ANTIOXIDANTS: HEALTHIER LIFE PROJECTION

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ABSTRACT
The aim of this article is to highlight the need to maintain adequate health especially from the fifth decade of life with the use of antioxidants. All recent findings show that these substances are actively involved in the neutralization of oxidative stress, promoted by the excess of free radicals. These molecules, generated in the process of tissue respiration that constitute approximately 5% of all oxygen consumed, would be the price we must pay for making use of this potentially toxic molecule such as oxygen. We also point out that in a totally physiological process there is a production of free radicals controlled by different metabolic pathways, since as we know, they constitute the first line of defense in our economy. However, oxidative stress, which is the imbalance between endogenous antioxidants versus oxidants, in favor of the latter, is or constitutes the previous step for a number of pathologies of all kinds, including infectious. It is also mentioned in the present work, some sources of exogenous antioxidants, especially fruits and vegetables that would complement the therapy of various diseases.
Likewise, preliminary (unpublished) results of the assimilation of an antioxidant by the aortic tissue of rats, subjected to increases in the temperature of the culture medium, which would promote its greater incorporation into endothelial cells, are included.
Keywords: antioxidants, free radicals, oxidative stress, cell assimilation, health.

RESUMEN
El objetivo de este artículo es resaltar la necesidad que se tiene para mantener una salud adecuada en especial a partir de la quinta década de vida con el empleo de antioxidantes. Por todos los hallazgos recientes se demuestra que estas sustancias, participan activamente en la neutralización del estrés oxidativo, promovido por el exceso de radicales libres. Estas moléculas generadas en el proceso de la respiración tisular que constituyen aproximadamente el 5% de todo el oxígeno consumido, sería el precio que debemos pagar por hacer uso de esa molécula potencialmente toxica como lo es el oxígeno. Igualmente señalamos que en un proceso totalmente fisiológico existe una producción de radicales libres controlado por diferentes rutas metabólicas, ya que como sabemos, constituyen la primera línea de defensa en nuestra economía. Sin embargo, el estrés oxidativo, desbalance entre los antioxidantes endógenos versus los oxidantes, en favor de estos últimos, son o constituyen el paso previo para un sinnúmero de patologías de toda índole, inclusive las infecciosas. Se menciona también en el presente trabajo, algunas fuentes de antioxidantes exógenos, en especial de frutas y verduras que servirían de complemento a la terapia de diversas enfermedades.
Asimismo, se incluyen los resultados previos (no publicados) de la asimilación de un antioxidante por parte de tejido aórtico de ratas, sometido a incrementos de temperatura del medio de cultivo, lo que promovería su mayor incorporación a las células endoteliales.
Palabras clave: antioxidantes, radicales libres, estrés oxidativo, asimilación celular, salud.

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Introduction

We pay a price for consuming oxygen, because not all the oxygen we consume (considered as 100%) serves to form energy in the form of adenosine triphosphate or ATP since 5% is lost producing the so-called free radicals [1].

The understanding of free radicals was not carried out systematically but in the last three decades. There was no demand for it, because aging was considered a natural and irreversible process except in the fields of radiation, preservation of food, among others, until the year of 1969, McCords and Fridovich discovered the enzyme superoxide dismutase (SOD) isolated from erythrocytes, which catalyzed the reaction:

$$2O_2^- (O_2\bullet + O_2) + 2H + \rightarrow H_2O_2 + O_2$$

This knowledge of the existence of superoxide dismutase involved the immediate recognition of the physiological existence of the superoxide radical, based on the teleology that the enzyme implies the existence of the substrate. What subsequently led to the biological recognition of free radicals and thus, oxidative stress [2].

Superoxide anion (O_2^-) as well as nitric oxide (NO) are important mediators of tissue damage and organic dysfunction, for instance in inflammatory processes, where NO is produced in high quantities.

In this work we seek to better interpret the knowledge we have about those endogenous and exogenous molecules produced to fight free radicals; the so-called antioxidants and the role they play in human health. As well as, the role that this indispensable molecule fulfills for life, as is oxygen, which, due to its high reactivity, is also capable of becoming a toxic element. At the same time, we see with concern the impact that the oxidation-aging relationship has had on the population, which has promoted the high consumption of antioxidants and that is expanding more and more worldwide on a daily basis, even though it has not yet elapsed, which will be its possible consequences.

