OXIDATIVE STRESS IN ATHLETES

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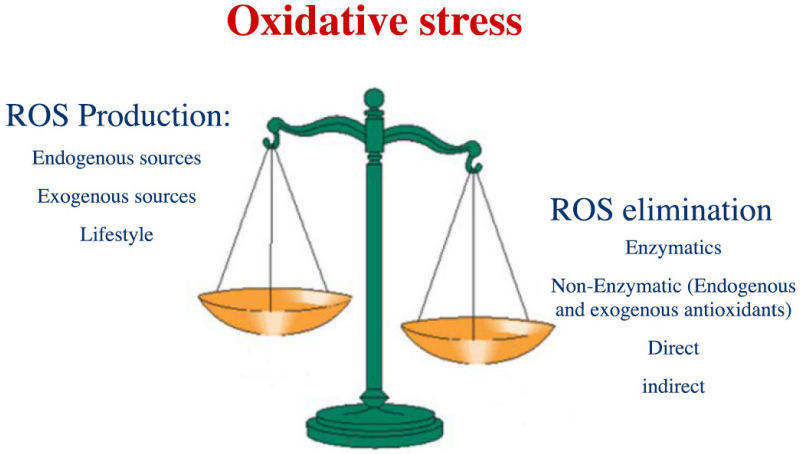
Oxidative stress is the result of an imbalance between the processes of synthesis of reactive oxygen species (ROS) and the processes of their elimination. The balance in favour of synthesis produces an excess of ROS that reacts with the molecular components of cells and fluids, both structural and functional, affecting their capacities, function and cell cycle.

Oxidative stress is associated with the origin or cause of cardiovascular and inflammatory pathologies, metabolic syndrome, diabetes, obesity, cancers and is also present during physical activity and sport, and can affect the results of training, competition and recovery. Such a broad spectrum of influence of oxidative stress requires the need to understand the mechanisms by which reactive species are able to produce these alterations that can lead to pathologies. On the other hand, a balance favourable to the processes of elimination of reactive species also generates a situation of reductive stress, which is also associated with certain cellular dysfunctionalities and can be just as harmful as oxidative stress.

ROS are also signalling molecules that mediate the cellular response necessary for adaptation to changing physiological situations such as hypoxia and reperfusion, physical activity, tissue regeneration, immunity, etc. The combination of these functions suggests that in the pathological situation of oxidative stress, excess ROS production cannot be counteracted by the scavenging processes and a high concentration of ROS is maintained over time; however, when, as a result of high ROS production, the scavenging mechanisms are activated, a transient increase in ROS can occur which is necessary for cell signalling and which is rapidly counteracted by the action of the scavenging processes, which are also necessary to be able to terminate the signal. A balanced situation between production and elimination is appropriate for maintaining a healthy state.



The ROS generated during cellular functioning are the result of the partial reduction of the oxygen molecule giving rise to superoxide anion (O2-), hydrogen peroxide (H2O2) and hydroxyl radical (OH-), including other reactive species that are produced as a result of the reaction of these with cellular components such as lipids, proteins, amino acids, inorganic ions and carbohydrates and that still maintain a high reactivity and capacity to produce free radicals; These include reactive nitrogen species, hypochlorite, peroxynitrite, unsaturated fatty acid hydroperoxides and monosaccharide derivatives.

Reactive species

Radicals		Non-radicals	
O_2^{*-}	Superoxide anion	H_2O_2	Hydrogen peroxide
OH*	Hydroxyl radical	$^1O_2$	Singlet oxide
HO_2*	Hydroperoxyl radical	HOCl	Hypochlorite
NO*	Nitric oxide	ONOO*	Peroxynitrite

The processes that generate ROS are activated during physical activity. The production of metabolic energy at the mitochondrial level appears to be one of the processes that generates the greatest production of ROS. The mitochondrial respiratory chain is where the main reduction of oxygen to water occurs in parallel to the production of metabolic energy in the form of ATP. In this oxygen reduction process, partially reduced molecules such as superoxide anion are generated and from this, hydrogen peroxide can be generated, which can be transformed into the hydroxyl radical. During physical activity, oxygen consumption at the mitochondrial level increases in order to obtain metabolic energy to support the physical activity and thus also the partial reduction of oxygen and the production of superoxide anion.

