

Clinical Studies supporting the use of Antioxidants during Chemotherapy and Radiation

**POLY-MVA™**



Poly-MVA ORAC Analysis

As you are reading the 5 Clinical Studies below, **pay close attention to the list of Antioxidants that demonstrated substantial clinical benefit.** It is important to understand the superiority of Poly-MVA's liquid crystal polymer when compared to these standard vitamins and compounds.

Data suggests that **polymers like Poly-MVA have greater antioxidant potential than monomolecular structures like vitamins.** Any monomolecular antioxidant absorbs electrons, but it also donates them, acting as a pro-oxidant.

Dr. Garnett's electrochemistry papers demonstrate that the lipoic acid-palladium compound (Poly-MVA) has far better antioxidant potential than any other vitamin tested.

Dr. Antonawich sent samples of Palladium Lipoic Complex to *Brunswick Laboratories in Wareham, Massachusetts*, **for an ORAC analysis**, which measures the ability of a substance to absorb free radicals in comparison to other vitamins.

The results were pretty stunning, as expressed in vitamin E equivalents per gram:

Vitamin A = 1.6

Melatonin = 2.04

Vitamin C = 1.12

Lipoic Acid = 1.4

Vitamin E = 1.0

Poly-MVA (Palladium Lipoic Complex) = 5.65

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Article 1

1: Int J Cancer. 2008 Sep 15;123(6):1227-39.

Impact of antioxidant supplementation on chemotherapeutic toxicity: a systematic review of the evidence from randomized controlled trials.

Block KI, Koch AC, Mead MN, Tothy PK, Newman RA, Gyllenhaal C.

Institute for Integrative Cancer Research and Education, Suite 350, Evanston, IL, USA.

Much debate has focused on whether antioxidants interfere with the efficacy of cancer chemotherapy. The objective of this study is to systematically review the randomized, controlled clinical trial evidence evaluating the effects of concurrent use of antioxidants with chemotherapy on toxic side effects.

We performed a search of literature from 1966-October 2007 using MEDLINE, Cochrane, CinAhl, AMED, AltHealthWatch and EMBASE databases. Randomized, controlled clinical trials reporting antioxidant-based mitigation of chemotherapy toxicity were included in the final tally. Searches were performed following a standardized protocol for systematic reviews. Only 33 of 965 articles considered, including 2,446 subjects, met the inclusion criteria. **Antioxidants evaluated were: glutathione (11), melatonin (7), vitamin A (1), an antioxidant mixture (2), N-acetylcysteine (2), vitamin E (5), selenium (2), L-carnitine (1), Co-Q10 (1) and ellagic acid (1).**

The majority (24) of the 33 studies included reported evidence of decreased toxicities from the concurrent use of antioxidants with chemotherapy. Nine studies reported no difference in toxicities between the 2 groups. Only 1 study (vitamin A) reported a significant increase in toxicity in the antioxidant group. **Five studies reported the antioxidant group completed more full doses of chemotherapy or had less-dose reduction than control groups.** Statistical power and poor study quality were concerns with some studies.

This review provides the first systematically reviewed evidence that antioxidant supplementation during chemotherapy holds potential for reducing dose-limiting toxicities. However, well-designed studies evaluating larger populations of patients given specific antioxidants defined by dose and schedule relative to chemotherapy are warranted.

QUOTES FROM AUTHORS

Co-author **Dr. Robert Newman, Professor of Cancer Medicine at M. D. Anderson Cancer Center** said, "This study, along with the evolving understanding of antioxidant-chemotherapy interactions, suggests that the previously held beliefs about interference do not pertain to clinical treatment."

"This review demonstrates that there is no scientific support for the blanket objection to using antioxidants during chemotherapy. In addition, it also appears that these supplements may help mitigate the side effects of chemotherapy," said **Keith I. Block, MD**, lead author of the study and Medical Director of the Block Center for Integrative Cancer Treatment. "This is significant because it increases the likelihood that patients will be able to complete their treatment."



Article 2

1: Altern Ther Health Med. 2007 Mar-Apr; 13(2): 40-7. Links

Antioxidants and other nutrients do not interfere with chemotherapy or radiation therapy and can increase kill and increase survival, Part 2.

Simone CB 2nd, Simone NL, Simone V, Simone CB.

Simone Protective Cancer Institute in Lawrenceville, NJ, USA.

PURPOSE: Some in the oncology community contend that patients undergoing chemotherapy and/or radiation therapy should not use food supplement antioxidants and other nutrients. Oncologists at an influential oncology institution contended that antioxidants interfere with radiation and some chemotherapies because those modalities kill by generating free radicals that are neutralized by antioxidants, and that folic acid interferes with methotrexate. This is despite the common use of amifostine and dexrazoxane, 2 prescription antioxidants, during chemotherapy and/or radiation therapy.

DESIGN: To assess all evidence concerning antioxidant and other nutrients used concomitantly with chemotherapy and/or radiation therapy. The MEDLINE and CANCELIT databases were searched from 1965 to November 2003 using the words vitamins, antioxidants, chemotherapy, and radiation therapy. Bibliographies of articles were searched. All studies reporting concomitant nutrient use with chemotherapy and/or radiation therapy (**280 peer-reviewed articles including 62 in vitro and 218 in vivo**) were indiscriminately included.

RESULTS: Fifty human clinical randomized or observational trials have been conducted, involving 8,521 patients using beta-carotene; vitamins A, C, and E; selenium; cysteine; B vitamins; vitamin D3; vitamin K3; and glutathione as single agents or in combination.

