When oxygen can be toxic? A Mini review

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The sole author designed, analyzed, interpreted and prepared the manuscript.

Abstract

No one within the past later a long time had in intellect that the oxygen we breathe that contributes to sparing the lives of millions of patients and the most component of life has no harmful impacts on the body. Oxygen and water are the soul of living beings in common but beneath certain conditions such as weak immune status and lack of the body's ability to excrete natural antioxidants happens that the oxygen atom responds as a receptor for electrons, since its structure within the case of electronic soundness has two electrons that are not bound and as a result of progressive responses that create a few intermediate compounds. (Such as hydroxyl radical ($^{\bullet}OH$), hydrogen peroxide (H_2O_2) and superoxide anion ($^{\bullet}O^-_2$) that are hurtful to human' organs and influence the extraordinary degree of cell division process and the physiological activities that it performs since it could be a capable oxidizer. These reactive atoms and free radicals inferred from atomic oxygen are called Reactive Oxygen Species (ROS). In spite of the fact that ROS play a key part as a flag-bearer in ordinary cell flag transduction and cell cycling, they have long been known to be a component of the immune reaction of safe cells to microbial invasion. ROS are created as byproducts during the mitochondrial electron transport of aerobic respiration or by oxido/reductase proteins and metal-catalyzed oxidation. The primary step in ROS generation is the reduction of atomic oxygen (O_2) to anion superoxide ($^{\bullet}O^-$

$_2$), is the antecedent of other responsive species. For this reason, the significance of normal cancer prevention agents has gotten to be vital to urge freed of the poisonous quality of ROS and particular antioxidant supplement ought to be given to improve the diet. Among the well-known antioxidants and cancer prevention agents are glutathione, vitamins C and D as well as enzymes such as, superoxide dismutase, catalase and peroxidase which contribute successfully to the disposal of these oxidizing substances.

Keywords: Interaction of oxygen, Reactive Oxygen Species (ROS), Oxidative damage, Anti-oxidative defense.

1. Introduction

There are indications that oxygen was not present in the atmosphere of the earth at the time of its formation, that's, from almost 4.5 to 4.8 billion years ago, and there was much contention that oxygen existed within the environment approximately two billion years ago as a result of the advancement of the action of photosynthetic life forms, the primary of which was blue-green green growth. Since then, the organisms present at that time were anaerobic microorganisms and the evolution of photosynthetic organisms was accompanied by a gradual accumulation of oxygen that had a great impact on the emergence of aerobic organisms about 1.5 billion years ago [1,2]. By using oxygen as a final oxidizing agent, air cells can extract more energy from non-oxidizing nutrients such as glucose, because it can be fully oxidized to carbon dioxide (CO_2). Thus, aerobic life images flourished and compared to those in anaerobic organisms, and on the other hand, oxygen were defined as deadly or toxic to some forms of life, such as, some obligatory anaerobic organisms such as those that live in the soil thrive only in the absence of oxygen and die in its presence, like Clostridium [3]. Many questions come to mind, such as, why is oxygen, toxic to some organisms? How can anaerobic organisms survive and thrive in the presence of this toxic substance (oxygen)? It can be answered by these two questions that the oxygen in the case of electronic stability is not toxic or harmful to the organism, but because its electronic structure has two electrons that are not bound, there are restrictions on the possibility of the oxygen molecule interacting as a receptor for the electrons. For example, when the oxygen molecule is converted into a union of hydrogen atoms to form water, It occurs in four consecutive steps, each step in which one electron transfer takes place [4]. If the oxygen reacts in such a way, and it often

happens, this results in the appearance of intermediate compounds that lead to many problems of life, because it is one of the strongest oxidizing materials. Examples of these oxidizing materials (ROS) are the superoxide anion, hydroxyl radical, and hydrogen peroxide [5]. The present review article deals with different sorts of ROS, their production, and their role as messenger and inducer of oxidative stress and to focus on the anti-oxidative defense system against ROS.

