

# Orthomolecular Oncology Review: Ascorbic Acid and Cancer 25 Years Later

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The effect of ascorbic acid on cancer has been a subject of great controversy. This is a follow-up review of the 1979 article by Cameron, Pauling, and Leibovitz published in *Cancer Research*. In this updated version, the authors address general aspects of ascorbic acid and cancer that have been presented before, while reviewing, analyzing, and updating new existing literature on the subject. In addition, they present and discuss their own mechanistic hypothesis on the effect of ascorbic acid on the cancer cell. The objective of this review is to provide an updated scientific basis for the use of ascorbic acid, especially intravenously as adjuvant treatment in pharmacological nutritional oncology.

**Keywords:** *vitamin C; intravenous ascorbic acid; cancer; tumor growth; nontoxic chemotherapy; antioxidant; prooxidant*

Twenty five years ago, an important review by Pauling, Cameron, and Leibovitz presented the scientific basis to support the use of ascorbic acid (AA) as a therapeutic agent in the treatment of cancer. A group of clinicians failed to reproduce Pauling and Cameron's earlier reports on the therapeutic effect of vitamin C on cancer patients. While this discrepancy generated controversy, the medical establishment rapidly settled the issue without further research and analysis. However, new knowledge on the pharmacokinetics and pharmacodynamics of AA and new clinical data have given a more complete understanding of the critical aspects of AA's therapeutic effect on cancer. This review will summarize these new findings and discuss our own mechanistic hypothesis on the effect of AA in the cancer cell. The objective of this review is to provide an updated scientific basis for the use of AA (intravenous route) as adjuvant treatment for cancer patients.

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## AA Characteristics

### Biochemistry

AA (vitamin C, ascorbate,  $C_6H_{12}O_6$ ) is a ketolactone with a molecular weight of 176.13 g/mL. A basic identified biochemical role for AA is to accelerate hydroxylation reactions in a number of biosynthetic pathways. In many of these reactions, ascorbate directly or indirectly provides electrons to enzymes that require prosthetic metal ions in a reduced form to achieve full enzymatic activity. The best-known biochemical role of ascorbate is that of cofactor for prolyl and lysyl hydroxylase enzymes in the biosynthesis of collagen.<sup>1</sup> The molecular structures of AA and its oxidized form dihydroascorbic acid are similar to that of glucose. Its structure is similar to glucose because of several hydroxyl groups (OH) that are next to each other (see Figure 1).

### Biological Functions

Ascorbate, present in most biological settings (pk = 4.2), is an essential vitamin for humans.<sup>2</sup> Scurvy, the deficiency disease arising from the lack of ascorbate, can reach a life-threatening level and even death.<sup>3</sup> Most mammals synthesize ascorbate from glucose; however, humans and other primates lack the enzyme

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