ENVIRONMENTAL EXPOSURE TO IONIZING RADIATION AND ITS EFFECT ON SUPEROXIDE DISMUTASE ENZYME AND LIPID PEROXIDATION IN HUMAN VULNERABLE GROUPS

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By

SOHEIR SAAD KORRAA
Pharmacist At The National Centre
For Radiation Research And Technology
(ATOMIC ENERGY AUTHORITY)

Supervised By

Prof.Dr.ALY ABDEL HADY MASSOUD
Prof. of Community, Environmental
and Occupational Medicine - Faculty
of Medicine-Ain Shams University

Prof.Dr.MOHAMOUD MOHAMED MAHFOUZ
Prof. of Radiotherapy, Oncology
and Nuclear Medicine - Faculty of
Medicine-Cairo University

Prof. Dr. AHMED ALY EL MILIGY
Prof. of Radiation Chemistry
and Chairman of The National
Centre For Radiation, Research
and Technology

615.842
S.S

40765

Institute of Environmental Sciences
and Research
Ain Shams University

Cairo - Egypt

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Introduction and Aim of the Work

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Introduction and Aim of The Work

Since the creation of life (during preceding centuries) all bio-systems have been exposed to natural back-ground of ionizing radiations (cosmic and terrestrial irradiation). However, associated with the development of industrialization and civilization in this century; man-made radiation technology has increased in peaceful applications as well as military uses. Ionizing radiations are now incorporated in industry, agriculture, research and medicine (treatment, diagnosis and research). Such applications resulted in the employment of large numbers of workers, thus the problem of radiation occupational exposure has arisen.

Effects of ionizing radiation are mediated through free radicals formed either by direct or indirect effects of irradiation, where most of the latter are mediated by reactive oxygen metabolites. Though the mechanism(s) are not fully elucidated, the superoxide radical ($\bar{O}_2^{\cdot}$) has been shown to be formed directly and through secondary reactions of ionizing radiations (Marklund *et al.*, 1984). Thus $\bar{O}_2^{\cdot}$ is a toxic oxygen species and is regarded as the parent of a series of oxygen metabolites formed in the biological system in response to many external stresses including ionizing radiations (Cerutti, 1985).

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The deleterious effects of oxygen metabolites have been shown to follow two main routes:

1. Destruction of biomembranes and subcellular organelles due to the presence of polyunsaturated fatty acids in such membranes, thus inducing lipid peroxidation which can be measured in terms of the level of plasma malondialdehyde (MDA).

2. Attack over cellular proteins and nucleic acids, thus inactivating enzymes and inducing strand break scission of DNA and consequently chromosomal aberrations (Weiss 1986).

Fortunately, living systems in order to avoid damage to various biological structures from $\bar{O}_2^{\cdot}$ radical, the latter's concentration is strictly controlled by an inducible enzyme termed the "Superoxides Dismutases", where the protein synthetic apparatus of the cell becomes programmed to elevate the level of this endogenous enzyme , and deficiency in its production may lead to undesirable effects (Stevens and Autor, 1977) and (Storz et al., 1990)

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Current periodic occupational worker's medical examination for detection of radiation exposure damage depends mainly on:

- Clinical examination.
- Blood picture.
- Biochemical analysis.
- Chromosomal aberrations.

Although detection of chromosomal aberrations is considered the most reliable test ,still it is difficult to be applied routinely as it is expensive, complicated and time consuming (Stojanovic et al., 1983) and (UNSCEAR, 1988).

Consequently this thesis was an attempt to:

1. Assess the possibility of early detection of radiation exposure effects by comparative estimation of plasma malondialdehyde and blood superoxide dismutases enzyme .

2. Provide a quantitative and sensitive biological test for identification of high and low radiation risk groups among radiation exposed workers.

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Review of Literature

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Superoxide Radical and Superoxide Dismutases

Introduction:

It is a well known fact, that levels of oxygen supplied at concentrations above that of ambient air bring about damage to plants, animals and aerobic bacteria. Even 21% oxygen has been shown to slowly manifest damaging effects. which are dependent on the type of organism, physiological state, age and nutritional status. (Gilbert, 1963).

In 1954, Rebecca Gershman and Daniel L. Gilbert proposed that many of the damaging effects of oxygen could be attributed to the formation of oxygen radicals (Harman, 1992). This hypothesis was then developed by Fridovich, (1976) and (1978), into the superoxide theory of oxygen toxicity, which states that the formation of superoxide radical *in vivo* plays the major role in the toxic effects of oxygen.

Oxygen and Its Molecular forms:

A free radical is any species that has one or more unpaired electrons in its outer most orbital. Accordingly,