2. Interaction of oxygen molecule as an electron receiver

There is no doubt that the oxygen we breathe represents the element of life for humans and all living things except for anaerobic bacteria. In the case of patients who have difficulty in breathing, they are given oxygen in balanced quantities through an oxygen mask (Fig 1). The supplement compounds, interior the cell, are oxidized through complex enzymatic forms and small amounts of ROS are formed as byproducts of oxygen metabolism. These species have a vital role in cell signaling and homeostasis [6]. ROS levels can increase significantly during environmental stress conditions such as heat or Ultraviolet (UV) exposure. This may result in critical harm to cell structures and typically well-known as oxidative stress. In plants, the generation of ROS is primarily influenced by stress factor responses. These conditions include drought, nutrient deficiency, salinity, chilling, metal toxicity, and Ultraviolet radiation [7]. During many biochemical reactions inside the cell, ROS are produced especially within mitochondria, endoplasmic reticulum, and perisomes [8,9]. During the process of oxidative phosphorylation, mitochondria convert energy into adenosine triphosphate (ATP). In this process, proton transport over the internal mitochondrial membrane by the electron transport chain, this passes through an arrangement of proteins through oxidation/reduction responses in which each acceptor protein along the chain having a more prominent reduction potential than the previous. The last goal of an electron in the chain is an oxygen molecule. Normally, O_2 is reduced to produce water and about 1% of electrons passing through the chain and in this case, oxygen is incompletely reduced to give the superoxide anion [10]. The reduction of molecular oxygen (O_2) produces superoxide anion ($^{\bullet}O^-_2$), the precursor of most other reactive oxygen species [equation 1]. Dismutation of $^{\bullet}O^-$2 produces hydrogen peroxide

(H_2O_2) [equation 2]. Hydrogen peroxide, in turn, may be partially reduced forming hydroxide ion and hydroxyl radical (•OH), or fully reduced to water [equation 3 & 4] [11]. Increasing levels of ROS formation can be stimulated by different pollutants, heavy metals and xenobiotics [12]. Another sort of reactive oxygen species is singlet oxygen ($^1O_2$) which is created, as a by-product of photosynthesis in plants. In the presence of light and oxygen, photo-sensitizers (chlorophyll) may change over triplet oxygen ($^3O_2$) to singlet oxygen ($^1O_2$) [13].

$O_2 + 1e \longrightarrow {}^{\bullet}O^-_2$ **[Superoxide anion radical].......... equation 1**

${}^{\bullet}O^-_2 + 1e + 2H^+ \longrightarrow H_2O_2$ **[Hydrogen peroxide] .... equation 2**

$H_2O_2 + 1e + H^+ \longrightarrow H_3O_2 \longrightarrow H_2O + {}^{\bullet}OH$ **[Hydroxyl radical] .... Equation 3**

${}^{\bullet}OH + 1e + H^+ \longrightarrow H_2O$ **................ equation 4**

$O_2 + 1e + H^+ \longrightarrow 2H_2O$

In the first step, an electron is transferred to the oxygen molecule, leading to the formation of the superoxide anion radical (${}^{\bullet}O^-_2$). In the second step, the electron moves from the superoxide anion radical (${}^{\bullet}O^-_2$) that formed in the previous step in the presence of a pair of protons ($2H^+$) leading to the formation of a molecule of hydrogen peroxide (H_2O_2), and in the third step, hydrogen peroxide is converted in the presence of a proton and an electron to give a molecule of water (H_2O) and a hydroxyl radical (${}^{\bullet}OH$) through the central compound H_3O_2 and finally the hydroxyl radical is combined with a proton (H^+) and an electron (1e) to give a molecule of water (H_2O). The result of the previous steps is the interaction of a molecule of oxygen (O_2) with four electrons and four protons to give two molecules of water ($2H_2O$). Fig.2 represents the structures of the oxygen molecule, hydroxyl ion, and reactive oxygen species (ROS).