Oxidation Process

We know that the process of generating energy within the mitochondria consists basically in the transfer of electrons from one molecule to another arranged from lower to greater oxidation potential, in such a way that 95% of the oxygen used by the body is reduced to water by the action of the cytochrome oxidase complex of the mitochondrial respiratory chain that leads to the acceptance of the 4 circulating electrons in order to form two water molecules.

As a consequence of having two unpaired electrons in its external orbital; unlike other molecules in which each pair of electrons rotate in the opposite direction, present the same spin. This prevents O_2 from capturing two electrons simultaneously and forced it to accept the electrons one by one. In other words, the reduction is done in 4 univalent steps: It captures the first electron and forms the superoxide anion (O_2^-), a second electron and forms hydrogen peroxide (H_2O_2), a third electron and forms hydroxyl radical form (^-OH) and, finally it captures the 4 electron and forms water ($2H_2O$) [3].

As a result, about 5% of oxygen molecules do not complete the capture of the 4 electrons and escapes from the mitochondria, becoming very unstable chemical entities and therefore highly reactive with a half-life of only microseconds. The most typical example for the high percentage that is produced from the total of radicals, is the superoxide anion (1-2%). As a consequence of the need to stabilize itself, acquiring an electron with which it would complete its orbit, it spreads rapidly within the cell, responding to its enormous capacity to combine, which is achieved, in a non-specific manner in most cases, with the diversity of molecules that make up the cellular structure, such as: carbohydrates, lipids, proteins, nucleic acids and derivatives of each one of them. In turn, the combination of the functional molecule with the free radical gives rise to a dysfunctional molecule, which

can have an impact on cell life. A classic example is the reaction of free radicals with unsaturated lipids (which have double bonds) of the cell membranes, a reaction called lipoperoxidation. The phospholipids of the membranes contain a large amount of polyunsaturated fatty acids, very vulnerable to peroxidation since carbon-carbon double bonds weaken the carbon-hydrogen bond of the neighboring carbon atom. In this way, the hydroxyl radical (OH*), when attacking the double bond of the fatty acid subtracts a hydrogen atom and creates a new organic radical (initiation) giving rise to two fragments of fatty acid, each of one becames a free radical capable of attacking the double bond of another fatty acid. These free radicals, by attacking a neighboring lipid and subtracting a hydrogen atom produce a hydroperoxide and with it a new radical (propagation). The lipid hydroperoxides are stable in the pure state, but in the presence of transition metals decompose, giving an alkoxyl radical. This is how both peroxyl and alkoxy radicals stimulate the chain reaction by subtracting hydrogen atoms from other lipids, a process that ends up functionally damaging the cell membrane. This reaction is of such magnitude, that a single free radical can affect approximately one million molecules during the chain reaction producing all the variety of reactive oxygen species (ROS) although there is also reactive nitrogen species (RNS) derived from the Nitric oxide. (4).

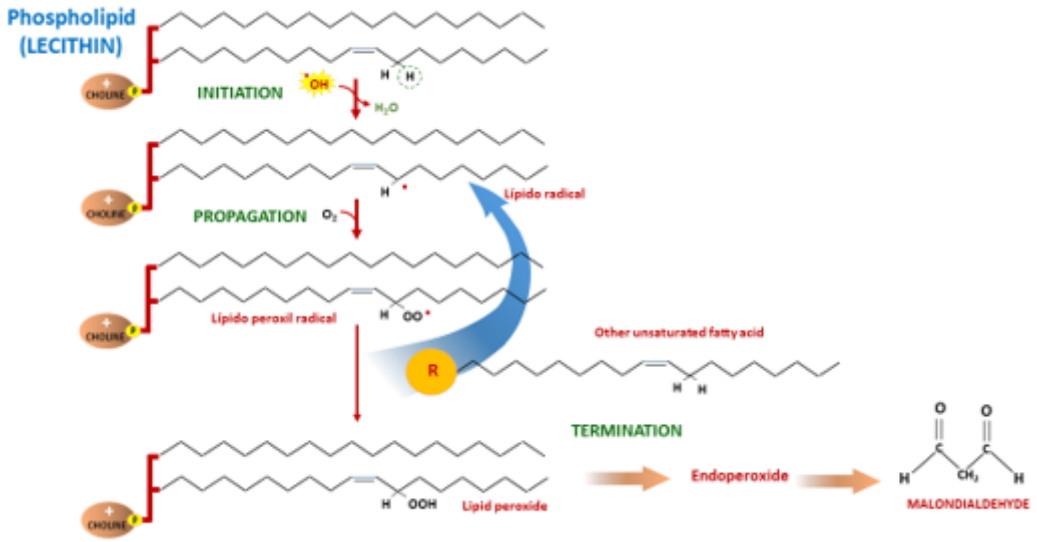

Figure 1. Mechanism of lipid peroxidation (Initiation, propagation and termination).

