Guest Editorial

The Pro-oxidant and Antioxidant Effects of Vitamin C

The paper entitled, "Vitamin C Exhibits Pro-oxidant Properties," which appeared recently in the journal *Nature* has attracted considerable attention. Authors Podmore, Griffiths, Herbert, *et al* describe the potential pro-oxidant effects of daily supplementation with 500 mg of vitamin C on DNA base oxidation *in vivo*.[1] Their conclusion raises concern because a vast number of individuals regularly supplement their diets with vitamin C in the belief that it has *antioxidant* effects.

The results of the study are paradoxical. The authors found that the oxidation of guanine (a purine) in DNA was significantly reduced after vitamin C supplementation, but the oxidation of adenine (also a purine) was significantly elevated. The oxidation of nucleic acids is indicative of oxidative stress being placed on DNA with the concomitant exposure to reactive oxygen species, such as hydroxyl radical. The oxidation of adenine suggests that vitamin C (supplemented at 500 mg) participated as a pro-oxidant, whereas the reduced level in the oxidation of guanine suggests it acted as an antioxidant.

Is vitamin C a pro-oxidant or an antioxidant? The answer to this question is not available from the data or its interpretation in the paper. The results are contradictory. The failure of the authors to point out this paradox in the conclusions drawn from their work is a significant oversight. They focus solely on the oxidation of adenine, and conclude that a supplement of 500 mg vitamin C acts as a pro-oxidant, while ignoring the observed antioxidant effects with regard to guanine. It is certainly well established that vitamin C can serve as a pro-oxidant through formation of ascorbyl radical. It is also known this radical is quenched by vitamin E to yield tocopheryl radical, which, in turn is reduced by the conversion of glutathione to oxidized glutathione. High doses of vitamin C could increase the concentration of ascorbyl radical that, if not quenched by vitamin E, could result in an increased oxidant burden. The observation in the Podmore *et al* study that guanine oxidation was reduced with supplementation of 500 mg vitamin C strongly suggests this was not the case. The presence of oxidized adenine remains a contradiction.

It has recently been pointed out that adenine is easily oxidized in the extraction procedure of lymphocytes for DNA.[2] Therefore, it is possible that the observed adenine oxidation was not a result of vitamin C intake, but rather a result of experimental techniques used in the extraction of the DNA. Although the study opens the door for more investigation, it should not lead to the conclusion that a supplement of 500 mg vitamin C is dangerous. Until the apparent contradiction in the data relative to the oxidation of adenine versus the antioxidation of guanine is resolved, this paper simply represents an interesting observation in the absence of replication or mechanistic understanding.

by Jeffrey S. Bland, Ph.D.

References

1. Podmore ID, Griffiths HR, Herbert KE, et al. Vitamin C exhibits pro-oxidant properties. *Nature* 1998;392:559.
2. Jenner A, England TG, Aruoma OI, Halliwell B. Measurement of oxidative DNA damage by gas chromatography–mass spectrometry: ethanethiol prevents artifactual generation of oxidized DNA bases. *Biochem J* 1998;331:365-369.

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