

Product Monograph for  
 Nutritional Therapeutics, Inc.  
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# Propax Ingredients: Cellular Functional Management in Cancer

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**INTRODUCTION**

This monograph is meant to provide detailed, accurate, and current information pertaining to the safety and efficacy of the individual ingredients contained in Propax. These ingredients have been shown to exhibit anti-cancer properties in various laboratory and clinical settings.

Propax is not intended to be used as a treatment, nor is it marketed as such. It does not replace standard treatments. It is intended as a nutritional adjunct to standard treatment, providing nourishment for normal cells and tissues, and thereby improving a variety of QOL indicators.

**PROPAX™ WITH NT FACTOR®**

**DIRECTIONS:** As a dietary supplement take 2 or 3 packets over the course of the day. The 4 multi-tablets may be taken with or without food and should be consumed at least 20 minutes before or one hour after the softgel fish oil capsule. The softgel fish oil capsule is best taken with food.

Supplement Facts Serving Size 1 Packet		
Amount per 1 Packet	% Daily Value	
Calories	14	
Calories from Fat	10	
Total Fat	1 g	1.5%
Saturated Fat	<1 g	<1.0%
Polyunsaturated Fat	<1 g	*
Monounsaturated Fat	<1 g	*
Cholesterol	6 mg	2.0% †
Carbohydrate	<1 g	<1.0% †
Protein	<1 g	<1.0% †
Vitamin A (as acetate)	4375 IU	87.5%
Vitamin A (as natural beta-carotene)	3750 IU	75.0%
Vitamin C (as calcium ascorbate)	150 mg	250.0%
Vitamin D-3 (as cholecalciferol)	32 IU	8.0%
Vitamin E (as d-Alpha tocopherol)	145 IU	483.0%
Vitamin K (as phytonadione)	2.5 mcg	3.1%
Vitamin B-1 (thiamine HCL)	6.25 mg	416.7%

Vitamin B-2 (as riboflavin/ribose-5-phosphate)	30 mg	1764.7%
Vitamin B-3 (as niacinamide)	60 mg	300.0%
Vitamin B-6 (as pyridoxine/P-5-P)	40 mg	2000.0%
Folic Acid (as folate)	200 mcg	50.0%
Vitamin B-12 (cynocobalamin)	25 mcg	416.7%
Biotin	25 mcg	8.3%
Pantothenic Acid (as d-calcium pantothenate)	25 mg	250.0%
Calcium (as phosphate, ascorbate, citrate, sulfate, borogluconate)	360 mg	36.0%
Iodine (as kelp)	18.75 mcg	12.5%
Magnesium (as carbonate, oxide, glycinate, sulfate)	160 mg	40.0%
Zinc (as methionate)	12.5 mg	83.3%
Selenium (as selenomethionate)	75 mcg	107.1%
Copper (as tyrosinate)	300 mcg	15.0%
Manganese (as glycinate)	2.5 mg	125.0%
Chromium (as nicotinate)	50 mcg	41.7%
Molybdenum (as glycinate)	20 mcg	26.7%
Potassium (as citrate)	12.8 mg	0.4%
<b>NT Factor</b>		
Bioflavonoids (as citrus, rutin, rosehips, quercetin)	165 mg	*
Boron (as calcium borogluconate)	500 mcg	*
L-Carnitine Tartrate	160 mg	*
Grape Seed Extract (Proanthocyanadins)	5 mg	*
Inositol (Inositol/Inositol nicotinate)	25 mg	*
Pantethine (as coenzyme A precursor)	70 mg	*
Vanadium (as vanadyl sulfate)	12.5 mcg	*
Alpha-Keto Glutarate	125 mg	*
Glutathione (as reduced)	5 mg	*
L-Tyrosine	60 mg	*
N-Acetyl-L-Cysteine	25 mg	*
Taurine	110 mg	*
Green Tea Extract	50 mg	*
Horsetail (as silica)	12.5 mg	*
Phosphoglycolipids	160 mg	*
EPA (as Eicosapentaenoic Acid)	180 mg	*
DHA (as Docosahexaenoic Acid)	120 mg	*
INT Factor (as tablet base)	1400 mg	*

**Other Ingredients** - Gelatin (softgel capsule), microcrystalline cellulose, methylcellulose, croscarmellose sodium, vegetable magnesium stearate, silica, water and glycerine.

