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The effect of oxidative stress on the kidneys

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Abstract

Free radicals have a strong ability to harm and destroy vital molecules in the body's cells, such as carbohydrates, lipids, proteins, and nucleic acids. The harm resulting from free radicals plays a major role in constantly increasing these radicals and in a series of reactions that lead to the destruction of vital molecules in the cell. Free radicals play a helpful role in destroying malignant tumor tissues by radiation, and they also have a role in demonstrating the action and effect of toxic substances and drugs. They also participate in various vital processes within the body's tissues as intermediate compounds, as biochemical stimulants work to stimulate enzymes through the association of the free radical with the protein part of the enzyme, thus stimulating the working mechanisms of that enzyme, such as the enzymes Catalase, Reductase , Peroxidase, and Oxidase.

Therefore, the current review dealt with a study on oxidative stress, including free radicals and antioxidants, and the effects of oxidative stress resulting from the use of drugs and antibiotics on some organs such as the liver, heart, aorta, lung and testicles in general, and the kidneys in detail by studying their effects on blood dynamics within the glomerulus and tubule cell toxicity and inflammation. And crystal nephropathy, rhabdomyolysis, vascular disorders, and nephron toxicity.

Keywords: Free Radicals; Antioxidants; Drugs; Antibiotics; Kidneys

1. Introduction

Oxidative stress is defined in the biological system as an imbalance in the balance of antioxidants and free radicals. This imbalance is due to excessive production of free radicals or a deficiency in antioxidants, which therefore leads to the destruction of large biomolecules in the body. Oxidative stress occurs when the level of oxidant compounds exceeds the ability of antioxidants to remove them (H Sekhon *et al*., 2010).

Antioxidants are complex compounds with biological properties that are extremely important to the bodies of living organisms, as they act as a protective shield against many diseases that affect the organism, including heart disease, cataracts, cancer, atherosclerosis, and aging. They also have an important role in maintaining health. The organism, especially in the late stages of the organism's life (Chen *et al*., 2012).

Many studies have been conducted on the effect of oxidative stress, and the levels of (MDA and GSH), the activity of the enzyme (SOD), and catalase (CAT) in kidney tissues were estimated, as oxidative stress showed histopathological changes such as infiltration of inflammatory cells, dilatation in tubules, tubular atrophy, and reduction. of Bowman's space, congestion, hemorrhage, and nicrosis as a result of kidney injury and oxidative stress caused by increased MDA levels (Elbe *et al*., 2016).

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It was found that oxidative stress leads to a significant increase in biomarkers in the kidneys such as blood urea nitrogen and creatinine, an increase in the inflammatory process, and other pathological changes resulting from an increase in effective oxygen species, lipid peroxidation and protein carbonyle level, an increase in peroxynitrite, and a decrease in the glutathione level, and thus the crucial role of oxidative damage and inflammation in nephrotoxicity (Shaki *et al*., 2016). In studies conducted on the kidneys, it was found that oxidative stress causes renal diseases and acute interstitial nephritis (Aloy *et al*., 2020).

1.1. Oxidative stress

Oxidative stress occurs due to an increase in the concentrations of many reactive oxygen species (ROS), such as hydroxide radicals (OH-), superoxide radicals ($^{-}O_2$), and hydrogen peroxide (H_2O_2), in quantities that exceed defensive antioxidants. These radicals cause damage and damage to tissues, and are accompanied by an increase in In the peroxidation of fats to tissues, leading to the breakdown of unsaturated fatty acids, resulting in damage to various tissues of the body (Ighodaro and Akinloye, 2018). Oxidative stress resulting from a high-cholesterol diet led to histological disorders in the aorta, including Elastic Sheets Detachment, accumulation of cholesterol crystals, Inflammatory Infiltration, Adventitia Degeneration, Smooth Muscle Fibers Degeneration, and increased Aorta Thickening, in addition to Blood Colloid within the lumen of the aorta (Ahmed *et al*., 2020; Mohammed and Ahmed,2024b).

