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## BASIC SCIENCES RESEARCH

# Effects of High Dose Ascorbate Administration on L-10 Tumor Growth in Guinea Pigs

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Sodium ascorbate is preferentially toxic to tumor cells at high concentrations. It has not been established, however, whether sufficient intra-tumor ascorbate concentrations are safely achievable *in vivo*. We administered sodium ascorbate subcutaneously or orally for eighteen days to Sewall-Wright strain-2 guinea pigs bearing intradermal L-10 hepatocarcinoma tumors. Tumor masses and intra-tumor ascorbate concentrations were determined at necropsy. L-10 cells formed tumors that metastasized to the lymph nodes, with tumor burdens reaching nearly 50 grams in untreated animals. Subcutaneous injections of

ascorbate (500 mg/kg/day) inhibited tumor growth by as much as sixty-five percent, with oral supplementation reducing it by roughly fifty percent. Tumor growth correlated inversely with intra-tumor ascorbate concentration, the latter exceeding 2 mM in some cases. Ascorbate concentrations sufficient to kill tumor cells can be safely achieved in solid tumors *in vivo*, suggesting a possible role for high dose intravenous ascorbate in treating cancer.

*Key Words:* Ascorbic acid, Vitamin C, Neoplasm, Guinea pig

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**M**ost tumors are commonly treated with chemotherapy and radiation, interventions that can compromise the immune system and cause harsh side effects. Nutrient-based strategies that support overall patient health while reducing tumor burden would, if available, provide an appealing alternative to the current standard of care. One such strategy, first proposed by Cameron and Pauling in the 1970's, calls for the administration of vitamin C (ascorbic acid, ascorbate) to cancer patients at doses two to three orders of magnitude above the United States government's recommended daily allowance of the vitamin (1). While a pair of clinical trials conducted at the Mayo clinic suggested that oral administration of vitamin C (10 g/day) did not benefit terminal cancer patients (2, 3), other clinical studies indicate that ascorbate can be effective against tumors when it is administered intravenously (4-7).

The pharmacokinetics of vitamin C are such that intravenous administration may elevate plasma ascorbate

levels one or two orders of magnitude above those attainable with oral dosing. This may be important in light of the fact that, at millimolar concentrations, sodium ascorbate can generate cytotoxic levels of hydrogen peroxide (8, 9). Since tumor cells are often catalase deficient, they are more sensitive to hydrogen peroxide than normal cells. Published reports indicate that intravenous ascorbate protocols can be safely used to achieve plasma ascorbate concentrations equivalent to those necessary to kill tumor cells in culture (10-12). It is not known yet what ascorbate concentrations can be achieved in solid tumors, though it has been observed that vitamin C accumulates in solid tumors at concentrations higher than those in surrounding normal tissue (13, 14). If millimolar ascorbate concentrations can be attained in tumors, vitamin C may prove useful as an anti-cancer agent.

The purpose of the research described in the present report was to simultaneously measure tumor growth rates and intra-tumor ascorbate concentrations in tumor bearing guinea pigs treated with injected or orally administered sodium ascorbate. We chose a guinea pig model because guinea pigs share with primates the inability to produce vitamin C. A transplantable hepatocarcinoma model, the L-10 cell line, is available for use with inbred Sewall-Wright strain 2 guinea pigs. L-10 cells can be injected intradermally to form metastatic solid tumors that are fatal in ninety

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