**NT Factor®** - is a nutrient complex extracted and prepared using proprietary processes. It is composed only of food and food components listed as:

**Phosphoglycolipids** - includes polyunsaturated phosphatidylcholine, glycolipids and other polyunsaturated phosphatidyl nutrients.

**Bifido Bacterium, L. Bacillus, L-Acidophilus** - freeze-dried and microencapsulated in a state of suspended animation with potential to form healthy microflora colonies.

**Growth Media** - foods and bacteria growth factors to support microflora colonies including rice bran extract, arginine, beet root fiber, black strap molasses, glycine, magnesium sulfate, para-amino benzoate, leek, pantethine (bifido growth factor), taurine, garlic, calcium borogluconate, artichoke, potassium citrate, calcium sulfate, spirulina, bromelain, natural vitamin E, calcium ascorbate, oligosaccharides, B-6, niacinamide, riboflavin, inositol, niacin, calcium pantothenate, thiamin, B-12, folic acid, chromium picolinate.

does not contain starch, salt, wheat, dairy products, soy protein, animal by-products, artificial flavoring, artificial coloring, animal stearic acid, digestible plastics, or sugar.

## VITAMIN A (RETINOL)

Plays a crucial role in maintaining epithelial cell integrity by regulating the synthesis of muco- and glyco- proteins in mucous membranes.<sup>1</sup> It supports proper immune function by promoting normal cellular differentiation and growth while effectively inhibiting the growth of transformed cells.<sup>2,3,4,5</sup> This inhibition effect is also shown in transplanted or induced tumors, resulting in slowed tumor growth, and prolonged survival time.<sup>6</sup> Studies have demonstrated that it lowers the recurrence of colon polyps<sup>7</sup> and reduces the risk of cervical cancer by stopping the progression of cervical dysplasia.<sup>8,9</sup> This is accomplished through the inhibition of protein kinase C,<sup>10</sup> a major enzymatic mechanism for neoplastic growth and proliferation. The growth-inhibiting effects of chemotherapeutic agents are enhanced when combined with other antioxidants,<sup>11,12,13,14,15,16</sup> as are the effects of radiation therapy.<sup>17</sup>

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## ALPHA-KETOGLUTARATE

Glutamine derivative has been shown to increase macrophage cytostatic activity and NK cell cytotoxicity in tumor-bearing rats. These results suggest that it increases the immune response to metastasis and chemotherapy.<sup>1</sup> The effect of the tumor burden on host rats with Morris hepatoma 7777 was lessened,<sup>2</sup> and enhanced protection, repair and healing of the intestinal mucosa was also observed.<sup>3</sup>

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## BETA-CAROTENE

A precursor of retinol which has anti-cancer effects independent of its conversion to vitamin A.<sup>1</sup> Low carotenoid activity has been directly linked to increased cancer risk.<sup>2,3</sup> It exerts antigenotoxic actions through antioxidant and immunoregulatory effects, as well as cell signaling mechanisms.<sup>4</sup> It is an efficient free radical scavenger of singlet O, and as such, inhibits free radical damage. It also acts as a cellular sunscreen, protecting against UV radiation effects, including oxidizing damage of singlet O to membranes.<sup>5</sup> The transformation process subsequent to carcinogen exposure has been shown to be inhibited by Beta-Carotene<sup>6</sup> as have the prostaglandin pathways utilized by neoplastic cells for growth and proliferation.<sup>7</sup> In immunological studies, elevations in T-helper and NK cells have been stimulated in a dose-dependent manner.<sup>8</sup> Direct oncogene suppression by beta-carotene was observed after irradiation. Inhibition of transformation due to its ability to induce gap junction intercellular communication was also shown. The effect is apparently triggered by its interaction with genes coding for connexin 43mRNA.<sup>9</sup> In combination with cyclophosphamide chemotherapy, the long term cure rate of adenocarcinoma increased from 0-90%.<sup>10</sup>

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## VITAMIN B-1 (THIAMINE)

B-group vitamin with antioxidant properties. A reversible deficiency leads to increased cell mortality and partial necrosis due to impairment of oxidative metabolism, condensation of chromatin, disorganization of mitochondrial cristae, and impairment of TDP-dependent alpha-ketoglutarate dehydrogenase.<sup>1,2,3</sup> In case-control studies on gastric, colon, rectal, and prostate cancers, high intake of thiamine was associated with a decreased risk.<sup>4,5,6</sup>

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## VITAMIN B-2 (RIBOFLAVIN)