Oxidative stress in the liver also led to the leakage of enzymes and the accumulation of iron in the liver tissue, Fibrosis, Central Vein Well Thickening, and Lymphocytes Infiltration at a high rate, with the occurrence of Bile Ducts Sclerosis and Congestions, and the observation of Degeneration and Necrosis (Ahmed *et al*., 2022a; Aljaff *et al*., 2023). In the heart, oxidative stress led to Fibrosis, Coronary Vessels Thickening, and Myocardial Fibers Hypertrophy at a moderate rate, along with Inflammatory Infiltration and Hemolysis between cardiac muscle fibers, Myocardial Fibers Degeneration, and Disintegrates of cardiac muscle fibers (Ahmed *et al*., 2022b).

In addition, oxidative stress in the lung led to many histological changes, including Alveolar Damage, Alveolar Sacs, Thickening Vessels, Thickening Bronchioles, Fibrosis, Inflammatory Infiltration, Hemorrhage, Congestions, Degeneration, Necrosis, and Karyolysis (Ahmed, 2023). As for the testes, oxidative stress led to a decrease in the number of seminal tubules, the destruction of some entire tubules, a reduction in the number of germ cells, the separation of the sperm progenitors from each other and the basement membrane, degeneration and atrophy in the germ cells with degeneration in the sperm precursors and a reduction in the number of sperm, degeneration in the Sertoli cells and a decrease in their numbers to a significant degree. It degenerates in the cytoplasm of leydig cells and reduces their number, with congestion and bleeding between the seminal tubules (Ahmed *et al*, 2021).

1.2. Free Radicals

It is a molecule or atom that contains in its outer orbit one or more single electrons, and this is what makes it more highly effective than others and unstable due to the presence of a single electron in its outer shell, as it tends to gain an electron from the surrounding molecules to become stable by producing an electron double It has high energy and high affinity to interact with biological molecules in the body (Huang *et al*., 2005). Oxygen, which is an important element of life, can cause serious damage to the body in special circumstances because the reduction of oxygen by one electron leads to the formation of a number of active chemical compounds known as Reactive Oxygen Species (ROS), such as hydrogen peroxide (H_2O_2) and the radical Hydroxyl (OH^-) and superoxide radical (O_2^-) (Kumar, 2011). Therefore, free radicals can be defined as molecules from which, during chemical reactions, a single electron was taken from one of the electron pairs and became a container in its outer orbit for a single electron, forming free oxygen radicals (Block *et al*., 2002).

1.3. Antioxidants

Antioxidants work to donate an electron to the free radical and transform it into a stable, harmless compound that is unable to interact with various biological molecules in the body, thus working to remove its harmful activity against the body (Shih *et al*., 2002). Thus, oxidation is known in its simplest sense as a chemical reaction that transfers electrons from the basic substance to oxidation reactions, thus producing free radicals that search for a positively charged substance to combine with (Rodrigo, 2009).

Exogenous antioxidants include antioxidants derived from food, such as folic acid, lipoic acid, ferrous ions, and minerals such as manganese, copper, zinc, and other antioxidants taken with food, as well as vitamin E (α-Tocopherol) and vitamin C (Ascorbic acid), selenium, and some secondary metabolites of plants, such as flavonoids (Bouayed, 2010).

Vitamin C is a powerful antioxidant in blood plasma and is effective in eliminating free radicals. It reduces the risk of cancer. It helps in the absorption of iron not bound to globin. It may help in the collagen synthesis process and is also involved in the process of thyroxine metabolism and drug metabolism (Padayatty and Levine, 2016). Regarding the importance of Vitamin E (α- Tocopherol), a study (Ahmed *et al*., 2023) showed positive improvements in testicles when using Vitamin E to treat rabbits, which included an increase in Spermatogenesis percentage, Primary Spermatocytes Percentage, and Secondary Spermatocytes Percentage, with a high degree, and an increase in Spermatozoa Percentage, and Mature Sperm Percentage, in addition to a higher level of testosterone compared to the control group.

