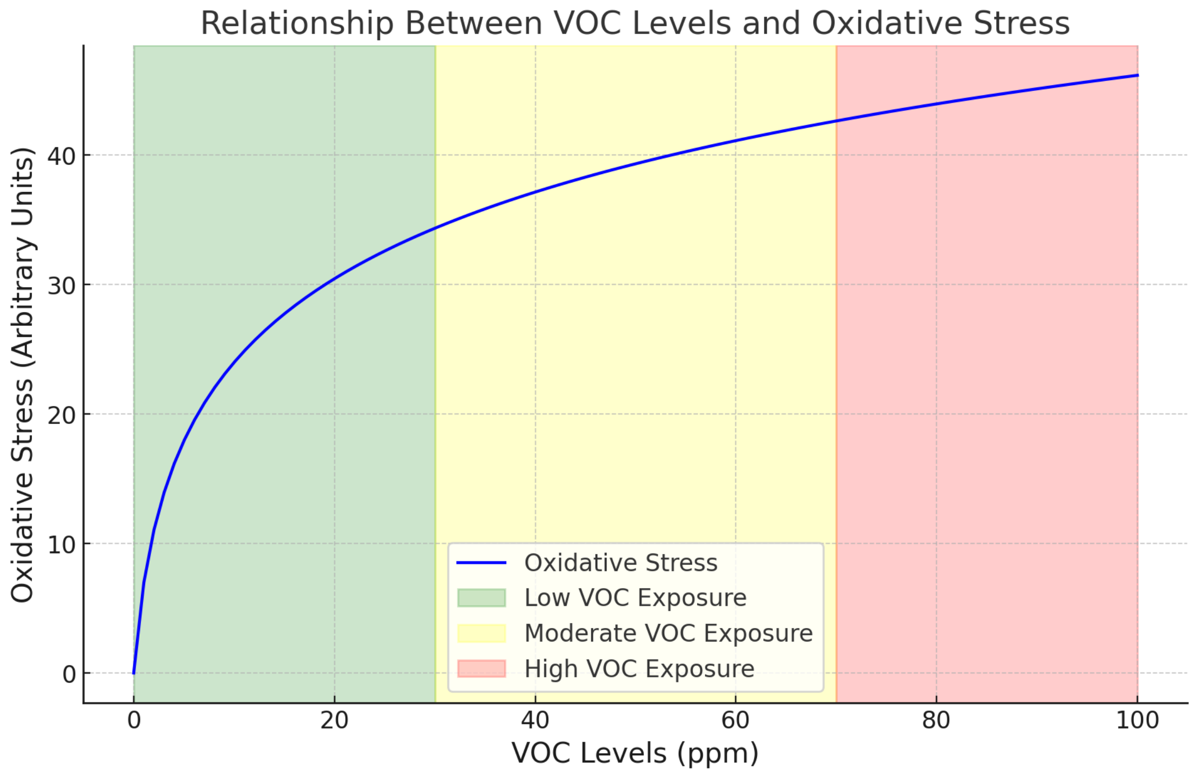
Keywords: Volatile organic compounds, oxidative stress, domestic painters, salivary biomarkers, malondialdehyde, 8-hydroxydeoxyguanosine, total antioxidant capacity, superoxide dismutase, glutathione peroxidase.

Literature Review:

Domestic painters are routinely exposed to volatile organic compounds (VOCs) in their work environment. VOCs are chemicals that easily evaporate at room temperature, found in paints, thinners, and other materials used in painting. Chronic exposure to VOCs has been linked to various health issues, including respiratory problems, skin irritations, and neurological effects. One significant consequence of VOC exposure is the induction of oxidative stress, a condition where there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to counteract their harmful effects. This review explores the existing literature on salivary oxidative stress biomarkers in domestic painters exposed to VOCs.

Oxidative Stress and VOCs

Oxidative stress is a well-documented consequence of exposure to environmental pollutants, including VOCs. VOCs such as benzene, toluene, xylene, and formaldehyde can penetrate biological membranes and generate ROS, leading to cellular damage. The biological impact of VOC exposure has been extensively studied, with findings indicating that prolonged exposure to these compounds leads to increased oxidative stress markers in various biological fluids and tissues.