The reaction of metal complexes with lipoperoxides generates a wide range of products which in turn can be harmful to the cell, such as gases, ethane, pentane, ethylene or aldehydes (4-hydroxy-transnonenal, malondialdehyde, MDA).

Currently, we know that there are several mechanisms by which we increase the presence of free radicals and with it, oxidative stress. Although it is true, its production is greater during the organic metabolism, properly in the mitochondria, it is also attributed an increase in oxidation resulting from an inadequate diet without leaving aside, the bad habits of life; excessive intake of alcohol, tobacco consumption, exposure to solar radiation, the mechanisms of action of certain drugs, the action of toxic substances, increased physical or psychological stress that ultimately promote the proliferation of free radicals, the imbalance of the compensatory mechanisms and , finally, oxidative stress accelerating their aging [4].

Defense Process: Antioxidants

In view of the foregoing, life in presence of molecular oxygen requires a multiple system of defense against the various free oxygen radicals that physiologically prevent their formation and neutralize their destructive activity at the same time.

At the moment, we consider the production of free radicals as a product of the normal metabolism of the cell and therefore our organism is designed to neutralize them. This group of enzymatic and other entrapment substrates, which are normal components of cells and tissues, are generically called natural or endogenous antioxidants. Thus we see that physiologically our organism is designed until approximately 46 years of age to neutralize that natural oxidation.

As we can appreciate, our cells are exposed to oxygen everyday all day and this leads to oxidation despite the fact that oxygen is important for the health of our body. It is because of that in the presence of oxidation, an antioxidation is produced that allows us to always be in a condition of equilibrium. The imbalance is generated when there is an increase in oxidation over that of antioxidant production; this is called oxidative stress. Consequently, the body uses antioxidants to stabilize free radicals. This prevents them from causing more damage in other cells. Antioxidants can protect and reverse, to some extent, the damage that oxidants have caused.

Today there is a lot of interest in the concept of oxidative stress to the point that its study is considered one of the few cases in the history of medicine that has promoted such a profound impact since its discovery. Numerous investigations have demonstrated their importance among physiologists and clinicians on their participation in all biological systems reaching the conclusion that practically all pathologies occur or begin with a state of oxidation.

The antioxidant mechanism acts fundamentally at five levels:

1. A first level is precisely at the inner membrane of the mitochondria, where the cytochrome oxidase complex of the mitochondrial respiratory chain, which prevents the production of oxidants is greater than 5%, preventing the univalent reduction of oxygen by means of enzymatic systems capable of effecting the consecutive tetravalent reduction without giving the option of releasing the partially reduced intermediates (O_2^-, H_2O_2 and OH*).

2. A second level is at the enzymes capable of blocking the superoxide anion radical, such as superoxide reductase (SOD). In the cells of eukaryotic organisms there are two different isoenzymes depending on the metal present in its active center one, is cytoplasmic and contains a Cu^{2+} and a Zn^{2+} atom in its active site and a second, is mitochondrial by its position, and contains Mn^{3+} in its active site. This group of metalloenzymes catalyses the dismutation of the superoxide radical to H_2O_2 and O_2, with an efficiency so great that it approaches the theoretical limit of diffusion. This last finding reinforces the symbiotic theory of mitochondria [5].

$$O_2^- + O_2^- + 2H^+ \xrightarrow{\text{(Cu-Zn-SOD, Mn-SOD)}} H_2O_2 + O_2$$

3. A group of enzymes specialized in neutralizing hydrogen peroxide constitutes the third level of defense. Among them is the enzyme present in peroxisomes, called catalase that catalyzes the reduction of hydrogen peroxide by various electron donors, including more importantly, glutathione-peroxidase (GPH) present in the cytoplasm of mammalian cells containing selenium. Its active site convers reduced glutathione into oxidized glutathione.