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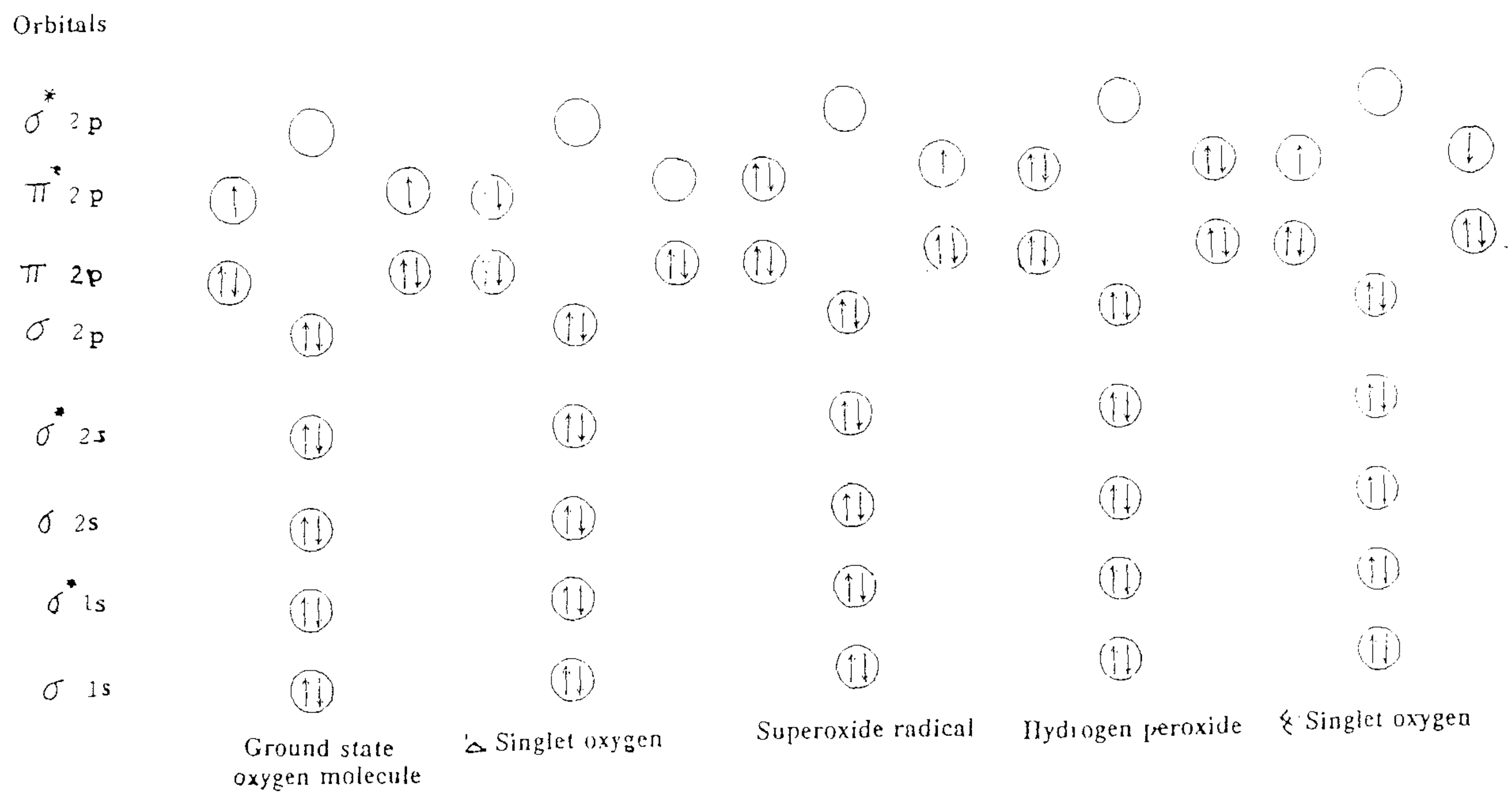

Fig. (1): Molecular forms of oxygen

(↑↓) orbital electrons

orbital name

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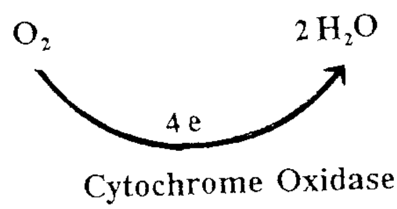
Oxygen molecule itself is a radical since it has two unpaired electrons each located in a different π antibonding orbital, Fig. (1). Fortunately, these two electrons are of parallel spins, thus for oxygen, in order to oxidize a two electron donor an inversion of spin is necessary. But the life time of collisional complex between oxygen and a potential 2 electrons donor is short while the time required for an inversion of spin is relatively long, thus oxygen mediates a two electron oxidation only at slow rates (Nonhebel <u>et</u> <u>al</u>., 1979). However, in a biological system, oxygen oxidizes biologically relevent two electron donors at rapid rates, but the presence of a catalyst is a must; e.g. cytochrome oxidase enzyme which reduces oxygen directly to water:-



Removing the unpaired electrons of oxygen molecule in a way that alleviates the spin restriction provides the probability of two singlet oxygen states:

Singlet Δ O_2 : This is not a radical, as it does not have an unpaired electrons. It is biologically important

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as it is normally formed in the lens and retina of mammalian eyes and is also responsible for the illumination of biological pigments such as chloroplast, chlorophyll, retinal flavins and porphyrins (Weiss, 1986).

2. Singlet Σ O_2: Despite of the fact that singlet sigma oxygen has been shown to decay quickly, it has been reported to oxidize cholesterol to 5-hydroperoxide and has been also shown to be produced during the myeloperoxidase system of neutrolphils. (Koppenol,1976) and (Ogryzlo, 1978).

Superoxide radical ($\bar{O}_2^{\cdot}$): Is said to be formed when a single electron is accepted by the ground state of oxygen molecule after entering one of the π antibonding orbitals. It is almost formed in all biological aerobic systems, and its chemistry shows that it may react as a reducing agent donating its electron or as an oxidizing agent in which it is reduced to H_2O (Weiss, 1986).

Peroxide H_2O_2: Which is not a radical is formed by adding an electron to $\bar{O}_2^{\cdot}$. However, the peroxide formed at physiolgical pH ,immediately protonates producing hydrogen peroxide H_2O_2 . The latter may be formed in a biological cell as a result of two types of reactions:

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