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Oxidative stress and free radicals related to diabetes: A review

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Abstract
Diabetes mellitus has attracted tremendous attention in the field of molecular biology and Biochemistry. Free radicals are very harmful or may be helpful to the body. In certain cases where there is an imbalance between the formation and removal of free radicals which actually cause the oxidative stress. Thus to remove the oxidative stress, antioxidants are required in the body which plays an important role for scavenging the free radicals. As diabetes mellitus is also caused by certain oxidative stress. Antioxidants are required to remove the oxidative stress generated by free radicals and thus helps in curing diabetes mellitus disease both type-1 and type-2. In this review paper all the factors leading to oxidative stress and as well as the factors of antioxidants are mentioned and can be correlated from the entire reading of the paper.

Keywords: oxidative stress, free radicals, antioxidants, diabetes mellitus, reactive oxygen species

1. Introduction
Diabetes mellitus may be defined as a group of metabolic disorder that has been characterize by the increased level of glucose in blood which is also known as hyperglycemia. Insulin may be defined as a protein synthesize in Beta cell of pancreas as a response to various stimuli such as glucose. glucose is considered as a major determinant in the diabetes mellitus disease [1]. It has been observed that the long term elevation of the blood glucose level are associated with micro and macro vascular complication like stroke and blind ness [2]. Similarly to hyperglycemia the other factors that relates to the pathogenesis of diabetes are the oxidative stress that leads to high risk of complication [3].
It might be believed that oxidative stress might be playing a major role in the vascular complication in diabetes particularly in the patients suffering from type-2 diabetes mellitus [4]. It has been estimated that the ROS level has been elevated which might happen due to decrease in destruction or increasing production of catalase (CAT) and superoxide dismutase (SOD), glutathione peroxidase (GSH-px) antioxidants. The variation in the levels of this type of enzyme might make tissue susceptible to the oxidative stress which might lead to development of diabetic complications [5].

2. Types of Diabetes
Diabetes mellitus can be classified in different ways but one form of classification is as follow (American Diabetes Association, 2004):
1. Type I diabetes (Insulin dependent) is due to immune mediated beta-cells destruction, leading to insulin deficiency.
2. Idiopathic diabetes is the type 1 diabetes with no known etiologies and is strongly inherited.
3. Type II diabetes (Non-Insulin dependent) is due to insulin secretory defect and insulin resistance.
4. Gestational diabetes mellitus is any form of intolerance to glucose with onset or first recognition of pregnancy.

However diabetes is mostly classified basically into TWO major types: Type I Diabetes (IDDM) and Type II Diabetes (NIDDM) [6].

3. Oxidative stress and free radicals
Oxygen might be regarded as the element which is the most essential part of our life. Cells that use oxygen generates huge amount of energy free radicals which are produce in the mitochondrial cells. These products which are released as a byproduct are known as reactive oxygen species (ROS) and in other words they are termed as reactive nitrogen species as a result of cellular redox reaction [7]. This is the state which is called as oxidative stress that might result in serious cell damage if the mentioned stress is prolonged. Oxidative stress might play a major role in development chronic disease such as cancer, arthritis, and other auto immune disorder [8]. It has been estimated that the imbalances in free radicals levels as well as the antioxidant in saliva play a major role in periodontal disease [9]. It might be said that the cells which take up oxygen is converted to water by cellular enzymes action. In this phenomenon some enzymes leak electrons in to the oxygen molecules leading to the formation of free radicals [10]. These formations are normal biochemical reaction that involves oxygen. The two most important sources of free radicals are normal cellular metabolism like mitochondrial electron transport chain, endoplasmic reticulum oxidation and other enzymatic activities [11].

4. Necessity of free radicals
In the low concentration of ROS which is essential of normal physiological functions that includes gene expression cellular growth and defense against infection. Sometimes they may also act as an agent that cause stimulation for biochemical process with in the cell [12]. ROS also participate in biosynthesis of

macromolecules such as prostaglandin, thyroxin that might be stimulating the process involved in development. Immune system also uses ROS. In certain cases macrophages and neutrophils generates ROS by which they kill bacteria by engulfing which is also known as phagocytosis. Proteins, lipids, carbohydrates and nucleic acid are all effected by free radicals. The fact might be considered as free radicals generate free radicals from normal compound which is a part of the chain reaction. These free radicals might damage cell membranes and as well as lipoproteins in a process which is called lipid peroxidation. Proteins are also destroyed by ROS leading to structural changes and loss of activity of enzymes [13].