Salivary Biomarkers for Oxidative Stress

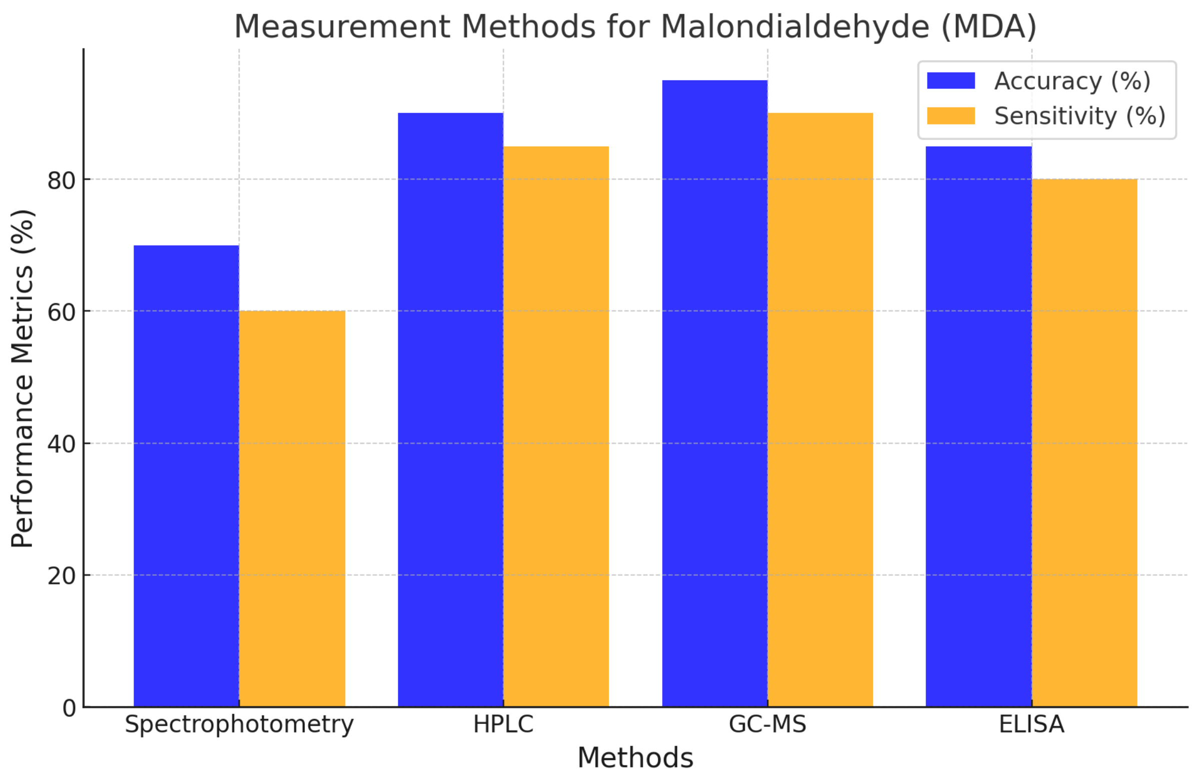
Saliva is increasingly recognized as a valuable biofluid for monitoring oxidative stress due to its non-invasive collection method and the presence of various biomarkers that reflect systemic oxidative stress. Key salivary biomarkers used to assess oxidative stress include:

Malondialdehyde (MDA)

Definition and Importance

Malondialdehyde (MDA) is a byproduct of lipid peroxidation, which occurs when reactive oxygen species (ROS) attack polyunsaturated fatty acids in cell membranes. MDA is one of the most commonly used biomarkers for oxidative stress and lipid peroxidation because its levels increase significantly in response to oxidative damage.

Measurement Methods
Several methods are used to measure MDA levels in biological samples, each with its own advantages and limitations:



Here's a bar chart comparing different methods for measuring Malondialdehyde (MDA) based on their accuracy and sensitivity:

Methods:

Spectrophotometry: Widely used but less sensitive.
HPLC (High-Performance Liquid Chromatography): High accuracy and sensitivity.
GC-MS (Gas Chromatography-Mass Spectrometry): Gold standard with the highest performance.
ELISA (Enzyme-Linked Immunosorbent Assay): Balanced performance and ease of use.