4. In the fourth and last level are the defenses against the OH*; this radical once formed, is an extremely reactive oxidant that interacts with almost all the molecules found in living organisms, at speeds only limited by the diffusion speed. These defenses are constituted by vitamins C and E, the latter also called α-tocopherol which, due to its

hydrophobicity, is present in biological membranes [6]. Its antioxidant action within the cell is very effective on the OH* produced in the Haber-Weiss cycle from the H2O2 formed in the presence of the Cu^{2+} or Fe^{2+} (Fenton reaction described in 1894). Whereas, vitamin C or ascorbic acid, is a hydrophilic electron donor or reducing agent, that reacts rapidly with O_2^-. and OH*, as well as a captor of singlet oxygen (atomic) and hypochlorous acid, a powerful oxidant generated at the site of inflammation [7]. Ascorbic acid is also used in the body as a cofactor of the enzymes proline hydroxylase and lysine hydroxylase, involved in the biosynthesis of collagen and the enzyme dopamine p-hydroxylase that converts dopamine into noradrenaline [8].
However, the administration of ascorbic acid to patients with iron overload can produce serious reactions because ascorbic acid can reduce Fe^{3+} to Fe^{2+}, which, in the presence of H2O2 can stimulate the formation of the OH* by the reaction of Fenton [9].
5. A fifth level is related to the response of the organism once the molecular damage has occurred. Thus, due to the fact that most of the molecules of the organism suffer a constant change, they are periodically replaced, which allows the damage to disappear. In the case of genetic material, oxygen free radicals are capable of causing breaks in the DNA chain and even of inducing mutagenesis, but there are enzymatic mechanisms of repair that allow the reestablishment of genetic information.

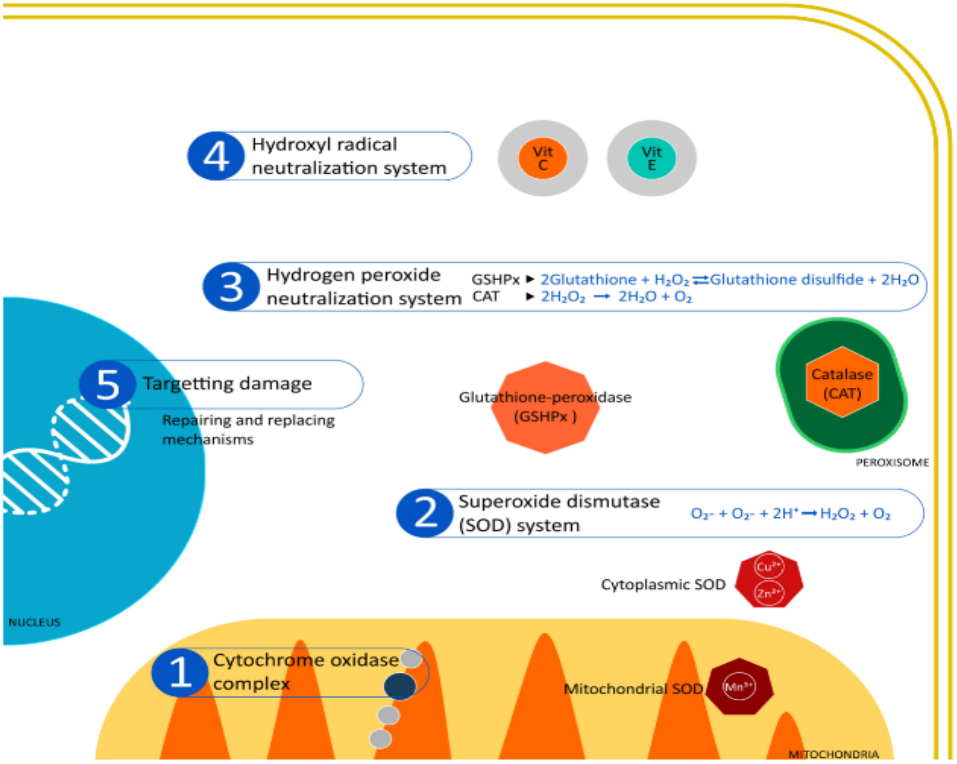

Figure 2. The five levels of the mechanism of action of antioxidants

As mentioned above, our body produces some antioxidants in order to fight free radicals that are formed during normal bodily processes. Whereas another important group is obtained when a healthy diet is consumed. A diet that incorporates fruits and vegetables (vegetables) with high content of nutrients such as beta carotenes, lutein, lycopene, selenium and A, B and C vitamin.
There is relevant evidence that suggest consumption of these nutrients greatly reduces the risks of suffering from certain pathologies. Nevertheless, it is not yet clear if this is due only to the antioxidants present, or to something else (other factors) that contain these foods [10].

