

CANCER RESEARCH

Inhibition of Human Breast Carcinoma Cell Proliferation by Ascorbate and Copper

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We tested the effect of different concentrations of ascorbic acid (AA), 50, 100, 250 mg/500 mg/dL with copper sulfate (CS), 10 mg/dL on human breast carcinoma (MDA-MB231) cell proliferation *in vitro*. Cell proliferation was measured using a colorimetric assay (Cell proliferation kit II (XTT), Boehringer, NJ). The results of the mean absorbance of the tissue culture at different AA concentrations and a constant CS concentration were as follow: 0.82 ± 0.03 (control, mean \pm SE), 0.64 ± 0.02 (CS above); 0.48 ± 0.03 (50 mg/dL AA), 0.21 ± 0.02 (100 mg/dL), 0.08 ± 0.01 (250 mg/dL AA), 0.60 ± 0.05 (500 mg/dL). These results show that a combination of AA and CS inhibits human breast

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carcinoma cell proliferation *in vitro*. This cell proliferation inhibitory effect is directly proportional to the AA concentration with the exception of the 500 mg/dL AA dose. This chemotherapeutic effect was optimally enhanced when AA was added at a concentration of 250 mg/dL. The AA concentrations of 500 mg/dL had a biphasic effect on tumor cell proliferation probably due to back and forth redox reactions between AA and dehydroascorbic acid in a closed system. This study provides preliminary evidence that AA and SC can be used as biological response modifiers (BRM) for tumor growth inhibition.

Key words: Vitamin C, Koper, Cancer

Effective treatment of solid tumors and their metastases has been extremely toxic and with limited success. Moreover, in the last two decades different combination protocols have not changed disease-free survival and total survival (1, 2). Current cancer therapy focuses on cell killing by directly attacking the cell's reproductive cycle, combining several highly toxic agents that have an array of secondary adverse effects. Little attention has been given to manipulating the local environment where these malignant cells develop as a means of treatment. This environment favors uncontrolled cell reproduction, tumor growth and metastasis probably due to a low generation of oxidative

species (3). Cellular environmental conditions highly depend on intermediary metabolism, which can be influenced by biological response modifiers (BRM). It is known that solid tumor cells have a reduced concentration of catalase; this particular deficiency increases their susceptibility to oxidative reactions (4, 5). Thus, nontoxic chemotherapy consisting of the addition of pro-oxidant cations, vitamins with oxidation-reduction potential and certain fatty acids that may generate cystostatic and/or cytotoxic effects would be expected to produce a significant suppression of tumor growth. In order to explore this possibility, we embarked on preliminary studies utilizing ascorbic acid (AA) and copper as potential BRM for cancer due to their redox potential.

Methods

Human breast carcinoma cells MDA-MB231 were prepared for cell culture using D-MEM/F12 media with antibiotic/antimycotic solution and fetal bovine serum. The cell proliferation study in human breast carcinoma cell lines MDA-MB231, Metastatic to pleura and metastatic to bone, exposed to (CS), 10 mg/dL and different concentrations of AA (50, 100, 250 and 500 mg/dL) was done under normal (ambient, 21%) oxygen conditions. Cell

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