B-group vitamin involved in protein and lipid metabolism, oxygen transport and tissue repair, and catalyzes redox reactions in its coenzyme forms. A deficiency in infancy leads

to impaired iron metabolism resulting in irreversible significant morphological and cytokinetic changes in the small intestine.<sup>1</sup>Supplementation reverses DNA-binding of carcinogen caused by a deficiency.<sup>2</sup> It plays a role in regulating the carcinogenic activity of AFB. An endogenous supply inhibits the Aflatoxin B1 reactions and DNA adduct formation.<sup>3</sup> This effect was attributed to the coenzyme forms, which are an integral part of the microsomal monooxygenase that catalyzes the activation reactions.<sup>3</sup> B-2 prevents an elevation in lipid peroxides,<sup>4</sup> and according to a double-blind intervention trial, high serum levels of B-2 prevent precancerous esophageal lesions.<sup>5</sup> The incidence of esophageal and stomach cancers in rats caused by NSEE was shown to be reduced by B-2 supplementation,<sup>6</sup> as was DNA breaks induced by hepatocarcinogens.<sup>7</sup> Substantial reductions in tumor growth were reported in rats fed supplemental B-2.<sup>8</sup>

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#### VITAMIN B-3 (NICOTINAMIDE)

Nucleotides of this vitamin (NAD, NADP) act as coenzymes in a wide range of enzymatic processes. It assists in repairing DNA breaks by maintaining NAD levels required for poly-ADP repair of DNA damage.<sup>1,2,3</sup> A deficiency of this nutrient prevents the proper repair of DNA breakage. When deficiencies of folate and antioxidants also exist, these are expected to act in synergy with a nicotinamide deficiency, which may result in DNA damage and cancer.<sup>4</sup>

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#### VITAMIN B-6 (PYRIDOXINE)

Pyridine derivative, precursor of pyridoxal phosphate functions as a co-enzyme in numerous metabolic reactions. A deficiency causes a decrease in the methylene-THF pool, which results in uracil incorporation, with subsequent chromosome breaks.<sup>1</sup> An inverse association was shown with prostate cancer, in a case-controlled study.<sup>2</sup> High dietary vitamin B-6 levels are speculated to inhibit tumors by immune enhancement through the mediation of T lymphocyte-dependent mechanisms.<sup>3</sup>

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#### VITAMIN B-12 (CYANOCOBALAMIN)

Precursor of methionine exhibits anti-cancer properties in concert with vitamin C or

folate. A B-12 deficiency may cause chromosome breaks by the same mechanism as folate deficiency, since both B-12 and methylene-THF are required for the methylation of dUMP to dTMP.<sup>1</sup> Deficiencies of folate and B-12 may act synergistically, and supplementation above RDA levels is necessary to prevent chromosome breakage.<sup>2</sup>

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## BIOFLAVONOIDS

Naturally occurring co-factors found in plants which enhance the assimilation and effects of antioxidants. They have been found to be cyto-protective against the toxic effects of chemotherapy.<sup>1</sup> Evidence also exists that they enhance the cytotoxic activity of cancer drugs on drug-resistant tumors. Quercetin has been demonstrated to exhibit these effects.<sup>2,3</sup> Curcumin has been found to reduce the toxicity of adriamycin on cardiac tissues, while many bioflavonoids diminish the inflammatory effects of some cancers.<sup>4,5,6</sup> Phase II detoxification, vital to carcinogen detoxification, is enhanced by several flavonoids.<sup>7</sup>

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## BIOTIN

Coenzyme upregulates the utilization of B-vitamin complexes. Was shown to have a significant effect in protecting against cisplatin-induced nephrotoxicity, while preserving cisplatin's anti-tumor properties.<sup>1</sup> Pretreating tumor necrosis factor (TNF) with biotin-avidin improves its antitumor activity while reducing its systemic toxicity substantially.<sup>2</sup>

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## BORON

Essential trace component of hydroxyapatite, which is the main substance in bone. It is critical for the uptake of calcium into hard tissue. In rat Ehrlich ascites carcinomas, the effect of antitumor drugs was enhanced,<sup>1</sup> survival time increased, and cytotoxic damage was minimized by boron incorporation within those compounds.<sup>2</sup> The growth reducing effects were significantly increased when a combination of boron compounds was administered.<sup>3</sup> In fact, a 25% cure rate and minimized cytotoxic effect in incurable rat glioma was noted.<sup>4</sup> The anti-tumor activity of 2 boronated dipeptides was demonstrated to reduce lymphoid leukemia DNA, RNA and protein synthesis, and this effect was shown to be caused by protein-linked DNA breaks resulting from inhibition of topoisomerase II phosphorylation.<sup>5</sup>

