

## Oxidative Stress and Aging Prevention

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### DEAR EDITOR,

It has been considered that free radicals might damage to cells by excess reactive oxygen species. Oxidative stress denotes increased free radicals that can damage deoxyribonucleic acid and mitochondria due to excess energy stores. It causes or accelerates many hard curative complications such as diabetes,<sup>[1]</sup> atherosclerosis,<sup>[2,3]</sup> cancer,<sup>[4,5]</sup> hepatic<sup>[6,7]</sup> and kidney damage.<sup>[8-12]</sup> The theory of oxidative stress involvement in aging which was proposed 56 years ago has received high attention with indisputable controversies. It has also been proposed that decreasing oxidative stress-induced cell damage will prolong the life-span of the cells. The antioxidant term is used for a group of chemicals that scavenge or bond the reactive oxygen molecules.<sup>[13]</sup> Antioxidants are critical to cell homeostasis by removing free radicals resulting in protection of cells. They have been shown to be able to prevent or cure a lot of disabling diseases; however, there are controversies about their clinical efficacies of these compounds. In regard to aging, although the current basis of the free radical theory is that oxidative stress leads to cell aging and introduction of antioxidants during periods of oxidative stress will slow down aging, however, the concept of excess oxidants has been shown mostly in *in vitro* studies when cells are stressed by culture media changes and

in clinical trials there are some controversies.<sup>[14]</sup> It has been suggested that antioxidants are not always beneficial; even they can be harmful and can function as pro-oxidant precursors.<sup>[15]</sup> The question is that when antioxidants act properly and why they are not always beneficial in stressed conditions. The answer might be found in the complexity of antioxidant system in human being. Specific vitamins directly reduce free radicals and up-regulate physiologic antioxidant enzymes. Vitamins A, C and E and folate have been shown to be effective supplemental antioxidants in decreasing free radicals *in vivo* and *in vitro*. However the results of the large studies offer little evidence that taking vitamin E, vitamin C, beta-carotene or other single antioxidants protect against chronic diseases such as cancer and atherosclerosis. The findings about combinations are also complicated and not entirely clear.<sup>[13]</sup> It seems that natural whole products such as vegetables and fruits are effectively able to prevent or cure a variety of chronic diseases and prevent aging in clinical trials, but single antioxidants or even their combination do not always act the same. Antioxidants almost certainly evolve as parts of elaborate networks. This means that no single substance can do the work of the whole collection of antioxidants. It might be because the antioxidant system in the body is a complex system and oxidation of one part of this system affects other parts. Hence,

although a single antioxidant might be able to enhance the whole antioxidant capacity, but it might not be able to restore the antioxidants in all parts of this system.<sup>[16]</sup> Furthermore, antioxidants in certain conditions, such as at high doses or in the presence of metal ions can display pro-oxidant activities 47-50. The pro-oxidant or antioxidant activity depends upon antioxidant concentration. For example, quercetin has shown antioxidant activity at low doses (0.1-20  $\mu\text{m}$ ) while at 50  $\mu\text{m}$  or higher concentrations decreased cell survival and viability, thiol content and superoxide dismutase, catalase or glutathione S-transferase activities. It also potentiated the superoxide radical ( $\text{O}_2^-$ ) generation within isolated mitochondria and cultured cells.<sup>[17]</sup> In conclusion free radicals may contribute to aging as well as chronic complications such as diabetes, heart diseases, nephrotoxicity and cancer, however not all antioxidants in all situations are effective in counteracting oxidative stress. Abundant evidence suggests that eating whole vegetables, fruits and grains, which all are rich in antioxidants, usually protect the body against oxidative stress; however, they are not effective equally when taken out of their natural context. The dose of single antioxidants is also important, but the complex antioxidants in their natural context might be less hazardous in high doses.

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