Oxidative Stress

Under normal conditions, there is a balance between the production of free radicals or other reactive species versus the generation of endogenous antioxidants. This dynamic balance allows the cells to work effectively and therefore there is no cell damage. However, as a result of an increase in free radicals or a deficient antioxidant state, the balance is broken, producing a state known as oxidative stress which, in short, is nothing more than the increase in cellular oxidation, causing a structural and functional change, which accelerates its aging reaching even cell suicide (apoptosis).

This oxidative damage leads to cellular aging (loss of cellular youth), which leads to the deterioration of the tissues with the consequent absence of regeneration, which leads to several diseases and, ultimately, to death. Pathologies such as cerebrovascular, cardiovascular, metabolic, degenerative diseases and even cancer are related to aging [9].

In summary, oxidative stress conditions cellular metabolism through the oxidation of proteins, sugars, lipids and nucleic acids, to the extreme that they alter normal functioning, which causes rupture or mutation of DNA, for example [11].

Perspective of the Antioxidant-Human Aging Relations

The theories that explain aging affirm two pillars for the development of this: a genetic basis that characterizes each living being and a non-genetic base that includes free radicals or oxidative stress [11].

During the first steps of knowledge of oxidative stress, Denham Harman of the University of Nebraska proposed in 1956 the direct connection between free radicals and the aging process, noting that life expectancy could increase by reducing the impact of oxidative processes. Thus, it was reported that reactive oxygen species (ROS), among other free radicals, can damage the inner membrane or the mitochondrial genetic sequences which, in turn, leads to an increased production of ROS, thus increasing damage and oxidative stress already present. Consequently, as a result of the loss of balance due to the increased production of oxidants on antioxidants, the mitochondrial genome becomes vulnerable to the attack of free radicals produced by this organelle [10].

During the aging process, the antioxidant protection mechanisms are reduced so that the cells become more susceptible and with it, more prone to their molecules being damaged. These forms of injury are manifested in particular in different substrates, whether carbohydrates, lipids or proteins.

As an outstanding example, it is worth mentioning the case of lipids: during peroxidation, malondialdehyde is produced, a metabolite that, without contemplation, reacts with lipids and proteins, producing formation of so-called Schiff conjugated bases. These finally bind to the fluorescent and insoluble product deposited in the tissues (lipofuscin) and used as a marker of cellular aging [11].

On the other hand, the scientific literature [11] states that longevity seems to be prolonged maintaining a diet that includes adequate levels of antioxidants and with a low-calorie but healthy one; this can be based on the less mitochondrial degradation, cell metabolism and oxygen consumption. A scenario of persistent oxidative stress during old age can lead to alterations in the immune mechanisms. The decrease of antioxidants (such as glutathione) is characteristic in the senescence process, especially in the blood tissue and in some organs. The degenerative changes of the immune system potentially lead to the formation of cataracts and characterize Alzheimer's, Parkinson's or cardiovascular diseases. It is fairly clear from the aforementioned, that a good immune system is associated with health, well-being and longevity [12].

Our Organism Uses the Oxygen-Free Radicals to Our Favor

The respiratory discharge of activated phagocytes does not fill an energetic need, but is directed to the production of oxygen metabolites, some of them true radicals, destined to destroy the phagocytized invading bacteria, thanks to its powerful oxidizing activity. Such an efficient defense must have a price, since the same bactericidal molecules O_2^-, H_2O_2, OH*, and $^1O_2$ can cause damage in the same environment in which the phagocytes act. In fact, the infection is commonly associated with inflammation and the latter type of damage can be related not only to the attacking forces but also to the activity of the defending cells. The respiratory discharge and primary production of the O_2^- is catalyzed by an enzyme in the phagocyte membrane, NADPH-oxidase, which is activated by phagocytosis. The biological importance of NADPH-oxidase is evident in the congenital chronic granulomatosis disease, whose victims suffer from serious and recurrent infections because this enzyme is functionally defective. Activated phagocytes also release unsaturated fatty acids from phospholipids, probably by activation of a latent phospholipase.

