

Vitamin C and cancer revisited

Balz Frei* and Stephen Lawson

+ Author Affiliations

Linus Pauling Institute, Oregon State University, Corvallis, OR 97331

In this issue of PNAS, Chen *et al.* (1) show that i.p. injection of “pharmacologic doses” of vitamin C decreases the growth and weight of human, rat, and murine tumor xenografts in athymic, nude mice. This work follows a number of articles by the same group, led by Mark Levine at the National Institute of Diabetes and Digestive and Kidney Diseases, showing that millimolar concentrations of extracellular vitamin C kill cancer cells but not normal cells in a hydrogen peroxide (H₂O₂)-dependent manner (1–3). Such millimolar concentrations of vitamin C can be achieved in humans by i.v. infusion but not by diet or supplements (4). Hence, vitamin C is postulated to exert local pro-oxidant effects in the interstitial fluid surrounding tumor cells, killing them or inhibiting their growth, while leaving normal cells intact (1–3).

It is well known that vitamin C, or ascorbic acid, is an effective biologic antioxidant and does not act as a pro-oxidant under normal conditions (5) because it does not readily autoxidize, i.e., react with oxygen (O₂) to produce reactive oxygen species, such as superoxide radicals (O₂^{•-}) or H₂O₂. However, ascorbate readily donates an electron to redox-active transition metal ions, such as cupric (Cu²⁺) or ferric (Fe³⁺) ions, reducing them to cuprous (Cu⁺) and ferrous (Fe²⁺) ions, respectively (Reaction 1). In fact, reduction of copper or iron in the catalytic site of certain enzymes underlies ascorbate's well known biologic function as a co-substrate in procollagen, carnitine, and catecholamine biosynthesis (6). Reduced transition metal ions, in contrast to ascorbic acid, readily react with O₂, reducing it to superoxide radicals (Reaction 2), which in turn dismutate to form H₂O₂ and O₂...

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*To whom correspondence should be addressed at:

Linus Pauling Institute, Oregon State University, 571 Weniger Hall, Corvallis, OR 97331.

E-mail: balz.frei@oregonstate.edu

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From the Cover: Pharmacologic doses of ascorbate act as a prooxidant and decrease growth of aggressive tumor xenografts in mice

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