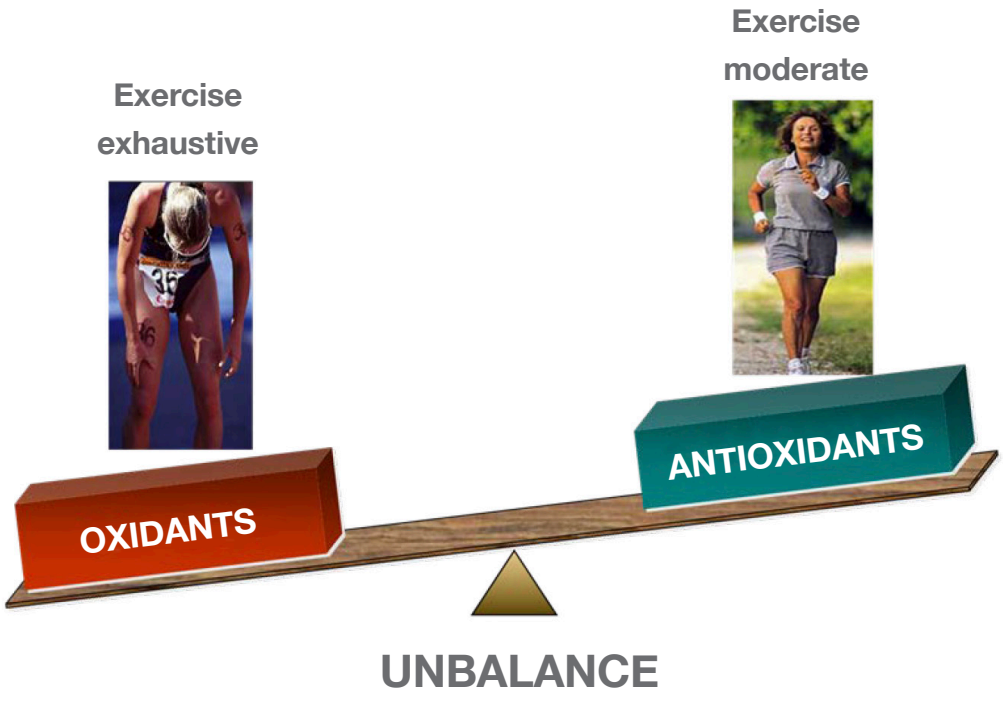
Oxygen transport in the blood is another process in which ROS can be produced. Haemoglobin is the molecule that binds oxygen for transport within erythrocytes. Haemoglobin is an allosteric protein, so its affinity for oxygen changes in the lung environment, which is higher than in the tissue environment (skeletal muscle), which is lower. This change in affinity allows it to take up oxygen in the lung and release it into the tissues. Oxygen travels bound to haemoglobin and haemoglobin can be oxidised, giving up an electron to oxygen which is reduced to superoxide anion. Control mechanisms exist to minimise the effects of this reaction; however, an increase in oxygen transport also leads to an increase in erythrocyte ROS production. During physical activity, oxygen transport in the blood is greatly increased, so ROS production can be increased by this pathway. Other proteins also have the ability to bind oxygen in a similar way to haemoglobin, the so-called haemoproteins, many of them oxidative enzymes such as glucose oxidases, which also generate ROS as a result of their normal activity. Other oxidases such as the flavoproteins xanthine oxidase and oxidonitric oxidase also spuriously generate superoxide anion. These two enzymes may be activated during physical activity and be a source of ROS.