The release of arachidonic acid in particular, which is part of phospholipids of cell membranes, is the precursor of the biosynthesis of eicosanoids through cyclooxygenase and lipoxygenase pathways, all of which are promoters of the formation of oxygen free radicals. Thus, prostaglandins, thromboxanes, leukotrienes and other eicosanoid derivatives, promote vasodilation, platelet aggregation and leukotaxis. As there is an attack on the cell membranes, necrosis and release to the environment of oxygen free radicals occurs which can rapidly depolymerize hyaluronic acid and collagen from the intercellular space. In addition, phagocytes release proteolytic enzymes that contribute to the attack of intercellular structures. The beneficial effect of the experimental application of bovine superoxide dismutase directly on the inflamed tissues or injected in the joints inflamed by osteoarthritis, tend to think that the radical superoxide anion is an important part of the inflammatory mechanism. Moreover, it has been shown that the radical superoxide anion can mobilize ferritin iron and hydrogen peroxide can release iron from hemoglobin thereby increasing the potential for formation of the hydroxyl radical, much more aggressive and dangerous than the own superoxide.

Food: Key in Our Health

Health is one of the great topics that occupy the minds of developed societies. However, the accelerated and unconcerned lifestyles of today have led to neglect healthy eating habits, an elementary factor in the prevention of chronic diseases.

According to the WHO, chronic diseases are increasing and, in 2020, will be responsible for 75% of all deaths worldwide. However, the key that helps us to face the risk of suffering from these noncommunicable diseases is within our reach. Experts agree that when humans follow a balanced and constant diet, the body acquires a greater repertoire of defense mechanisms against potential health conditions.

Thus, nutrition along with a healthy lifestyle are the key to prevention of various chronic pathologies. The adjustments in alimentary habits not only take part in health in the short term, but whether a person suffers from chronic diseases depends on these.

In fact, the components that make a diet healthy have always been present in nature (fiber, calcium, soy, fatty acids, antioxidants, among others) but it was not until the last decades that researchers have begun to identify them in isolation and in a structured form. Thus, they managed to determinate in a concrete way the benefits that these components provide to our body, beyond those that are essentially nutritional.

These investigations have been carried out in parallel to a widespread concern about health. Until a few years ago a main concern of people worldwide was the quality or

safety of food availability, but nowadays, the requirement that these products should be also healthy is added.

Promotion of Antioxidants in Food

In the same way that the relationship between oxidative stress and various diseases has been proven, the key role played by the contribution of antioxidants through diet or nutritional supplements in reducing the impact of these same pathologies has also been demonstrated. [14] Hence, nutrition is a key factor in the prevention and treatment of oxidative stress.

In order to reduce oxidative stress, the body can make use of exogenous sources of antioxidants. Thus, flavonoids are among the most popular antioxidants supplements [15,16].

However, flavonoids such as quercetin, myricetin and kaempferol can induce lipid peroxidation together with the breakdown of chains of genetic material through the decrease of nuclear glutathione (GSH) and the reduced activity of glutathione S-transferase (GST) [17]. Being compounds that oxidize easily and therefore acquire the character of oxidants in a high concentration, it is important not to influence excessive consumption of these as this can reverse the originally beneficial effects [18].

It is affirmed that the ingestion of vitamin E, in a diet or supplementation with a high content of γ- and δ-tocopherols, prevents cancer; however, its supplementation with high amounts of α-tocopherol does not possess such property [19]. It has been demostrated that adding vitamin C to an iron therapy for the treatment of anemia helps not only in its absorption, but in the prevention of liver damage due to an excess of iron because of its antioxidant properties [20].

Ferulic acids are also promising antioxidants due to their intracellular and extracellular actions and their variable action against neoplastic, diabetes, cardiovascular and neurodegenerative diseases [21].

Despite not being a true antioxidant, selenium stimulates the antioxidant systems in cells by a positive regulation of the activity of glutathione and glutathione peroxidase, which has been propitious to reduce radiotoxicity as a result of radiotherapy in some clinical trials [22].