Thiobarbituric Acid Reactive Substances (TBARS) Assay: The Thiobarbituric Acid Reactive Substances (TBARS) assay is a widely used method for measuring lipid peroxidation, which is an indicator of oxidative stress and cell membrane damage. The assay quantifies malondialdehyde (MDA), a byproduct of polyunsaturated fatty acid peroxidation, which reacts with thiobarbituric acid (TBA) to form a colored complex. Here are the key points about the TBARS assay:

Principle: The assay is based on the reaction of MDA with TBA under acidic and high-temperature conditions. This reaction produces a pink chromogen with a peak absorbance at 532 nm, which can be measured spectrophotometrically.

Procedure: Sample Preparation: Biological samples (e.g., plasma, serum, tissue homogenates) are prepared and mixed with TBA reagent.

Incubation: The mixture is heated to induce the reaction between MDA and TBA.

Measurement: The absorbance of the resulting solution is measured at 532 nm using a spectrophotometer.

Quantification: The concentration of MDA in the sample is determined by comparing the absorbance to a standard curve prepared using known concentrations of MDA. Results are typically expressed as MDA equivalents (e.g., nmol MDA/mg protein or nmol MDA/mL).

Applications: The TBARS assay is commonly used in research to assess oxidative stress in various biological samples. It is used to evaluate the extent of lipid peroxidation in conditions such as cardiovascular diseases, neurodegenerative disorders, diabetes, and aging. The assay can also be used to test the efficacy of antioxidants and other protective agents.

Advantages: Simple and relatively inexpensive. Can be applied to a wide range of biological samples.

Limitations: The TBARS assay is not entirely specific for MDA; other compounds (e.g., aldehydes) can react with TBA, potentially leading to overestimation of lipid peroxidation. The assay conditions (e.g., acidity, heating) can artificially induce lipid peroxidation in some samples, which can affect the accuracy of the results.

Improvements and Variations: Modifications to the assay have been developed to improve specificity and sensitivity, such as using high-performance liquid chromatography (HPLC) to separate MDA-TBA adducts from other interfering substances. Alternative methods and assays, such as the F2-isoprostanes assay, are sometimes used alongside or instead of TBARS for more specific and accurate measurements of lipid peroxidation.

The TBARS assay remains a popular and useful method for assessing lipid peroxidation and oxidative stress, despite its limitations. It provides valuable insights into the oxidative status of biological systems and the potential impact of interventions aimed at reducing oxidative damage.

The TBARS assay is a widely used method for measuring lipid peroxidation by detecting malondialdehyde (MDA) and other thiobarbituric acid (TBA)-reactive substances. It is commonly used in food science, biochemistry, and medical research to assess oxidative stress in biological samples.

Principle of TBARS Assay

Lipid peroxidation leads to the formation of malondialdehyde (MDA) as a secondary product.

MDA reacts with thiobarbituric acid (TBA) under acidic and high-temperature conditions, forming a pink-colored complex.

The complex absorbs light at 532–535 nm, which can be quantified using a spectrophotometer or fluorometer.

Reagents Required

Thiobarbituric Acid (TBA) – Reacts with MDA to form a colored complex.

Trichloroacetic Acid (TCA) – Precipitates proteins and prevents further oxidation.

Hydrochloric Acid (HCl) or Phosphoric Acid – Provides an acidic environment.

Butylated Hydroxytoluene (BHT) – Prevents artificial oxidation during the assay.

Standard MDA Solution – Used for calibration and quantification.

Protocol for TBARS Assay

Sample Preparation: Biological samples (plasma, serum, tissue homogenates) are mixed with TCA and centrifuged to remove proteins.

Reaction with TBA: Supernatant is mixed with TBA reagent and incubated at 95–100°C for 15–60 minutes. This step allows the formation of the MDA-TBA complex.