As for Endogenous antioxidants, they include Enzymatic Antioxidants, which mean the antioxidants present within the body of the organism, which include Glutathione Peroxidase, Glutathione-s-Transferase, Glutathione Reductas (GSSG - Red), and Super Oxidedismutase -SOD Catalase- CAT (Jeeva *et al*.,2015).

As for the non-enzymatic antioxidant system, it includes Glutathione, Sulfhydryl groups, Uric acid, Alpha lipoic acid, Histidin, Bilirubin, and Myoglobin. These antioxidants have low molecular weights, and glutathione is considered one of the most important non-enzymatic antioxidants as it works to prevent damage resulting from Oxidative stress, and it is one of the most prominent antioxidants for free radicals (Young, 2001).

2. The effect of oxidative stress on the kidneys

Oxidative stress caused by excess fat leads to tissue diseases in the kidneys, including Inflammatory Infiltration, Congestion, Blood Vessels Fibrosis, Necrotic Materials Accumulation in the Kidneys, Urinary Tubules Damage, Glomerulus Segmentation, Fibroblast Collection, and Hemolysis (Mohammed and Ahmed, 2024a). Drugs are also a major source of acute kidney damage, as they cause approximately 20% of acute kidney failure cases, especially with the increasing incidence of cardiovascular disease and diabetes, which require the use of several chemical drugs that may cause damage to kidney functions (Bao *et al*., 2018). Most drugs that cause nephron toxicity exhibit their toxic effect through several disease-causing mechanisms, and these mechanisms include intraglomerular hemodynamics, tubular cell toxicity, inflammations, crystal nephron pathies, rhabdomyolysis and thrombotic microangtopathy (Chang *et al*., 2017).

Drugs that have antiprostatic activity, such as non-steroidal anti-inflammatory drugs, or anti-Angiotensin II activity, such as angiotensin converting enzyme inhibitors and angiotensin Receptor Blocker, can interfere with the kidney's ability to regulate glomerular filtration and pressure the glomerular filtration rate. There are other medications, such as calcineyrin and tacrolinus, which cause constriction of the afferent artery vessels, which causes weakness in the kidneys, and their risk is determined by the development of the person’s disease condition (Bao *et al*., 2018).

2.1. Renal toxicity (Nephrotoxicity)

Nephrotoxicity is one of the most common kidney diseases and appears when the body is exposed to drugs or toxins that cause damage to the kidneys. When damage appears to the kidneys, they become unable to rid the body of excess urea and metabolic wastes from the body. The level of electrolytes in the blood, such as potassium and magnesium, also increases (AlQahtani *et al*., 2019). Nephron or kidney toxicity may be temporary due to a temporary rise in urea and creatinine levels, which rise due to temporary conditions such as dehydration, and may develop into acute kidney failure if it is not diagnosed early and the necessary therapeutic measures are taken (Barnett and Cummings, 2018).

2.2. Nephron toxicity indicators

Blood urea nitrogen refers to the amount of nitrogen that appears in the body in the form of urea due to metabolic products. It is used to find out whether there are excess nitrogenous wastes in the bloodstream that are supposed to be filtered in the kidneys. The failure of the kidneys to filter excess urea is one of the most important symptoms of kidney problems, as the increase in nitrogenous compounds in the blood leads to uremia, as the normal rate of urea in humans is 10-25 mg/100 ml (Andreucci *et al*., 2017). Creatinine also appears in blood serum after the body breaks down creatine to produce energy for muscles. The kidneys usually have the ability to filter large molecules of creatinine on a daily basis, but when health disorders occur in the kidneys, the level of creatinine in the blood serum will increase, indicating kidney damage (Wasung *et al*., 2015).

3. Conclusion

The results of the current review showed that oxidative stress results when the rate of free radical production exceeds that of antioxidants, and thus leads to an imbalance of oxidation and a high concentration of free radicals, which causes

biochemical disorders, including urea and creatinine, in addition to histological disorders, mainly in the kidneys, and other organs, including the liver, heart, aorta, lung, and testicles.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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