Antioxidants Enhance the Effectiveness of Cancer Therapies  
(Chemotherapy and Radiation treatment)

By Samantha Coulson PhD

There is extensive discrepancy with regard to prescribing antioxidant nutrients to cancer patients who are undergoing chemotherapy and/or radiation treatment.

Many oncologists advise patients against the use of antioxidant supplements fearing that they will decrease the effectiveness of these standard cancer therapies.

It is commonly believed that antioxidants will exert a protective effect on the cancer cells. However, there are no cancer treatment trials indicating that high doses of multiple dietary antioxidants or their derivatives, when given before therapy and every day thereafter for the entire treatment period have protected cancer cells from radiation therapy or chemotherapy.

Cancer prevention trials with synthetic β-carotene, in which the incidence of lung cancer among male heavy smokers increased by 17%, are often quoted as evidence for the case against supplementing with antioxidants during cancer therapy. People who smoke heavily have a highly oxidative body environment; therefore, if a single antioxidant is given alone, it would itself become oxidized forming free radicals that can increase the risk of lung cancer. Thus, this study is an unsubstantiated claim against the use of antioxidants in cancer patients.

This review by Kedar N. Prasad, puts forward some very strong evidence to support the use of antioxidants in high doses in conjunction with chemotherapy and radiation treatments. He has however, mentioned that endogenously made antioxidants such as glutathione- or antioxidant enzyme-elevating agents are not recommended during radiation or chemotherapy because they MAY protect cancer cells against the cytotoxic effects of therapy.

An argument against this is that cancer patients are typically malnourished and are already prone to significant oxidative stress, with mitochondrial DNA representing a critical target for such oxidative damage. Glutathione modulates mitochondrial function and impacts on apoptosis, and has been shown to protect against chemically induced oral cancer and leukoplakia. A decrease in glutathione peroxidase activity in tumour cells is associated with a marked increase in their ability to undergo necrosis rather than apoptosis.

Selenium, a cofactor to glutathione peroxidase, significantly inhibits the induction of skin, prostate, liver, colon, and mammary tumours. Increasing glutathione levels are essential in maintaining mitochondrial function, detoxifying potentially carcinogenic reactive oxygen species and sustaining the glutathionation conjugation pathway in Phase 2 detoxification.

Excerpts taken from:

Multiple Dietary Antioxidants Enhance the Efficacy of Standard and Experimental Cancer Therapies and Decrease Their Toxicity:
(Kedar N. Prasad, PhD. Integrative Cancer Therapies, 3(4); 2004 pp. 310-322.)

In this review, the author proposes that an active nutritional protocol including high doses of multiple dietary antioxidants and their derivatives (vitamin C, a-tocopheryl succinate, and natural β-carotene), but not endogenously made antioxidants (glutathione- and antioxidant enzyme-
elevating agents) when administered as an adjunct to radiation therapy and chemotherapy, may improve their efficacy by increasing tumour response and decreasing toxicity.

At present, there is no effective strategy to reduce the risk of recurrence of the primary tumour or the development of a secondary tumour induced by treatment agents. In addition, acute damage to normal tissue occurs during radiation therapy or chemotherapy, and in some instances, such damage becomes the limiting factor for the continuation of therapy.

**Recommendation of Antioxidants by Oncologists**

Most oncologists do not recommend antioxidants to their patients during radiation therapy or chemotherapy. Some may recommend a multi-vitamin preparation containing low doses of antioxidants after the completion of therapy. This recommendation may be harmful because like normal cells, cancer cells need certain amounts of micronutrients including antioxidants for growth and survival. Indeed, low doses of individual dietary antioxidants may also stimulate the proliferation of some cancer cells[1] and at low doses, may protect cancer cells against free radical damage produced by chemotherapeutic agents or x-irradiation.