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### VITAMIN C (ASCORBATE)

Enhances immune response to cancer through several mechanisms. It acts in concert with Vitamin E as an antioxidant to prevent lipid peroxidation, exerts antimicrobial action, neutralizes toxins produced by tumorous cells, and activates NK cells.<sup>1,2,3</sup> In addition, it protects against carcinogen-induced chromosomal breakage, and aids in prevention of transformation and progression of normal cells to cancerous cells<sup>3</sup>. In the gastrointestinal tract, it suppresses the microbial-mediated production of the carcinogen N-nitrosamine,<sup>4</sup> and in combination with selenium, inhibits the transformation of nitrates to carcinogenic nitrosamines.<sup>5</sup> Vitamin C has been shown to have a significant protective effect in a variety of non-hormone dependent cancers, including renal and stomach,<sup>6,7,8,9,10</sup> and many studies indicate an enhancement of chemotherapy.<sup>11</sup>

### REFERENCES

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### CALCIUM

Macromineral which participates in virtually every system and organ in the body. A deficiency has been implicated in the development of colon cancer,<sup>1</sup> and its supplementation has been shown to exhibit an inverse association with colon carcinogenesis<sup>2,3,4,5,6</sup> and risk of polyp formation.<sup>7</sup> In fact, a randomized double-blind trial, calcium supplementation was shown to reduce colon cell proliferation<sup>8</sup> as well as the recurrence of polyps by 19% in individuals with previous colon cancer.<sup>8,9,10</sup> Evidence also exists in cell culture systems that it inhibits the oncogenic properties of colon cancer cells.<sup>9</sup> Complex interactions between calcium, phosphorus and vitamin D have been associated with prostate cancer risk.<sup>11,12</sup> In androgen-sensitive prostate cancer cells, the depletion of calcium stores associated with the presence of increased extracellular calcium triggers apoptosis.<sup>13</sup> This mechanism is enhanced by the use of anti-cancer drugs.<sup>14</sup>

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## CARNITINE

Vitamin-like nutrient ubiquitous in animal tissues. It acts as a shuttle to transport long chain fatty acids into the mitochondria for beta-oxidation, and to remove the short and medium chain by-products of metabolism. When an acetyl derivative of carnitine was fed to older rats for a few weeks, mitochondrial function was restored, and oxidant levels were lowered to that of a young rat.<sup>1</sup> In rat models of sarcoma-induced wasting, carnitine lowered plasma triglycerides and inflammatory cytokines. This therapeutic effect may be the result of decreased cytokine production and/or increased elimination.<sup>2</sup> In addition, carnitine reverses the dysfunction of the carnitine system in normal

tissues caused by anticancer drugs, without impairing their therapeutic efficacy<sup>3,4,5</sup>.

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## COPPER

Trace mineral component of several enzyme systems, including SOD. As a co-factor with metalloenzymes and proteins, it participates in the regulation of redox reactions controlling cellular responses to physiological responses. In addition to participating in vitamin C metabolism, it acts in the same way as Mn in reducing cellular oxidative stress.<sup>1,2,3,4</sup>

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## VITAMIN D (CHOLECALCIFEROL)

Group of sterols with hormone-like functions that regulate plasma calcium levels. Low serum vitamin D levels are a risk factor for renal cell carcinoma, which may be prevented through enhancement of intercellular gap junction communication by vitamin D

supplementation.<sup>1</sup> The results of a 19 year prospective study in men show that the risk of colorectal cancer was inversely correlated with dietary vitamin D and calcium.<sup>2</sup> Its administration is associated with inhibitory effects on the growth of in vitro cancer cell lines.<sup>3</sup> In studies of the effects of dietary vitamin D intake on the risk of prostate cancer, it was observed that high intakes of calcium and phosphorus from animal sources suppress Vitamin D production. Additionally, high fructose consumption results in a low plasma phosphate level, which results in higher vitamin D production.<sup>4</sup> Conversely, low serum phosphate levels lead to a lower risk of prostate cancer.<sup>5</sup> A synthetic analog of D<sub>3</sub> inhibits tumor growth in 30% of rats, and prevented the recurrence of these tumors.<sup>6</sup> The combined action of vitamin D and vanadium minimize the incidence of rat liver carcinogenesis induced by diethylnitrosamine and Phenobarbital.<sup>7</sup>

