A TREATISE ON FREE RADICAL IN THE BASIS OF HUMAN LIFE

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A chemical entity having an unpaired electron in its outermost shell is called free radical. It has an acute intension to capture electron from other molecule. Scientific knowledge about free radicals is very important for our biological system. Free radical mainly binds with lipid, protein and DNA in our body. They have some beneficial roles: (i) destroy of pathogen, (ii) kill cancer cells, (iii) keep brain active, (iv) keep muscles smooth, (vi) control of the internal organ etc. On the other hand, increase of concentration of free radical causes various disease such as Alzhimer's because various disease such as Alzhimer's perkinson's, rheumoid arthritis, aging, cancer etc.

Different types of free radicals

a. Singlet Oxygen (O_2): Due to presence of unpaired electron, oxygen by itself is a radical in its excited state.
b. Hydroxyl radical ($OH^{\cdot}$): Hydroxyl radical is very reactive. It is produced in two ways:

i. It is produced by the catalization of transition metal ion (Fe^{+2} or Cu^{+2}) up H_2O_2. This is called Fenton Reaction.

$$Fe^{+2} + H_2O_2 \longrightarrow Fe^{+3} + OH^{\cdot} + OH^{-}$$

ii. Super oxide radical ($O^{-\cdot}$)and Hydrogen peroxide reacting with each other produce hydroxyl radical (OH^{-})

$$O_2^{-\cdot} + H_2O_2 \longrightarrow O_2 + OH^{\cdot} + OH^{-}$$

c. Peroxyl Radical ($ROO^{\cdot}$) : The superoxide reacting with a proton produce the simplest peroxyl radical which is Perhydroxyl radical (HOO).

Diagnosis of free radical:

Diagnosis of free radical done by following techniques:

1. Electron spins resonance.
2. Nuclear magnetic resonance using a phenomenon called CIDNP.
3. Chemical labelling: using X-ray photo electron spectroscopy (XPS) or Absorption spectroscopy

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4. Use of free radical markers: stable specific or nonspecific derivatives of physiological substances can be measured .e.g. Lipid per oxidation products, Amino-acid -per oxidation products, pep tide oxidation products.

How it works in human body:

Sources of oxidants: Oxidants are produced from exogenous and endogenous sources. Mitochondria, endoplasmic reticulum and peroxisome are the main cell organelles of producing oxidants.

Mitochondria: Mitochondria is the 'power house' of a cell. It is the most abundant source of oxidants due to high metabolic reactions. Electron transport chain in which O_2 is reduced to H_2O is one of the major oxidant production sites. In Electron transport chain $O_{2.}^-$ produced from O_2 by the elimination of a electron from O_2.Mitochondrial superoxide dismutase (SOD) converts $O_{2.}^-$ to $H_2O_{2.}$. The recent experiments reveal nitric oxide synthase produce NO^-. from L-arginine.

Endoplasmic Reticulum: In endoplasmic reticulum H_2O_2 is produced by the transfer of electrons from dithiols to molecular oxygen. Cytochrome p-450 and b5 enzyme leads to produce Reactive Oxygen Species in ER

Peroxisomes: In peroxisomes the most produced ROS is H_2O_2. Peroxisomes are small granular bodies filled with electron dense substances and limited by a single membrane which are formed as dilations of the ER. The peroxisomes are filled with enzyme peroxidase as named except this also content catalase and D-amino acid oxidase, In peroxisome expect H_2O_2, other oxidantes like $O_2.^-$, $OH.^-$ and $NO.^-$ also produced. Acyl co-A oxidase,D-amino acid oxidase L-α amino acid oxidase, urate oxidase , xanthine oxidase enzymes produce various ROS.

Phagocytic Cells: Phagocytic cells are immune cells which kill the foreign particles or antigens by producing oxidant. When a neutrophil attacked by foreign microbes, a pyridine-nucleotide dependent oxidase is activated involving the action of a b type cytochrome, in this process O_2 produces O_2^-.

Inside the phagolysome the heme containing enzymes 'Myelo peroxidase' forming an complex with H_2O_2 catalyze halaides like Cl^-,Br^-,I^- by H_2O_2. When Cl^- is catalyzed HOCl produced, which is very reactive ROS.

Targets of Oxidants: Free radicals are very unstable they have an intention to get stabilize by taking electron from the other, as the other become unstable. Free radicals can damage the cell if the antioxidant and oxidant balance got disturbed. It can attack the three main condition of cells: Nucleic acid , Proteins and Lipids.