**Experimental Studies showing Effect of Individual or Multiple Dietary Antioxidants on Growth of Cancer Cells**

Antioxidants and their derivatives such as vitamin A (including retinoids), vitamin C, a-tocopheryl succinate, and natural ß-carotene at high doses induce differentiation, proliferation inhibition, and apoptosis depending on dose and type of antioxidant, treatment schedule, and type of tumour cell, without producing similar effects in most normal cells in vitro and in vivo. [17-24]

Treatment of cancer cells with a high dose of retinoic acid, a-tocopheryl succinate, or ß-carotene markedly alters expression of genes, levels of proteins, and translocation of certain proteins from one cellular compartment to another, causing differentiation, proliferation inhibition and apoptosis, depending on the type and form of antioxidant, and treatment schedule and type of tumour. [13], [17], [18]

A treatment time of at least 24 hours is needed to observe a significant reduction in proliferation of cancer cells. Therefore, it is essential that high-dose antioxidants are administered before therapy and every day thereafter for the entire treatment period. A combination of antioxidants is more effective in reducing proliferation of cancer cells than the individual agents. [25, 26]

**Enhancement of Radiation-Induced Damage on Cancer Cells by Dietary Antioxidants**

Dietary antioxidants and their derivatives enhance the effect of irradiation selectively on cancer cells while protecting normal cells against some injuries. For example, retinoic acid enhances the effect of irradiation on tumour cells by inhibiting the repair of potential lethal damage in cancer cells. [29] Vitamin E, when given in a single high dose before irradiation, enhanced the levels of radiation-induced decrease in mitotic accumulation [31] and chromosomal damage [32] in cancer cells.

Dehydroascorbic acid, the major metabolite of ascorbic acid, acts as a radiosensitizer for hypoxic tumour cells in culture. [34] Treatment with dietary antioxidants reduced the effect of irradiation on normal tissues in patients with small-cell lung carcinoma. [38], [39] ß-carotene reduced radiation-induced mucositis without interfering with the efficacy of radiation therapy in patients with cancer of the head and neck. [40]
Enhancement of Chemotherapeutic Agent-Induced Damage on Cancer Cells by Dietary Antioxidants

Several studies have revealed that vitamin C, α-tocopheryl succinate, α-tocopheryl acetate, vitamin A, and carotenoids including β-carotene, enhance the growth-inhibitory effect of most of the chemotherapeutic agents on some cancer cells in culture. For example, vitamin C enhanced the effect of 5-fluorouracil on neuroblastoma cells in culture. It is suggested that multiple antioxidants are also effective in enhancing the effect of certain chemotherapeutic agents on cancer cells.

The combination of two agents causes more cell death than the individual agents alone. For example α-tocopheryl succinate in vivo acts as an anti-angiogenesis agent, whereas radiation or chemotherapeutic agents do not; therefore the combination of α-tocopheryl succinate with these therapeutic agents may be more effective.

Mechanisms of Enhancement of the Effect of Standard Therapeutic Agents on Cancer Cells by High-Dose Dietary Individual Antioxidants

We propose the treatment of tumour cells with high doses of dietary antioxidants before standard therapy, can initiate damage in cancer cells but not in normal cells. Free radicals generated by therapeutic agents, even if completely quenched by antioxidants, become irrelevant because damaged cancer cells suffer further injuries by mechanisms other than free radicals associated with therapeutic agents. The damage to cancer cells is further enhanced by the fact that micronutrients such as retinoic acid can inhibit the repair of radiation damage in cancer cells.

Dosage Of Antioxidants:

The supplemental dose of antioxidants proposed by Prasad for patients undergoing chemotherapy or radiation therapy included:

* 8g of vitamin C
* 800 IU vitamin E as alpha-tocopheryl succinate
* 60 mg of beta carotene.

All micronutrient supplements described should be taken orally and in divided doses because the biological half life of most of them is about 6 to 12 hours. He recommended that the active treatment protocol should be started at least 48 hours prior to standard therapy and should be continued for 1 month after completion of therapy, after which a maintenance protocol can begin.

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2 Van Houten B, Woshner V, Santos JH. Role of mitochondrial DNA in toxic responses to oxidative stress. DNA Repair (Amst). 2005 May 3;


7 Prasad KN. Multiple Dietary Antioxidants Enhance the Efficacy of Standard and Experimental Cancer Therapies and Decrease Their Toxicity. Integrative Cancer Therapies, 3(4); 2004 pp. 310-322.