

# Oxidative Stress Applied in *Diabetes Mellitus*-A New Paradigm <sup>†</sup>

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**Abstract:** Although obesity and a sedentary lifestyle are well-known risk factors for type 2 diabetes, at molecular level, the oxidative stress is regarded as the primary contributor to the pathogenic process. Our work intends to evidence how the thinking models influence the way that medical practitioners understand the pathogenic mechanisms. Some research groups focused lately on the system's dynamics and Complex Systems Theory. The living organisms as a complex system could be analyzed applying the network concept. Alternative methods for characterizing biological processes or phenomena based on feedback node structure have been developed [1].

**Keywords:** oxidative stress; antioxidants; complexity theory; algebraic fractals; diabetes mellitus; public health

## 1. Introduction

During last decade, many research groups proved that the oxygen species generate adverse effects [2,3] due to the imbalance between the production of ROS (reactive oxygen species) and the body's biological capacity to neutralize them (i.e., enzymes) [4,5]. In the meantime, the evolution of some significant diabetes complications, such as cardiovascular or renal disease, is related to the oxygen species as the primary pathogenic mechanism.

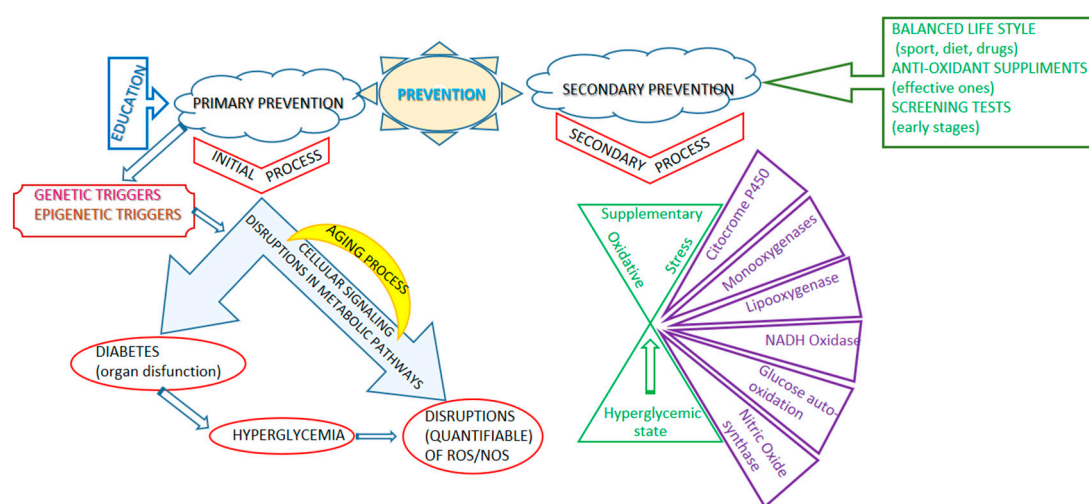
## 2. Discussion

Almost all of the chronic diseases have been associated with a high quantity of free radicals, or modified signal transductions. In dedicated medical research, two approaches could apply from nutritional interventions point of view: the situation when it is used to prevent a particular disease

or, when it is able to alleviate progression, symptoms or complications of the disease. In addition, the considered specific diseases are divided as follows: the group that involves the so-called mitochondrial oxidative stress conditions (cancer and diabetes) and the group that involves the inflammatory or oxidative conditions (atherosclerosis, chronic inflammation, ischemia and reperfusion injury) [6].

Hyperglycemia in diabetes mellitus is one of the main factors leading to specific structural changes, as protein and lipid oxidation, which are the most common (Figure 1). For instance, the free radicals induce damage to sulfhydryl groups. As consequence, the proteins are not recognized anymore, resulting in cross-reactions and finally triggering the autoimmune diseases.

In the meantime, abnormal LDL produced by the peroxidation of plasmatic lipids is not identified by liver's LDL receptors and subsequently, macrophage scavenger receptors take modified LDLs, forming engorged lipid macrophages (LEM), and infiltrate under blood vessel endothelium. It should be also considered that the lipid peroxidation mechanism is governed by the loss of membrane functionality and integrity [7].



**Figure 1.** Presentation of main primary and secondary prevention approaches.

The membrane lipids are influenced by the chain reaction between polyunsaturated fatty acids and ROS. Such chemical processes have as consequence increased cellular membrane permeability as well as an increased calcium influx. The subsequent effect of all these chemical transformations at the membrane level leads to mitochondrial damage. Another aspect to be considered is related to the effects of certain antioxidants whose molecules might change their first functionality *in vivo*. For instance, melatonin that is a proven antioxidant *in vitro* [8] generates circadian rhythm through protein-coupled receptors [9].

Considering the informational feedback of the oxidative stress (OS) process configured according to the feedback node structure, it was possible to establish which would be the main information necessary to characterize the OS process, namely: OS definition; ROS characteristics (primary –  $O_2$ , secondary – radicals formation through Fenton and Haber-Weiss processes); ROS behavior against bio-environment; OS action on body; OS quantification and strategies to be applied for OS and ROS. For our case, a complex structural type applies when multiple global feedback could be obtained. The nodes with same feedback can be merged horizontally into another node, leading to an interim feedback. There are two sequences of nodes: first with two nodes and second one with only one node. The feedback embraces one node within a sequence. For instance, the change of the environment (*in vitro* or *in vivo*) represents interactions between nodes using environment. Then the direct interaction between two neighboring nodes could be reduced. Taking the advantages of such integrated approach regarding the OS process connected to the *diabetes mellitus* the thinking models related to the pathogenic mechanisms applied by clinicians could be corrected.

### 3. Conclusions

In our work, we proved that the approach of the biological processes by help of complex mathematical models allows a correct understanding of pathogenic processes, without applying the simplifying hypothesis or artificial extension of general models.

It has been shown that it is possible to better interpret the oxidative stress using the feedback node model, which present same patterns at lower scale—as cells. The studies that we started could bring a significant difference on approaching the primary and secondary prevention and on other public health issues as well. Such dedicated research could be important for explaining the signaling pathways, which generate chronic diseases (i.e. diabetes).

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