Harber-Weiss reaction generates the highly reactive hydroxyl radical (${}^{\bullet}OH$) from an interaction between superoxide (${}^{\bullet}O^-_2$) and hydrogen peroxide (H_2O_2) as follows [14].

$$H_2O_2 + {}^{\bullet}O^-_2 \longrightarrow O_2 + OH^- + {}^{\bullet}OH \text{ [Hydroxy radical]}$$

Metal catalysis is necessary for this reaction. In the first step First, ferric ions (Fe(III)) are reduced by $^{\bullet}O^{-}_2$ to ferrous ions followed by oxidation by dihydrogen peroxide (Fenton reaction).

$$Fe^{3+} + {}^{\bullet}O^{-}_2 \longrightarrow Fe^{2+} + O_2$$

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{2+} + OH^{-} + {}^{\bullet}OH \text{ [Hydroxy radical]}$$

3. Oxidative damage of ROS

The reactive oxygen species are greatly destructive to life forms at high concentrations, and this state of oxidative stress can happen when the level of ROS surpasses the defense components. These species pose their harm impacts already by lipid peroxidation, nucleic acid damage, proteins oxidation, and enzyme inhibition. This leads to the activation of the programmed cell death (PCD) pathway [15,16]. ROS can moreover serve as second messengers in numerous cellular forms, including tolerance to environmental stresses [17,18]. The fact that ROS can act as harming or signaling atom depends on the sensitive balance between ROS generation and scavenging activities of cells. The overabundance of ROS is achieved by the anti-oxidative system including, enzymatic antioxidants such as superoxide dismutase, catalase, guaiacol peroxidase (GPX), glutathione reductase (GR) and mono-dehydroascorbate reductase [19], and non-enzymatic antioxidants such as glutathione (GSH), carotenoids, tocopherols ascorbate, and phenolics. Studies demonstrated that hydroxyl radical represents the most reactive among all ROS, since it includes a single unpaired electron, able to respond with oxygen within the triplet ground state. As cells have no enzymatic mechanisms, the end of the abundance of hydroxyl radical, eventually leads to cell death [20]. The oxidation of natural substrates within the cell by hydroxyl radicals may continue either by the addition of hydroxyl radicals organic molecules or by the release of a hydrogen atom from it. Hydroxyl radical (•OH) causes subsequent cellular damages and interacts with all biological molecules resulting in protein damage, lipid peroxidation, and membrane destruction [21]. On the other hand, superoxide anion and hydrogen peroxide are moderately reactive and can be inhibited by

superoxide dismutase and catalase, however, H_2O_2 can be generated in the cells under normal and stress conditions. The major sources of hydrogen peroxide in plant cells are photorespiration, photooxidation, NADPH oxidase, xanthine oxidase, and β-oxidation of fatty acids [22]. Fig.3 represents the stepwise oxidative damage of cells by over-production of ROS.

4. Site of ROS production

Reactive oxygen species (ROS) are produced either in stressed and unstressed cells at several locations in mitochondria, plasma membrane, chloroplasts, peroxisomes, endoplasmic reticulum, and cell walls. ROS are formed by the leakage of electrons onto oxygen from mitochondria, plasma membranes, chloroplasts, or as by-products of a few metabolic pathways localized completely different cellular compartments. Fig.4 demonstrates the different sites of ROS production in plants.

5. Antioxidative defense system against ROS

In ordinary conditions, there's an appropriate balance between production and quenching of ROS, this balance may be disturbed due to some adverse environmental factors which reflect on increasing ROS levels and subsequently can initiate oxidative damage of proteins, lipids and nucleic acids [23]. Such oxidative damage can be avoided by the manipulation of enzymatic and non-enzymatic components of the anti-oxidative defense systems. In this connection, glutathione (γ-glutamyl-cysteinyl-glycine (GSH) [24], ascorbate [25], tocopherol [26]), carotenoids [27], and phenolic compounds [28] represent the major non-enzymatic oxidative compounds. On the other hand, the enzymatic components of the anti-oxidative defense system operate totally in different subcellular compartments and react in concert when cells are exposed to oxidative stress conditions. These enzymes include glutathione reductase, superoxide dismutase [29], catalase [30], enzymes of the ascorbate-glutathione [31], guaiacol peroxidase [32], mono-dehydro-ascorbate reductase [33] and dehydro-ascorbate reductase [19].