The use of antioxidant therapy as a complementary therapy in cancer treatment has had some opposition because it is presumed that it could interfere in the mechanism of action of chemotherapy that as we know, is based precisely on the generation of free radicals to attack the cancerous tumors [23]. However, important recent studies show that the administration of antioxidants has a higher potential both to decrease chemotherapy toxicity and to increase its effectiveness [24]. Despite this, the controversy continues due mainly to the lack of solid evidence that antioxidants consumed in their pure chemical form reduce the incidence of neoplastic diseases, however, their consumption in foods may be more beneficial in this aspect [25].

Nevertheless, the positive repercussion that its administration has on management of oxidative stress present in various diseases is undeniable. This makes the need to rank each type of antioxidant (to know closely its pathophysiological mechanism of action) particularly relevant, in such a way that its use as a complementary medicine in form of drugs that can be prescribed in clinical practice were guaranteed and requiring for it knowledge of its pharmacodynamics and pharmacokinetics (including a good control of its dosage and toxicity [26].

Capacity of Cellular Assimilation of Antioxidants

Although there is a lot of scientific evidence that favors its administration, several studies developed in the last decade do not support the incorporation of antioxidants in diet, especially if we talk about people over 40 years. Therefore, before ruling out their benefit, more clinical studies should be carried out with antioxidants in which the reasons why those studies showed no benefit could be profoundly explored and their design properly revised. As one of these reasons, it could be possible that the endothelial tissue damaged by oxidative stress assimilates antioxidants from the internal environment with same efficacy as normal endothelium.

Recent work in our laboratory (unpublished data) point out the need to metabolically activate the damaged (oxidized) cell in order to get antioxidant substances into its cytoplasm, in particular antioxidants with a high partition coefficient.

The vasoactive response was observed in vitro of three increasing doses of acetylcholine (0.1, 1.0 and 10 µM) of isolated rings of thoracic aorta from rats with endothelial dysfunction in an organ chamber, finding a decrease in the deterioration of vasodilation due to oxidation, when the isolated rings were previously incubated with coenzyme Q10 (antioxidant) for 20 min; additionally, when the temperature of the incubation medium was increased from 36°C (initial) to 39°C (final), the vasodilator response increased further, thus demonstrating its dependence on bath temperature.

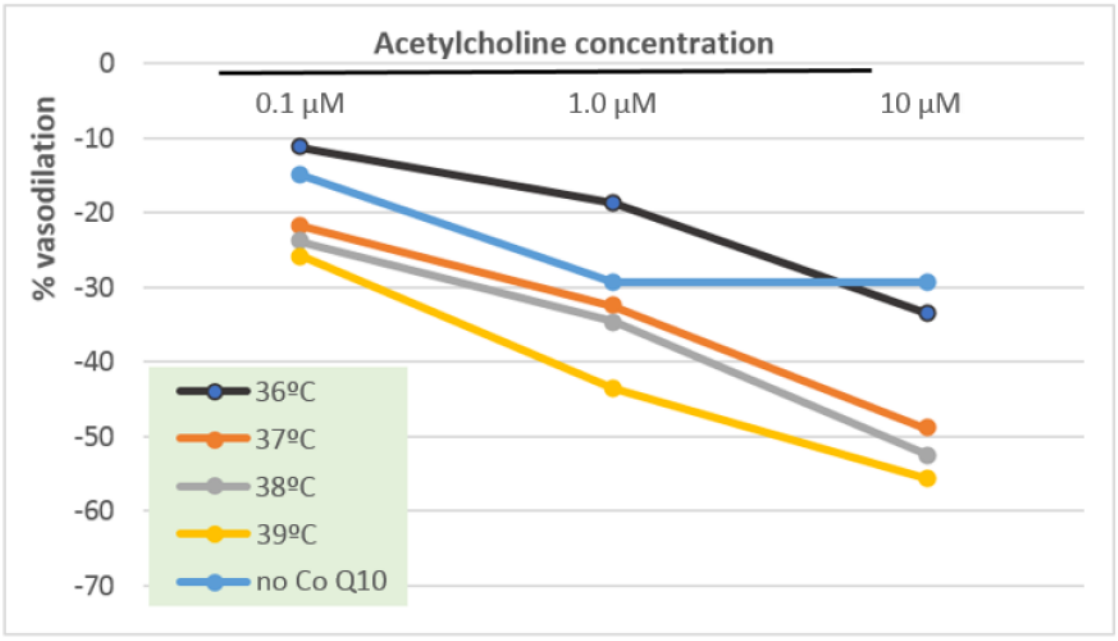

Figure 3. Effect of the incubation temperature (36-39° C) of aortic rings of rats with endothelial dysfunction with coenzyme Q_{10}, on their vasodilator response to 3 doses of Ach previously contracted with phenylephrine.