Cooling and Measurement: After cooling, the absorbance is measured at 532 nm using a UV-Vis spectrophotometer. A standard curve with known MDA concentrations is used for quantification.

Applications of TBARS Assay

Biomedical Research – Evaluates oxidative stress in diseases like diabetes, cardiovascular disorders, and neurodegeneration.
Food Industry – Monitors lipid oxidation in food products to assess freshness and shelf life.
Pharmaceuticals – Tests antioxidant activity of drugs and natural compounds.
Environmental Toxicology – Measures oxidative damage due to pollutants and toxins.

High-Performance Liquid Chromatography (HPLC): A more specific method that separates MDA from other thiobarbituric acid reactive substances before detection. This method can be coupled with UV detection or mass spectrometry for enhanced specificity and sensitivity.

High-Performance Liquid Chromatography (HPLC) is a powerful analytical technique used to separate, identify, and quantify components in a mixture. It operates on the principle of liquid chromatography, where a sample mixture is dissolved in a solvent and passed through a column containing a stationary phase. Different components in the mixture interact differently with the stationary phase and the mobile phase (solvent), leading to separation based on their properties such as polarity, size, and affinity for the stationary phase.

HPLC is widely used in various fields such as pharmaceuticals, biochemistry, environmental science, food and beverage analysis, and more, due to its sensitivity, accuracy, and ability to handle complex mixtures. It can detect and quantify very small amounts of substances, making it indispensable in both research and industrial applications.

Gas Chromatography-Mass Spectrometry (GC-MS): Another highly specific method that can accurately measure MDA levels by detecting and quantifying the MDA derivative formed after a derivatization step.

Gas Chromatography-Mass Spectrometry (GC-MS) is a powerful analytical technique used to identify and quantify components in a mixture. It combines the principles of gas chromatography (GC), where the sample is vaporized and separated by passing through a chromatographic column, and mass spectrometry (MS), where the separated components are ionized and detected based on their mass-to-charge ratio.

Here's how GC-MS works:

Gas Chromatography (GC): The sample is injected into the GC system, where it is vaporized and carried through a long, narrow column by an inert gas (usually helium or nitrogen). The components in the sample interact with the stationary phase inside the column based on their volatility and affinity for the column material. This separation results in each component eluting from the column at different times.

Mass Spectrometry (MS): As each separated component exits the GC column, it enters the mass spectrometer. Here, the molecules are bombarded with electrons, causing them to fragment into smaller ions. These ions are then separated based on their mass-to-charge ratio (m/z) and detected by a detector.

Data Analysis: The detector generates a chromatogram, which shows peaks corresponding to the separated components based on retention time in GC and abundance in MS. The mass spectrum obtained for each peak provides a unique "fingerprint" that can be compared against a database for identification.

GC-MS is widely used in various fields such as environmental analysis, forensic science, pharmaceuticals, food safety, and more. It offers high sensitivity and specificity, allowing for the detection of trace amounts of substances even in complex mixtures. This makes it a versatile and indispensable tool in analytical chemistry and research.

Enzyme-Linked Immunosorbent Assay (ELISA): A sensitive method that uses antibodies specific to MDA to detect and quantify MDA levels in samples.

Enzyme-Linked Immunosorbent Assay (ELISA) is a highly sensitive immunological technique used to detect and quantify specific proteins, antibodies, peptides, hormones, and antigens in biological samples. It relies on the interaction between an antigen (or antibody) and its corresponding antibody (or antigen) immobilized on a solid support.

Here's how ELISA typically works:

Coating: The first step involves immobilizing the antigen or antibody of interest onto a solid surface, such as a microplate well. This creates a solid-phase support.

Blocking: To prevent nonspecific binding, the remaining surface sites on the solid phase are blocked using an inert protein (e.g., bovine serum albumin, casein).

Binding: The sample containing the antigen (or antibody) is added to the well. If the antigen is present in the sample, it binds specifically to the immobilized antibody (or antigen).

Detection: After washing to remove unbound substances, a detection antibody linked to an enzyme (such as horseradish peroxidase or alkaline phosphatase) is added. This secondary antibody binds specifically to the antigen-antibody complex formed in the previous step.