Protein: ROS / RNS attack proteins and make them oxidised through P-P cross linkage as result denaturation, loss of enzymatic activity problem in function occur. The oxidation of

protein leads to various disease, like Alzheimer's disease Parkinson's disease, Rheumoid arthritis, Werner syndrome etc.

Lipid: Free radical mainly targets the polyunsaturated fatty acids residues of phospholipids to oxidize. The lipid peroxidation leads to loss of membrane functioning as result fluidity of membrane decreased, enzyme-receptor bound got inactivated. When free radical attacked a lipid molecule methylene group (CH_2) in a fatty acid produce lipid radical ($L.^-$). The lipid radical form lipid peroxy radical ($L00.^-$) by reacting with molecular oxygen. These lipid molecules farther propagates the peroxidation process by abstracting H atom from the other lipid molecule which leads to lipid damage.

DNA: When free radical attacks DNA is activates the poly (ADP-ribose) synthetase enzyme resulting splits of NAD^+ to aid the DNA. When, the damage is expensive, NAD^+ level decreased and the cell no longer to be able for function and damaged. ROS like OH radical directly interacts with DNA components and make some changes in single and double stranded DNA breaks which leads to mutation RNS like ($OONO^-$) interacting with guanine produces 8-nitroguanine and 8-oxodeoxyguanosine respectively 8-nitroguanine form is unstable can be spontaneously removed which leads to mutation.

RNA: RNA lack of an active repair mechanism for oxidation so, it is subjective to be more damaged than DNA. 8-dihydro-8-oxo-guanosine (8-oxoG) is the most extensively studied RNA damaging by product resulting various disease like Parkinson's disease, Alzheimer's disease Artherosclerosis, Hemochromastosis and Myopathies etc.

Some antioxidants against free radical

Antioxidant neutralised oxidant by giving them electron but not become free radical own self because of having another stable condition. There are 2 types of antioxidant by their nature 1) Enzymes 2) Vitamins

Enzymes: Antioxidant enzymes play vital role in first line of cellular defense from oxidative cellular damage. The antioxidant enzyme is catalase (CAT), GSH, super oxide dismutase (SOD), Glutathione peroxidase. Glutathione peroxidase is found in cytoplasm and mitochondria. It is the major antioxidant enzyme which prevents H_2O_2. It acts a vital role in the resistance lipid per oxidation.

CAT is another H_2O_2 metabolic enzyme. CAT converts H_2O_2 into H_2O and O_2. It is found in peroxisome and less in mitochondria.

SOD is an isoenzyme found in cytoplasm and mitochondria. SOD dismutase the superoxide radical to oxygen and hydrogen peroxide.

GSH (L- γ -glutamyl-L-cysteinyl-glycine) is a tripeptide. It is found generally in all living cells GSH is the cysteinyl reactive thiol group. GSH produce H_2O and alcohol by converting hydrogen and organic peroxide. It also prevents the exogenous and

endogenous toxins. GSH reduce S-S bond of protein and other molecule's remaining glycolytic and antioxidant enzyme in the reduce state.

Vitamins: Vitamins are also antioxidant they are micronutrients. Vitamin C, vitamin E , bioflavonoid and β- carotene are believed prevent the damage of oxidant.

1**) Vitamin C:** It is an antioxidant. It prevents body against oxidant. It also helps to make collagen (a tissue which holds muscle bone together). It helps to immunological activity Vitamin C keep body healthy and prevents anaemia by helping absorb ions and folic acid from blood. It breaks down free radicals. It found in all type of fruit and breast milk.

2) **Vitamin E:** it reduces the risk of cardiovascular disease by stabilising free radical. It also helps to prevent cancer. It acts against ageing.

3) **Flavonoids:** These are the group of phytonutrients with antioxidant which make defence against free radical. It helps to prevent cardiovascular disease cancer and urinary tract infections by bacteria.

4) C**arotenoid:** These are also a group of antioxidant. There are over 600 different types of carotenoids, but as common β-carotene, lycopene and lutein. Carotenoids prevent cancer eye disease and heart related disease and helps in immunological activities.

Conclusion

Work in the field of free radical is still in its infancy. There have been vast improvements in the knowledge of its structure and its basic science seems to be understood. Problems arise when trying to combine all these aspects into our biological system because the function of free radical in our biological system is still not explored well. Thus we need to understand more about the impacts of free radical on human body and develop better techniques for detection of its characteristics to safeguard our health. We are sure that this article will make huge impacts in this area.

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