6. Role of ROS in metabolic diseases and chronic inflammation

Previous studies demonstrated that reactive oxygen species (ROS) exert negative effects on human health that range from physiological regulatory functions to damaging alterations participating in the pathogenesis of an increasing number of diseases. Excess production of ROS is linked to pathological situations where redox damage and inflammation prevails in several chronic diseases. In the presence of excess glucose and saturated fatty acids, ROS generation and activation of the nuclear transcription factor-induced inflammation by upregulation of active inflammatory mediators involved in monocyte adhesion and chemotaxis [34]. Previous studies demonstrated that reactive oxygen species (ROS) exert negative effects on human health that range from physiological regulatory functions to damaging alterations participating in the pathogenesis of an increasing number of diseases. Excess production of ROS is linked to pathological situations where redox damage and inflammation prevails in several chronic diseases. In the presence of excess glucose and saturated fatty acids, ROS generation and activation of the nuclear transcription factor-induced inflammation by upregulation of active inflammatory mediators involved in monocyte adhesion and chemotaxis.

Antioxidant defence against ROS damage

The human body put in place several procedures to neutralize the impacts of ROS, free radicals, and oxidative stress based on enzymatic antioxidants (Catalase, glutathione reductase, superoxide dismutase) and non-enzymatic antioxidants (glutathione, lipoic acid, L-arginine, coenzyme Q10), all of them being endogenous antioxidants. Exogenous antioxidant molecules can be introduced by diet or by nutritional supplementation. The most effective nutritional antioxidants against ROS and their protective effects for human health can be summarized as follows:

a) Flavonoids

Flavonoids are found mainly in plants and are responsible for several pharmacological activities. Flavonoids are capable chelation of trace elements responsible for free radical generations and improve of antioxidant defenses [40].

b) Polyphenols

Prooxidant polyphenols seem to exert their cytotoxic activity by inducing apoptosis and cell cycle arrest via several pathways. In vitro studies investigated the prooxidative effects of polyphenols against cancer cell proliferation [41].

c) Vitamin E

Vitamin E is synthesized by vegetal organisms and contained in edible oils and seeds, as well as in food artificially enriched in α-tocopherol. Vitamin E is able to

prevent expression induced by cholesterol and play a beneficial role in preventing foam cell formation. Also, vitamin E is responsible for the activation of several signals in endothelial cells which are causative of ROS generation [42].

d) Ascorbic Acid

Ascorbic Acid is a natural antioxidant, reacts with ROS, quenching them and promoting the conversion into semi-hydro-ascorbate radical, as well as reducing the risk of cancer by suppressing free radicals and oxidative stress [43].

7. Conclusion

Prolongation of various negative environmental stress conditions to a certain extent leading to disrupt the cellular homeostasis and enhance the production of ROS. However, under normal growth conditions, ROS production in various cell compartments is low, in this condition act as signaling molecules that mediate several responses in cells. High level of ROS production causes oxidative harm to protein, lipid, and DNA, these impacts lead to altering membrane properties, loss of enzyme activity, protein inhibition, and cross-linking and ion transport resulting in cell death. These detrimental oxidative damages can be avoided by the understanding of anti-oxidative defense system comprising of enzymatic and non-enzymatic components. Recently, the future progress in proteomics, genomics, and metabolomics, will help in clear understanding of new pathways by which cellular cell responses to oxidative stress damage.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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Fig. 1: Oxygen masks deliver higher concentrations of oxygen for patients with serious respiratory conditions

