

## Bioprotective Anti-oxidants

### Health and Disease

*In this article, Dr Vladimir Badmaev and Dr Muhammed Majeed discuss the delicate balance between life supporting oxidation, the oxidant by-products and means to prevent the damage by free radicals to the body*



If the scientific and medical community has learned one lesson over time it is that patience and persistence are required to better understand the complex relationships between health and disease. Only such in-depth understanding can result in safe and effective prevention and management of a disease. The availability of oxygen to the body is crucial for its proper metabolism, functioning and well-being. This activity, however, does not occur without certain costs. These costs of oxygen utilization are known as oxidant by-products, free radicals, or reactive oxygen species abbreviated as ROS.

### The trade-off effect

Even the proverbial defence of the body against foreign invasion, like microbial infection, carries a high cost to pay and involves a trade-off. In fact, the defence mechanisms naturally produce oxidants which are able to kill the invading bacteria on one hand, yet cause collateral injury to the body cells.

For example, some white blood cells (neutrophils and monocytes) have an enzyme called myeloperoxidase, which is released from storage in those cells when the body is challenged by microbial invasion. This enzyme, together with hydrogen peroxide, has powerful oxidizing potential producing various ROS, e.g. hypochlorous acid, which is a body made antibiotic to control the impending infection. Nitric oxide, another example of ROS, is produced in tissues in response to various stimuli, and also in response to microbial infection. Like myeloperoxidase, nitric oxide plays a major role in the ability of white cells to defend the body against infection.

Perpetual physiological trade-offs are necessary to maintain balance in the body. These are typically handled by the major detox systems of the body, exemplified by a group of enzymes called monooxygenases (isoenzymes of cytochrome P450) and the glutathione system. Mono-oxygenases, found generously in the gastrointestinal tract, the liver and the lungs, oxidize numerous foreign substances, like drugs and environmental pollutants. This breakdown is an essential step that begins the process of eliminating toxins from the body, yet inevitably leads to the formation of ROS.

The backup mechanism used to counter monooxygenases generated ROS is the glutathione system. The glutathione molecule consists of three amino acids, and is designed to absorb the ROS before they do damage to tissues, an outcome known as oxidative stress. This all important interaction of glutathione with ROS is made possible by a selenium requiring enzyme called glutathione peroxidase. Unfortunately

in the process of absorbing ROS, glutathione itself becomes oxidized and becomes toxic to the tissues.

Therefore, glutathione itself is in need of salvaging by the enzyme called reductase. If this mechanism fails, oxidized glutathione is removed from the cell into the interstitial fluid and the blood stream. Thus high levels of oxidized glutathione in the blood are a reflection of oxidative stress in the body. In general, the glutathione status in the body is regarded as a biomarker of well-being and a good predictor of general health.

### **The mediating role**

In view of the above discussed trade-off mechanisms that involve inevitable ROS formation, the mediating role of certain biochemical mechanisms has been found necessary to preserve the integrity of cells and tissues. Glutathione, and its enzymes in the glutathione system, emerge as a proficient mediator between the useful and detrimental functions of oxidation. The particular relationships between ROS representatives, like nitric oxide, and the body's own anti-oxidant, glutathione system, may exemplify the importance of this mediating mechanism.

Nitric oxide is known to play several important physiological roles in the body. For example, characteristics of the so called endothelium relaxing factor, which may prevent cardiovascular disease, are identical to that of nitric oxide. This small compound plays a role in the central control of respiratory process, systemic blood pressure and neurotransmission in neuronal connections primarily by increasing the levels of 'second messenger' molecule or cyclic AMP. As previously mentioned, nitric oxide is also involved in the immune response as a natural antibiotic.

On the other hand, this compound can produce collateral reactions due to its ROS nature, leading to DNA damage and cell death. In experimental conditions it has been shown that the glutathione system, by maintaining adequate levels of reduced glutathione in the cell, is an effective defense mechanism in protecting cells from damage by nitric oxide. Thus the glutathione system indeed mediates and defines what the final role of an important ROS representative, nitric oxide, will be in the body.

### **All is in the balance between pro-oxidants and anti-oxidants**

The importance of both the pro-oxidant and antioxidant processes in maintaining health calls for balance of these two functions in the body. How well our body withstands aging process can be, to a large degree, determined by how well one can maintain the balance between essential pro-oxidant and anti-oxidant reactions.

It seems that the best way to maintain balance between the pro-oxidant and anti-oxidant processes is to support the natural built-in mechanisms to counteract free radicals. These mechanisms are collectively known as the body's anti-oxidant defense system and include, besides the discussed glutathione system, also some important enzymes disabling ROS, i.e. superoxide dismutase (SOD) and catalase.

Preventive steps to maintain the readiness of this defence system should not be based on the 'pill approach' alone. In fact, it would serve us well to also look to the

wisdom of long-standing medical traditions, like that of Ayurveda and related Tibetan medicine. According to this approach none of the techniques devised by man against any disease could be as helpful as the body's own means of fighting disease. These natural means should be supported, during critical moments, by specific treatments. But, in the first place, the individual should be maintained in good shape by: proper nutrition, good life-habits, proper adjustment to the seasons of the year, and awareness of our physical and psychological predispositions.

*To be concluded*

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