Vitamin C Doesn't Cause Cancer!

Balz Frei, Ph.D.
Professor of Biochemistry & Biophysics
Director and Endowed Chair
Linus Pauling Institute

A study in a recent issue of the highly respected journal *Science* reported that lipid hydroperoxides (rancid fat molecules) react with vitamin C to form products that could potentially harm DNA. Although the reaction of these products with DNA was not demonstrated in the study, the authors suggested that vitamin C can form genotoxins (DNA-damaging agents) from lipid hydroperoxides, titling their paper "Vitamin C-induced decomposition of lipid hydroperoxides to endogenous genotoxins." If these reactions were to occur in the human body, vitamin C in the presence of lipid hydroperoxides could potentially enhance mutagenesis and cancer risk. Not surprisingly, the study led to a spate of alarmist media reports warning that vitamin C "can lead to cancer," "Lab study finds vitamin C dangers," and "Vitamin C pills tied to DNA risk."

Such conclusions are unwarranted for a number of reasons. The study was conducted in a test tube (in vitro) under conditions far different from the infinitely more complex conditions in cells and tissues of the human body (in vivo). While the results show some intriguing chemistry of vitamin C, they have nothing to do with biochemistry or biology, and their relevance to reactions occurring in the human body is doubtful. Many reactions of vitamin C that occur in vitro do not also occur in vivo because the physiological environment of the cell and the body contains countless substances that may also react with either vitamin C or lipid hydroperoxides. A reaction observed between two isolated substances in vitro may be "out-competed" by other, more facile reactions in a complex biological system, such as blood, a cell membrane, or the cytoplasm (the fluid inside a cell).

In living organisms, enzymes called glutathione peroxidases efficiently dispose of lipid hydroperoxides. It is important to compare the reaction rate between lipid hydroperoxides and these enzymes with the reaction rate between lipid hydroperoxides and vitamin C. This latter reaction rate was not measured in the
"Science" study, but it was stated that "reactions were performed ... for 2 hours," an extremely long time in biochemical terms. We have done some follow-up experiments and found that the rate of reaction between lipid hydroperoxides and vitamin C is indeed slow. However, enzymatic reactions between lipid hydroperoxides and glutathione peroxidases take a fraction of a second to complete, not hours!

In other studies in my laboratory, we have shown that vitamin C effectively inhibits the formation of lipid hydroperoxides in the first place and also recycles vitamin E, which likewise inhibits the formation of lipid hydroperoxides. Thus, when human plasma is exposed to oxidizing conditions, vitamin C forms the first line of antioxidant defense, and no lipid hydroperoxides can be detected. Lipid hydroperoxides begin to form only *after* vitamin C has been completely exhausted. Lipid hydroperoxides and vitamin C are unlikely to co-exist in human plasma in significant amounts and do not have the opportunity to react with each other, as they did in the "Science" paper. We are now investigating whether adding lipid hydroperoxides to human plasma leads to their decomposition, and if so, whether this process is dependent on vitamin C. Our data thus far suggest that vitamin C *decreases*, rather than increases, the formation of genotoxins from fats under physiologically relevant conditions.

Another criticism of the "Science" study is that it used a concentration of lipid hydroperoxides of 400 µM, which far exceeds any concentrations observed in the body. Studies have shown that in human blood, lipid hydroperoxides may exist in concentrations of about 10 - 40 nM, which is 10,000-fold lower than what was used in the "Science" experiment. In fact, I predict that any individual with 400 µM lipid hydroperoxides in their circulation or tissues would die instantly, thereby forestalling any chance for vitamin C to generate genotoxins and cause cancer!

Given these criticisms, the authors' suggestion that vitamin C "could give rise to substantial amounts of DNA damage *in vivo*" is not justified. The notion that vitamin C increases cancer risk in humans contradicts hundreds of studies that have shown beneficial effects of vitamin C. Decades of clinical experience with vitamin C has demonstrated that it is not only remarkably safe, but also that, far from causing cancer, it protects against cancer. Epidemiological studies have consistently established that the intake of vitamin C-rich fruits and vegetables is associated with a substantially decreased risk of many cancers. These studies do not prove that vitamin C itself lowers cancer risk, and it is likely that the observed benefits are derived from the complex mixture of vitamins, phytochemicals, and fiber present in fruits and vegetables. Nevertheless, it would be nihilistic to ignore the apparent protective effect of vitamin C while waiting for the so-called "gold standard" of clinical trials to produce useful results, particularly considering the extensive supporting evidence from biochemical and animal studies, including animal cancer experiments carried out by Linus Pauling that showed a protective effect of vitamin C.

Based on the "Science" study, the media enthusiastically indicted "high-" and "megadose pills" of vitamin C, as reflected by the headline "Vitamin C pills tied to
DNA risk." In fact, the authors used vitamin C concentrations in their experiments that can be achieved in human plasma with a daily intake of 200 mg. Following conventional advice to consume five servings of fruits and vegetables a day easily provides 200 mg of vitamin C daily. The body does not distinguish between dietary vitamin C and supplemental vitamin C—it's all the same substance, ascorbic acid. Thus, if vitamin C indeed caused cancer, the advice would be not only to stop taking supplements, but also to stop eating vitamin C-rich fruits and vegetables—an absurd recommendation!

Many of the recent sensationalistic media reports on vitamin C have neglected to put results in the proper context, which deprives us of an appropriate perspective. An enormous amount of well-established evidence shows that vitamin C exerts numerous beneficial health effects. Vitamin C-rich foods not only lower cancer risk, but also the risk of heart disease, stroke, hypertension, cataract, and many other diseases. Therefore, the more fruits and vegetables you eat, the better off you are. If you choose to take vitamin C supplements, stick to it, as the scientific evidence indicates that you will do yourself a lot of good and certainly no harm!

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