Signal Generation: A substrate specific to the enzyme is added. The enzyme catalyzes a reaction that produces a detectable signal (such as a color change or fluorescence) proportional to the amount of antigen bound.

Measurement: The intensity of the generated signal is measured using a spectrophotometer or other detection device. This measurement allows for the quantification of the antigen or antibody present in the original sample.

ELISA is widely used in medical diagnostics, research laboratories, and biotechnology industries due to its high specificity, sensitivity, and ability to analyze multiple samples simultaneously. It plays a crucial role in detecting diseases, monitoring biomarkers, and assessing immune responses in various biological samples.

The Enzyme-Linked Immunosorbent Assay (ELISA) is a highly sensitive and specific biochemical technique used to detect and quantify proteins, peptides, antibodies, and hormones in biological samples. It is widely used in medical diagnostics, research, and pharmaceutical industries.

Principle of ELISA

ELISA is based on antigen-antibody interactions. A specific antibody binds to the target antigen, and an enzyme-linked detection system produces a measurable colorimetric, fluorescent, or chemiluminescent signal.

Types of ELISA

Direct ELISA

Antigen is immobilized on the plate, and a labeled antibody directly binds to it.
Advantages: Simple and quick.
Disadvantages: Less sensitive, higher background noise.

Indirect ELISA

Antigen is immobilized, and a primary antibody binds to it, followed by a secondary enzyme-linked antibody.

Advantages: Increased sensitivity.
Disadvantages: More steps, potential for cross-reactivity.

Sandwich ELISA (Most Sensitive)

A capture antibody is coated on the plate, which binds to the antigen, followed by a detection antibody and an enzyme-linked secondary antibody.
Advantages: Highly specific and sensitive.
Disadvantages: Requires highly specific matched antibody pairs.

Competitive ELISA

Antigen in the sample competes with a labeled antigen for antibody binding.
Advantages: Used for small molecules (e.g., hormones, drugs).
Disadvantages: Complex optimization.

Key Components of ELISA

Component	Function
Microplate (96-well plate)	Surface for antigen or antibody binding
Coating Antibody or Antigen	Captures the target molecule
Blocking Buffer	Prevents nonspecific binding
Primary Antibody	Binds specifically to the target antigen
Secondary Antibody (enzyme-linked)	Provides signal amplification
Substrate (e.g., TMB, OPD)	Reacts with the enzyme to generate a color change
Stop Solution	Stops the reaction for measurement
Plate Reader (Spectrophotometer)	Measures absorbance at a specific wavelength (e.g., 450 nm)

ELISA Assay Steps

Coating: Bind antigen or capture antibody to the microplate.
Blocking: Add a blocking agent (e.g., BSA, skim milk) to prevent non-specific binding.
Incubation: Add sample, primary antibody, and enzyme-conjugated secondary antibody.

Washing: Remove unbound substances with a buffer.
Substrate Reaction: Add substrate (e.g., TMB) for color development.
Detection: Measu

The concentration of the target antigen is determined using a **standard curve**:

$$\text{Concentration (ng/mL)} = \frac{(A_{sample} - A_{blank})}{\text{Slope of Standard Curve}}$$

Where:

- A_{sample} = Absorbance of the test sample
- A_{blank} = Absorbance of the blank
- **Standard Curve** is generated using known antigen concentrations.

absorbance at 450 nm to quantify antigen levels.

Applications of ELISA

Medical Diagnostics: Detection of viruses (HIV, COVID-19), cancer biomarkers, and autoimmune diseases.
Food Industry: Allergen detection (e.g., gluten, peanuts), contaminants, and pathogens.
Pharmaceuticals: Drug testing and vaccine development.
Environmental Monitoring: Detection of toxins, pesticides, and pollutants.

Significance in Occupational Health

MDA is a crucial biomarker for assessing oxidative stress in individuals exposed to environmental and occupational hazards, such as volatile organic compounds (VOCs). Elevated MDA levels indicate increased lipid peroxidation, which can lead to cell membrane damage and subsequent health issues. Monitoring MDA in saliva provides a non-invasive and convenient method for evaluating oxidative stress in workers, including domestic painters exposed to VOCs.