Conclusions

The increase in the vasorelaxant response, due to the increase in incubation temperature (39 ° C) with Coenzyme Q_{10}, suggests a greater assimilation of the antioxidant by the endothelial cells due perhaps to the increase of its metabolic activity in response to temperature.

This postulate, would lead us to dare to generalize that for a good assimilation of antioxidant in our body, is necessary the increase the metabolic activity of the cells, which can be achieved for example, with the performance of exercise.

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About Authors

Dr. Dr. Azael Paz-Aliaga received his PhD in Physiology and Biophysics from the Venezuelan Institute of Scientific Research (IVIC). Until the year of 1974 he studied Human Medicine at the Faculty of Medicine, National University of San Agustín de Arequipa where he was ad honorem assistant for 3 years in the chair of Physiology at the Department of Physiological Sciences. Shortly after he realized he was interested in research more than in general practice, so he moved to the Peruvian University Cayetano Heredia, joining the Biological Sciences career which he finished in 1977 in the laboratory of Physiology and Biophysics directed by Dr. Carlos Monge Cassinelli. Subsequently, as a grant holder of the Ford Foundation, he completed his Master's degree in Biophysics at the Pontifical Catholic University of Chile in the hands of Dr. Joaquín Luco Valenzuela, graduating from the Peruvian University Cayetano Heredia, in which at age 26 he entered as a teacher. The following year, he is called by his alma mater, the University of San Agustín, to take charge of the Chair of Physiology in charge of Dr. César Delgado Butrón in which he works for 2 years, to then receive a scholarship of the Nations United (UNDP) to do his doctoral studies in the IVIC of Caracas Venezuela. After finishing his studies, he is called to organize and create two faculties of medicine at the Francisco de Miranda University and then at the University de Oriente. After 20 years of traveling through several countries, always doing teaching and research, Dr. Paz-Aliaga returns to his homeland to take over the Chair of Physiology and Biophysics at the University of San Agustin in which he works until today. He creates the Scientific Research and Development Center of the Faculty of Medicine, being named its director. In 2007 he obtained a doctorate in Biological Sciences at the University of San Agustín. In 2010 he co-organized the VIII World Congress of Medicine and Physiology of Height. He was awarded the Hipólito Unanue Prize in 2012. Prize of the Peruvian Society of Physiological Sciences during the 1st International Congress of that society of which he was the organizer. His research interest in oxidative stress has allowed him to win research projects promoted by CONCITEC and UNSA-Investiga. He is the author of several publications including in the American Journal Physiology. The Invitation received by the Pharmacology Laboratory of the Autonomous University of Madrid, has allowed him to create a new novel method for the determination of body oxidation in a drop of blood.

Abel Fabio Cruz Oviedo is a student at the Faculty of Medicine at San Agustín National University Arequipa and he is doing his thesis within the framework of the research project: "Development of a laboratory test to determine the level of body oxidation in a drop of blood by PhD Azael Paz Aliaga". In 2016 he participated as vice president of the Circle of Research and Development in Physiology (CIDEF in spanish), a student association founded with the purpose of promoting and carrying out physiology research in both basic and clinical areas, in the organization of the 1st International Congress of the Peruvian Scientific Society of Physiological Sciences. Currently, he is president of the Circle of Research and Development in Physiology for the period 2018-2019 and is part of the Scientific Research and Development Center (CIDEC in spanish) at San Agustín National University.

Claudia M. Paz-Matellini is an undergraduate student of the Faculty of Medicine of the Peruvian University Cayetano Heredia. She is a member of the Cayetano Heredia Scientific Society of Students of Medicine (SOCEMCH), organization oriented to promote research in areas related to health during undergraduate education. She is also a member of the Student Society of Clinical Sciences (SECC) dedicated to the development of clinical sciences in undergraduate medicine at the Peruvian University Cayetano Heredia.