Vitamin C Metabolites, Independent of Smoking Status, Significantly Enhance Leukocyte, but not Plasma Ascorbate Concentrations

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ABSTRACT

Introduction: The objective of this study was to test the effects of acute doses of vitamin C alone, calcium ascorbate with vitamin C metabolites, and placebo, on total plasma and leukocyte vitamin C concentrations over 24 hours.

Methods: A double-blind, placebo-controlled, four-way crossover study was performed consisting of four separate phases lasting 24 hours each and utilizing one of four oral 1000-mg preparations within each phase (one of vitamin C alone, two separate vitamin C formulations of calcium ascorbate with vitamin C metabolites, and placebo). There was a 7-day washout between phases, and blood draws at seven time points within each phase of the study for a total of 28 serologic measurements per subject and 420 total measurements for the entire clinical trial. Vitamin C concentration in plasma and leukocytes were measured by high-performance liquid chromatography at baseline and at six sequential time periods over 24 hours.

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**Results:** Fifteen healthy males were enrolled, aged 18-39 years; nine were had never smoked and six were chronic smokers. No significant difference in plasma vitamin C levels was observed when comparing the different preparations. However, at 24 hours, calcium ascorbate with metabolites resulted in significantly higher concentrations of vitamin C in leukocytes ($P<0.0001$) compared with vitamin C alone. These results were similar for both metabolite formulations, and independent of smoking status.

**Conclusion:** Regardless of smoking status, vitamin C metabolites may enhance leukocyte utilization of vitamin C itself, despite no consistent difference in plasma levels among the different preparations. A larger clinical investigation is warranted to confirm these preliminary findings, and to determine the clinical relevance of this impact on overall immune function.

**Keywords:** ascorbic acid; calcium threonate; immune function; vitamin C; metabolites; white blood cells

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**INTRODUCTION**

Vitamin C’s antioxidant capacity and stability within the plasma milieu has been previously well described.\(^1\) Past and ongoing randomized trials rely on these specific blood measurements to assist in determining compliance rates and the overall significance or clinical impact of ingesting this specific nutrient compared with other agents.\(^3\) Vitamin C plasma levels are unique compared with the majority of other nutrients due to their sensitivity to physiologic stressors, such as alcohol or smoking, which cause significant and acute reductions in absorption or bioavailability.\(^6\) Plasma values obviously provide some insight and value for researchers and clinicians, but finding other blood and tissue markers that provide greater interpretation of the role of vitamin C in humans appears needed due to generally strict plasma concentration control, and a general lack of therapeutically tangible clinical range limits.\(^8\)\(^9\)

Less understood, but arguably just as critical, is the bioavailability, concentration, and specific function of vitamin C within white blood cells—or leukocytes. Vitamin C concentration in these cells appears critical to their function,\(^10\) where the concentration of vitamin C exceeds the amount found in plasma by as much as 100-fold.\(^11\) Utilizing vitamin C supplementation alone, or alternate formulations of vitamin C, are a plausible initial clinical step into the investigation of ascorbic acid uptake and concentration in cells such as leukocytes, because of its potential role in acute and chronic disease prevention or treatment enhancement.\(^12\)

The objective of this study was to determine plasma and leukocyte vitamin C concentrations over 24 hours after an acute morning 1000-mg dose was administered in the form of vitamin C alone, calcium