5. Oxidative stress pathophysiology relates to diabetes

Evidences has been reported with support that the oxidative stress has the major role in the pathogenesis of both type-1 and type-2 diabetes. Free radicals generation which occurs in diabetes in some times by non-enzymatic glycation of proteins, oxidation of glucose and peroxidation of lipid in excess that leads to enzymatic damage, cellular machinery and also increase resistance to insulin due to oxidative stress [14]. In latest research lipid is considered as the apolipoprotein component of LDL that has been found to form aggregates that are insoluble oxidatively due to hydroxyradicals inducing cross linkage between apo-b monomer which might be responsible for oxidative damage in diabetic complication [15]. During the oxidative metabolism in mitochondria, the utilize oxygen is reduce to water and smallest remaing oxygen gets transform to oxygen free radicals (O) that is important as a ROS that is converted in other form of reactive species such as ONOO, OH and H2O2 [16]. In certain insulin signaling, this is modulated by two ways involving ROS and RNS. In one way response to insulin, ROS/RNS exert its full physiological function and in other site the ROS and RNS negatively regulates insulin signaling interpreting them to develop a resistance to insulin which is actually a risk factor for diabetes type-2 [17].

6. Diabetes complications induced by oxidative stress

From the experiments the evidences which has given link between diabetes and oxidative stress by measuring biomarkers that includes the biomarkers that damage DNA and lipid peroxidation product it is also belived that the progression of diabetic complication is always done by free radicals that has a major role due to the ability of damaging of lipids, protein and DNA [18]. In the variety of pathological conditions that are induced by oxidative stress such as rheumatoid arthritis, diabetes mellitus, and cancer [19]. In certain in-vivo studies that support the role of hyperglycemia in the generation of oxidative stress that leads to endothelial dysfunction in the blood vessels of diabetic patients. Increase of glucose and insulin level along with dyslipidemia in patients who suffer from diabetes develops macro angiopathies that might cause oxidative stress leading to atherosclerosis [20].

7. Different types of biomarkers of oxidative stress in diabetes mellitus

According to certain studies ROS might be reacting with some amino acids *in vitro* that produces anything from a modified denatured and nonfunctional protein that might further be responsible for oxidative stress [21, 22]. In certain cases diabetes mellitus might produce disturbances in the lipid profile of the body which makes the cell more susceptible to lipid peroxidation [23]. Certain experimental result has shown that poly unsaturated fatty acid that are found in cell membrane are extremely attack by free radicals due to present of multiple bonds [24]. It has been also found that certain vitamins are important part of biological system as they might be playing an important role in different biochemical process. Among these are vitamin A, C, and E that acts as antioxidant which detoxifirs the free radicals. Diabetes mellitus might induce alterations in the activity of enzymes glutathione peroxidase and glutathione reductase. These enzymes are found in cells those metabolizes peroxide to water and convert glutathione disulfide back to glutathione [25]. In certain case catalase is a regulator of hydrogen peroxide metabolism that in excess might cause serious damage to lipids, RNA, and DNA. CAT might convert H2O2 in catalytically into the water and oxygen that neutralizes it. In some case of catalase deficiency the beta cells of pancreas which has a large amount of mitochondria undergoes oxidative stress by producing excess amount of ROS leads to beta cell dysfunction and ultimately leads to diabetes [26]. SOD which is also known as superoxide dismutase helps in providing the first line defense against ROS mediated cell injury by the help of catalyzation the proportion of superoxide, the primary ROS in oxygen metabolism to molecular oxygen and peroxide [27].

8. Antioxidant

Antioxidants may be defined as substances that protect the cell from damage which are caused by free radicals. Antioxidants are found to interact with and stabilize the free radicals which might prevent some of the damages caused by free radicals. The antioxidants are exogeneous and endogenous in nature. These are classified as superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase. The non enzymatic antioxidants are may devided into metabolic antioxidant and nutrient antioxidant. The metabolic antioxidants are lipoic acid, glutathione, L-arginine, uric acid while nutrients antioxidants are vitamin E, C, caratenoids and tress elements [28].

9. Conclusion

Different diseases which are caused within the human body results from oxidative stress and thus from free radicals. Over here we have discussed mainly about diabetes mellitus but there are other diseases which are also caused due to the oxidative stress. This can be prevented by antioxidants supplementations. Cells are well equipped with impressive number of antioxidants enzymes as well as small antioxidants molecules, these agents are not sufficient enough to normalize the redox status during oxidative stress. Before the contemplating the antioxidant supplementation the most important aspect is to consider whether a particular patient require antioxidant supplementation or not, and the decision behind it. Free radicals might be a continuous process that forms within the human body and there is enough evidence in their involvement most pathophysiological state where antioxidant might counteract the detrimental effect of free radicals. In the near future therapeutic strategies might be formulated in such a way that the antioxidant capacity may be

utilize within the cells which may be used for long term treatment function. Oxidative stress might be demonstrated in many studies in the progression of diabetes which plays an important role during diabetes which includes impairment of insulin and the elevation of complicated incidents. Antioxidants are major factor already shown to be prospective in the treatment of diabetes in both type-2 and type-2. The increased levels of oxygen and nitrogen free radicals has been linked with lipid peroxidation and non enzymatic glycation of proteins and oxidation of glucose which contributes in diabetes mellitus and it's complication. In all the cases a relationship has been found between oxidative stress and diabetes along with their complication related to heart, liver, kidney, eye etc. Lastly oxidative stress is a worrying in metabolic disorder specially type-2 diabetes mellitus.

10. Reference

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