Total Antioxidant Capacity (TAC)

Definition and Importance

Total Antioxidant Capacity (TAC) refers to the cumulative ability of antioxidants present in a biological sample to neutralize reactive oxygen species (ROS) and other free radicals. It provides a comprehensive measure of the antioxidant status of an individual, reflecting the combined effect of all antioxidants present in the sample, including vitamins, enzymes, and other small molecules.

Measurement Methods

Several assays have been developed to measure TAC, each differing in their principles and the types of antioxidants they can detect. Common methods include:

Trolox Equivalent Antioxidant Capacity (TEAC) Assay: This method measures the antioxidant capacity relative to Trolox, a vitamin E analog. It is based on the ability of antioxidants in the sample to quench a stable free radical, usually ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)).

Ferric Reducing Antioxidant Power (FRAP) Assay: This assay measures the ability of antioxidants to reduce ferric (Fe^{3+}) to ferrous (Fe^{2+}) ions. The change in absorbance at 593 nm is proportional to the antioxidant capacity of the sample.

Oxygen Radical Absorbance Capacity (ORAC) Assay: This method measures the antioxidant's ability to scavenge peroxyl radicals generated by the thermal decomposition of azo compounds. The decrease in fluorescence is monitored, and the antioxidant capacity is expressed as Trolox equivalents.

Cupric Reducing Antioxidant Capacity (CUPRAC) Assay: This assay is based on the reduction of cupric ion (Cu^{2+}) to cuprous ion (Cu^{+}) by antioxidants. The change in absorbance at 450 nm is used to calculate the antioxidant capacity.

Significance in Occupational Health

TAC is a valuable biomarker for assessing the oxidative stress status of individuals exposed to environmental and occupational hazards, such as VOCs. High levels of oxidative stress, indicated by reduced TAC, can signal an overwhelmed antioxidant defense system and potential health risks. Monitoring TAC in saliva provides a non-invasive and practical approach for evaluating the antioxidant status and oxidative stress in workers, including domestic painters exposed to VOCs.

8-Hydroxydeoxyguanosine (8-OHdG)

8-Hydroxydeoxyguanosine (8-OHdG) is a modified base that occurs in DNA due to oxidative stress. It is one of the most common markers used to measure oxidative damage to DNA, as it is a product of the reaction between DNA and reactive oxygen species (ROS). Here are some key points about 8-OHdG:

Formation: 8-OHdG is formed when the guanine base in DNA is oxidized by ROS. This can occur due to various environmental factors such as UV radiation, pollution, smoking, and certain chemicals, as well as biological processes that generate ROS.

Detection and Measurement: Levels of 8-OHdG can be measured in various biological samples, including urine, blood, and tissues. Techniques such as high-performance liquid chromatography (HPLC), enzyme-linked immunosorbent assay (ELISA), and liquid chromatography-tandem mass spectrometry (LC-MS/MS) are commonly used for its detection.

Biological Significance: High levels of 8-OHdG are indicative of oxidative stress and DNA damage, which can lead to mutations and contribute to the development of various diseases, including cancer, cardiovascular diseases, neurodegenerative disorders, and aging.

Clinical and Research Use: Monitoring 8-OHdG levels is useful in both clinical and research settings to assess the extent of oxidative damage and the effectiveness of antioxidants and other protective measures.

Health Implications: Elevated 8-OHdG levels are associated with increased risk of several diseases. Therefore, reducing oxidative stress through lifestyle changes, such as improving diet, quitting smoking, and minimizing exposure to environmental pollutants, can potentially lower 8-OHdG levels and reduce disease risk.

Understanding and measuring 8-OHdG is crucial for studying the impact of oxidative stress on health and for developing strategies to mitigate its effects.

Superoxide Dismutase (SOD):

Superoxide dismutase (SOD) is an essential enzyme that protects cells from oxidative stress by catalyzing the dismutation of the superoxide radical (O_2^-) into oxygen (O_2) and hydrogen peroxide (H_2O_2). Here are key points about SOD:

Function: SOD plays a critical role in the defense against oxidative damage by neutralizing superoxide radicals, which are harmful byproducts of cellular metabolism. By converting superoxide radicals into less harmful molecules, SOD prevents damage to proteins, lipids, and DNA.