Physical activity is associated with an acute-phase immune response similar to that during an infection. The intensity and duration of physical activity and the repetition of physical activity sessions influence this acute response of the immune system. Neutrophils, mononuclear immune cells and macrophages have reactive species generating systems as an essential part of their immune function. These cells generate hydrogen peroxide and hypochlorite as aggressor molecules against the invader in the case of infections and as part of the degradation systems for tissue renewal of damaged tissues and inflammation. The cellular capacity for ROS production is increased during physical activity, even at the circulating peripheral level, which, together with the increase in the number of these cells circulating in the blood, means that immune cells are an important cause of ROS generation during exercise and also during recovery from exercise.

We must not forget that there are exogenous processes of ROS production that can also influence the overall oxidative balance. Apart from environmental pollution, radioactivity and smoking, solar radiation can be one of the causes of reactive oxygen species generation. Light radiation is capable of activating oxygen to a high-energy state (singlet oxygen) from which direct oxidation reactions of unsaturated fatty acids can occur; in fact, photoxidation is a well-known process in food preservation and discolouration.

ROS scavenging processes are many and varied. Some are endogenous, generated by the organism itself to cope with ROS production processes. These include the synthesis of antioxidant enzymes, such as superoxide dismutase which eliminates superoxide anion, catalase which eliminates hydrogen peroxide, glutathione peroxidase which eliminates peroxides including hydrogen peroxide; the synthesis of proteins such as haptoglobin, ceruloplasmin and ferritin capable of sequestering prooxidant molecules and ions and also the synthesis of low molecular weight antioxidant molecules such as glutathione and xanthine. Other systems are exogenous, made up of low molecular weight molecules with antioxidant capacity that cannot be synthesised by the body: some of them are vitamins such as vitamins C and E, although others have not acquired this status and are also antioxidants such as phenolic and polyphenolic antioxidants. This group of exogenous antioxidants also includes trace elements such as selenium, which are necessary cofactors for the synthesis of antioxidant enzymes.

The different ROS scavenging processes act together and interact with each other in order to balance ROS production and maintain oxidative balance. Physical and sporting activity increases the production of ROS and is also observed to increase the levels of oxidative damage marker molecules. These molecules such as protein carbonyls, malonyl-dialdehyde or 8-hydroxy-guanosine are degradation products of proteins, polyunsaturated fatty acids or nucleic acids that have reacted with ROS. The production of oxidative damage is a function of exercise intensity and duration, so that with exhaustive exercise, ROS production is not counteracted, oxidative imbalance and high levels of oxidative damage occur; with moderate exercise oxidative damage production is lower and an increase in antioxidant potential is observed. Parallel to the increase in oxidative damage induced by physical activity is an increase in the activity and levels of antioxidant enzymes, which are responsible for scavenging ROS and deactivating some of the molecular oxidative damage. This adaptive enhancement of endogenous antioxidant defences as a result of physical activity may be one of the bases for the beneficial health effects observed with regular physical activity.



Dietary supplementation with exogenous nutritional antioxidants is another way to balance the increased production of ROS during and after physical and sporting activity. Increased consumption of these antioxidants provides a decrease in markers of oxidative damage in athletes during and after exercise; however, the dose of antioxidants ingested may also prevent the antioxidant adaptations inherent to the performance of physical activity from occurring. In other words, nutritional antioxidant intake is required at doses that reduce or prevent oxidative damage, but at the same time do not interfere with the body's adaptation to physical activity. The required doses of these antioxidant supplements vary depending on the antioxidant potential of the supplement. It has been shown that consumption of drinks enriched with vitamins C and E, which are also rich in polyphenols, are sufficient to prevent oxidative damage and maintain or even enhance antioxidant adaptation to intense exercise.

Excessive fortification of these functional foods or the consumption of high doses of antioxidant vitamins such as vitamin C has been shown to be detrimental to the antioxidant adaptation of the athlete to training. The intake of antioxidant nutrients in a varied diet, e.g. following the Mediterranean dietary pattern, is usually high and it can be questioned whether additional antioxidant supplements are necessary. In any case, the intake of exogenous antioxidants is an important variable to take into account when planning training and during the development of sports competitions; it is a nutritional tool that can contribute to the maintenance of a good state of physical fitness and sports performance.