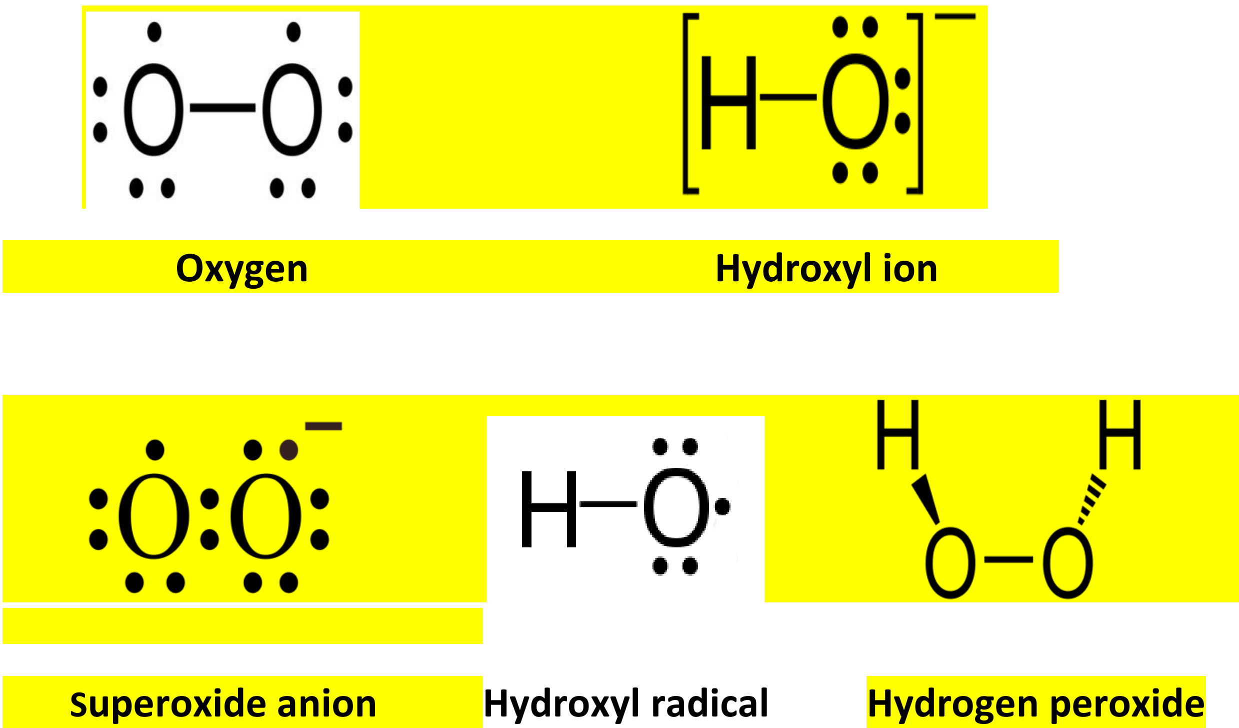

Fig 2: Structures of oxygen molecule, hydroxyl ion and Reactive Oxygen Species (ROS).