Types of SOD:

SOD1 (Cu/Zn-SOD): Found in the cytoplasm, this form contains copper and zinc ions.
SOD2 (Mn-SOD): Located in the mitochondria, this form contains manganese.
SOD3 (EC-SOD): An extracellular form, also containing copper and zinc ions, which functions outside of cells.

Health Implications: Proper functioning of SOD is crucial for maintaining cellular health. Deficiencies or malfunctions in SOD enzymes are linked to various diseases, including amyotrophic lateral sclerosis (ALS), cardiovascular diseases, and neurodegenerative disorders like Parkinson's and Alzheimer's disease.

Therapeutic Potential: Due to its role in combating oxidative stress, SOD has been explored for therapeutic use. SOD mimetics and gene therapy are areas of research aimed at enhancing SOD activity to treat or prevent diseases associated with oxidative damage.

Regulation: SOD activity can be influenced by several factors, including genetics, diet, and environmental stressors. Antioxidants in the diet, such as vitamins C and E, can support SOD function and overall antioxidant defense.

Research and Clinical Use: Measuring SOD activity can provide insights into the oxidative stress status of an individual or an experimental system. It is often used in research to study the effects of oxidative stress and the efficacy of antioxidant treatments.

SOD is a vital component of the antioxidant defense system, helping to maintain cellular homeostasis and protect against oxidative damage.

Glutathione Peroxidase (GPx)

Glutathione peroxidase (GPx) is an important enzyme in the body's defense against oxidative damage. It reduces hydrogen peroxide (H_2O_2) and organic hydroperoxides to water and corresponding alcohols, using glutathione (GSH) as a substrate. Here are some key points about GPx:

Function: GPx plays a crucial role in protecting cells from oxidative stress by catalyzing the reduction of harmful peroxides. This process helps to maintain cellular integrity and function by preventing the accumulation of peroxides, which can damage cellular components.

Types of GPx:

GPx1: The most abundant form, found in the cytoplasm of nearly all mammalian tissues, especially in the liver.
GPx2: Primarily located in the gastrointestinal tract.
GPx3: Found in plasma.
GPx4: Also known as phospholipid hydroperoxide GPx, it acts on lipid hydroperoxides and is found in cell membranes.

Mechanism of Action: GPx reduces peroxides by using glutathione (GSH), which itself gets oxidized to glutathione disulfide (GSSG). The enzyme then catalyzes the conversion of GSSG back to GSH with the help of glutathione reductase, thus maintaining the cellular redox balance.

Health Implications: Proper functioning of GPx is essential for protecting cells from oxidative damage, which can lead to various diseases, including cancer, cardiovascular diseases, and neurodegenerative disorders. Deficiencies in GPx activity have been linked to increased oxidative stress and related pathologies.

Nutritional and Therapeutic Aspects: Selenium is a critical component of GPx, and adequate dietary intake of selenium is necessary for optimal GPx activity. Supplementation with selenium or selenium-containing compounds can enhance GPx activity and provide therapeutic benefits in conditions associated with oxidative stress.

Regulation: GPx activity is regulated by the availability of its substrates (GSH and peroxides) and the presence of selenium. The enzyme's expression can also be influenced by oxidative stress and other cellular signals.

Research and Clinical Use: Measurement of GPx activity in blood or tissues is often used as a biomarker for oxidative stress. It is a valuable tool in research to study the effects of antioxidants, the role of oxidative stress in diseases, and the efficacy of therapeutic interventions.

GPx is a vital component of the antioxidant defense system, protecting cells from oxidative damage and maintaining overall cellular health

Conclusion

The existing literature underscores the impact of VOC exposure on oxidative stress and highlights the potential of salivary biomarkers as non-invasive tools for monitoring health effects. However, more targeted studies are required to fully understand the oxidative stress response in domestic painters and to validate saliva as a reliable biofluid for occupational health assessments. Such research could lead to improved monitoring and preventive measures for workers in the painting industry.

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