CONCLUSIONS: Since the 1970s, **280 peer-reviewed in vitro and in vivo studies, including 50 human studies involving 8,521 patients, 5,081 of whom were given nutrients**, have consistently shown that **antioxidants do not interfere** with therapeutic modalities for cancer. Furthermore, **non-prescription antioxidants and other nutrients enhance the killing of therapeutic modalities for cancer, decrease their side effects, and protect normal tissue.** In 15 human studies, **3,738 patients who took non-prescription antioxidants and other nutrients actually had increased survival.**



Article 3

1: Cancer Treat Rev. 2007 Aug; 33(5): 407-18. Epub 2007 Mar 23.

Impact of antioxidant supplementation on chemotherapeutic efficacy: a systematic review of the evidence from randomized controlled trials.

Block KI, Koch AC, Mead MN, Tothy PK, Newman RA, Gyllenhaal C.

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PURPOSE: Much debate has arisen about whether antioxidant supplementation alters the efficacy of cancer chemotherapy. Some have argued that antioxidants scavenge the reactive oxygen species integral to the activity of certain chemotherapy drugs, thereby diminishing treatment efficacy. Others suggest antioxidants may mitigate toxicity and thus allow for uninterrupted treatment schedules and a reduced need for lowering chemotherapy doses. The objective of this study is to systematically review the literature in order to compile results from randomized trials that evaluate concurrent use of antioxidants with chemotherapy.

DESIGN: MEDLINE, Cochrane, CinAhl, AMED, AltHealthWatch and EMBASE databases were searched. Only randomized, controlled clinical trials that reported survival and/or tumor response were included in the final tally. The literature searches were performed in duplicate following a standardized protocol. No meta-analysis was performed due to heterogeneity of tumor types and treatment protocols used in trials that met the inclusion criteria.

RESULTS: **Of 845 articles considered, 19 trials met the inclusion criteria. Antioxidants evaluated were:** glutathione (7), melatonin (4), vitamin A (2), an antioxidant mixture (2), vitamin C (1), N-acetylcysteine (1), vitamin E (1) and ellagic acid (1). Subjects of most studies had advanced or relapsed disease.

CONCLUSION: None of the trials reported evidence of significant decreases in efficacy from antioxidant supplementation during chemotherapy. **Many of the studies indicated that antioxidant supplementation resulted in either increased survival times, increased tumor responses, or both, as well as fewer toxicities than controls;** however, lack of adequate statistical power was a consistent limitation. Large, well-designed studies of antioxidant supplementation concurrent with chemotherapy are warranted.



Article 4

1: Radiat Res. 2009 Aug; 172(2):175-86. Links

Protective effects of dietary antioxidants on proton total-body irradiation-mediated hematopoietic cell and animal survival.

Wambi CO, Sanzari JK, Sayers CM, Nuth M, Zhou Z, Davis J, Finnberg N, Lewis-Wambi JS, Ware JH, El-Deiry WS, Kennedy AR.

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Abstract: Dietary antioxidants have radioprotective effects after gamma-radiation exposure that limit hematopoietic cell depletion and improve animal survival. The purpose of this study was to determine whether a dietary supplement consisting of l-selenomethionine, vitamin C, vitamin E succinate, **alpha-lipoic acid** and N-acetyl cysteine could improve survival of mice after proton total-body irradiation (TBI).

Antioxidants significantly increased 30-day survival of mice only when given after irradiation at a dose less than the calculated LD(50/30); for these data, the dose-modifying factor (DMF) was 1.6. Pretreatment of animals with antioxidants resulted in **significantly higher serum total white blood cell, polymorphonuclear cell and lymphocyte cell counts** at 4 h after 1 Gy but not 7.2 Gy proton TBI.

Antioxidants significantly modulated plasma levels of the hematopoietic cytokines Flt-3L and TGFbeta1 and increased bone marrow cell counts and spleen mass after TBI. Maintenance of the antioxidant diet resulted in **improved recovery of peripheral leukocytes and platelets after sublethal and potentially lethal TBI.** Taken together, **oral supplementation with antioxidants appears to be an effective approach for radioprotection of hematopoietic cells and improvement of animal survival after proton TBI.**

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Article 5

1: Radiat Res. 2008 Apr; 169(4): 384-96. Links

Dietary antioxidants protect hematopoietic cells and improve animal survival after total-body irradiation.

Wambi C, Sanzari J, Wan XS, Nuth M, Davis J, Ko YH, Sayers CM, Baran M, Ware JH, Kennedy AR.

Department of Radiation Oncology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA.

The purpose of this study was to determine whether a dietary supplement consisting of L-selenomethionine, vitamin C, vitamin E succinate, alpha-lipoic acid and N-acetyl cysteine could improve the survival of mice after total-body irradiation.

Antioxidants significantly increased the 30-day survival of mice after exposure to a potentially lethal dose of X rays when given prior to or after animal irradiation.

Pretreatment of animals with **antioxidants resulted in significantly higher total white blood cell and neutrophil counts** in peripheral blood at 4 and 24 h after 1 Gy and 8 Gy. **Antioxidants were effective in preventing peripheral lymphopenia only after low-dose irradiation.** Antioxidant supplementation was also **associated with increased bone marrow cell counts after irradiation.**

Supplementation with antioxidants was associated with increased Bcl2 and decreased Bax, caspase 9 and TGF-beta1 mRNA expression in the bone marrow after irradiation. Maintenance of the antioxidant diet was **associated with improved recovery of the bone marrow after sublethal or potentially lethal irradiation.**

Taken together, **oral supplementation with antioxidants appears to be an effective approach for radioprotection of hematopoietic cells and improvement of animal survival**, and modulation of apoptosis is implicated as a mechanism for the radioprotection of the hematopoietic system by antioxidants.