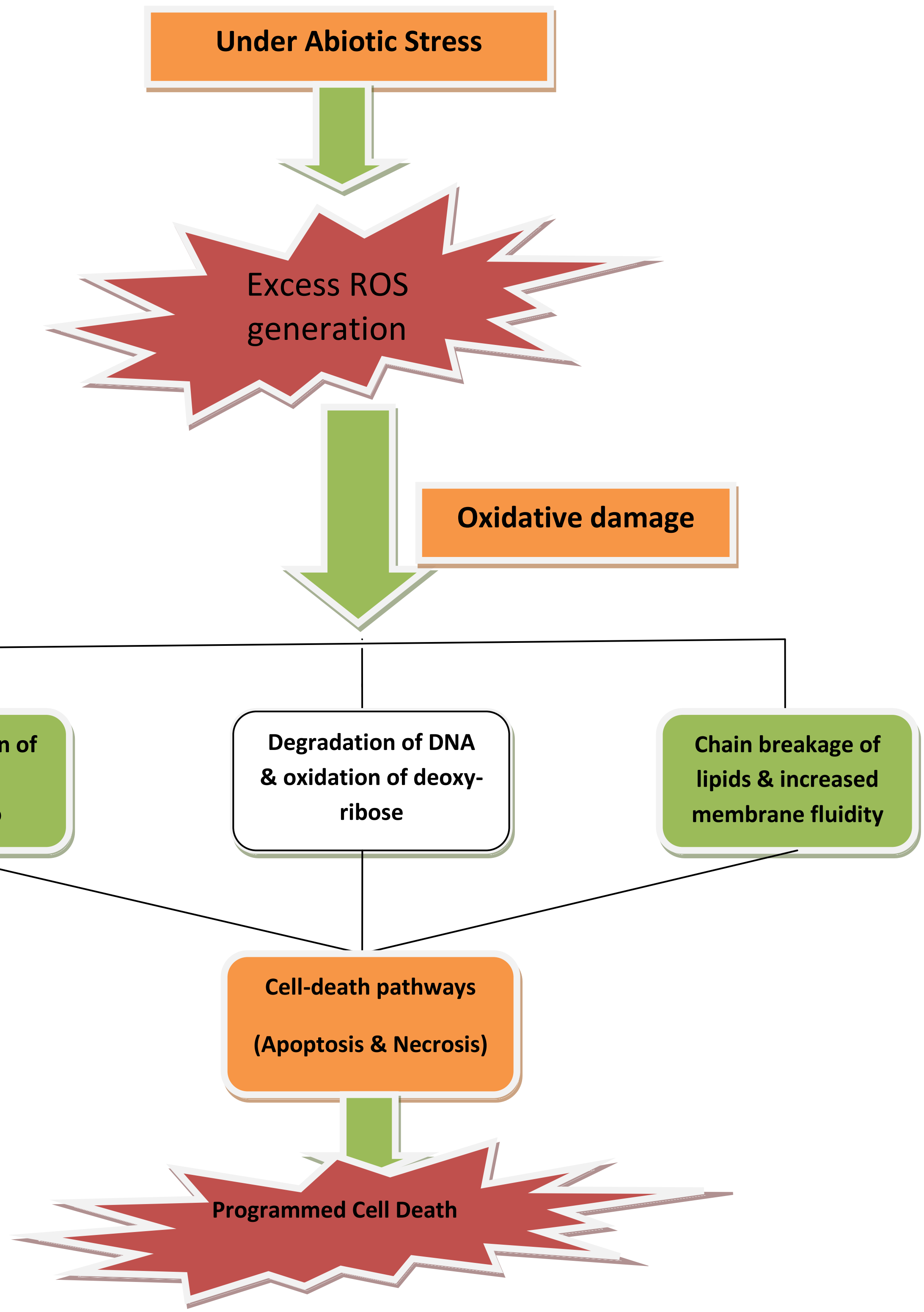

Fig.3: Stepwise oxidative damage of cells by overproduction of ROS.

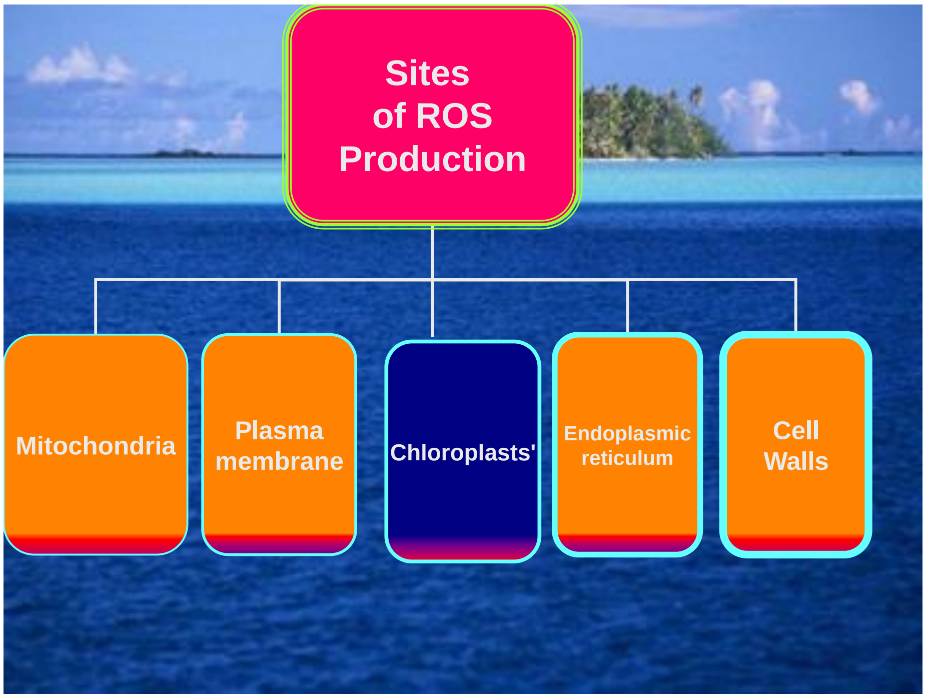

Fig.4: Sites of reactive oxygen species (ROS) production in plants.

Figure Legends:

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