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## DHA (OMEGA-3)

Highly unsaturated essential fatty acid precursor of neurotransmitters. It was found to attenuate linolenic acid induced tumor growth,<sup>1</sup>

and to reduce tumor cell proliferation by inhibiting the immune suppressing effects of PGE<sub>2</sub>.<sup>2</sup> DHA also appears to modulate angiogenesis through the same mechanism. Mice fed DHA showed reduced numbers of blood vessels within tumors, as well as tumor regression.<sup>3</sup> In leukemia cell lines, incorporation of DHA into plasma membranes increases their susceptibility to T lymphocytes.<sup>4</sup> It has been shown to stimulate immunity in cancer patients, most likely through PGE<sub>2</sub> inhibition.<sup>5</sup>

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## VITAMIN E (D-ALPHA TOCOPHEROL)

Its role as an antioxidant free radical scavenger has been well documented.<sup>1,2</sup> It has been shown to stabilize cell membranes by the interaction of its phytyl side chain with the fatty acyl chain of polyunsaturated phospholipids.<sup>3</sup> It inhibits the synthesis of prostaglandins and thromboxanes, and prevent platelet aggregation. Excess prostaglandins have been shown to suppress the immune system through adenylate cyclase activity. Alpha tocopherol reduces the adenylate cyclase response to PGE<sub>1</sub> and PGA<sub>2</sub> through a non-antioxidant mechanism.<sup>4</sup> In addition, it was found to induce TGF-beta induced apoptosis of human breast cancer cells.<sup>5</sup> A significant inverse relationship was found between Vitamin E intake and the incidence of prostate<sup>6,7</sup> breast and colon<sup>8</sup> cancers. Mortality from prostate cancer fell 41% in a supplemented group.<sup>9,10</sup> It has both a synergistic and protective effect in chemotherapy, where it has a

demonstrated benefit in cardiovascular protection, enhancement of cell killing effect, and diminished drug toxicity.<sup>11</sup> Data show that it enhances the effect of Tamoxifen through anti-inflammatory effects.<sup>12,13,14</sup> It plays an important role in preserving the anti-tumor function of Omega-3 EFAs.<sup>15</sup>

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## EPA (OMEGA-3)

Essential highly unsaturated fatty acid precursor of DHA, which has been shown to provide a protective effect against cancer in populations with fish-based diets.<sup>1</sup> In animal studies, it has been found to reverse the tumor growth promoting effects of linoleic acid (omega-6) by inhibiting its uptake through the mediation of a Gi protein coupled signal transduction pathway.<sup>2,3,4,5,6</sup> The resulting inhibition of cell division is linked to the inhibition of translation initiation<sup>1</sup>. Reduced tumorigenic activity was also observed to be due in part to an alteration in prostaglandin synthesis.<sup>7,8</sup> The induction of leukemia cell death through the uptake, activation and incorporation of EPA into lipids has also been demonstrated.<sup>9</sup> EPA modulates the inflammatory response which leads to weight loss in cancer patients. After EPA supplementation, weight was stabilized, and a median weight gain of .5 kg was noted after 4 weeks.<sup>10</sup>

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### FOLIC ACID (FOLATE)

A B-vitamin which interacts with B-12 in the metabolism of amino acids, and purines. Enhances tissue and cell repair through synthesis of RNA and DNA. Studies have shown an inhibition of tumor growths and lower mortality in folate-supplemented rats. A folate deficiency causes chromosome breaks through the deficient methylation of uracil to thymine, resulting in the incorporation of high uracil levels in human DNA.<sup>1,2</sup> Folate doubled the tumor suppression of cyclophosphamide.<sup>3</sup> It has also been associated with a lower incidence of cervical cancer,<sup>4</sup> a decrease in new colorectal adenoma formation,<sup>5,6</sup> as well as lower risk of colon cancer<sup>7,8</sup>.

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### GLUTATHIONE

A derivative of methionine which combines with selenium to form glutathione peroxidase (GP). In addition to its membrane-protective role of inhibiting lipid peroxidation,<sup>1</sup> it has been shown to have a synergistic effect with chemotherapeutic agents through interactions with antioxidants,<sup>2,3,4,5,6,7,8,9,10,11,12,13</sup> and to both enhance the therapeutic effects and diminish the toxic side effects of cisplatin.<sup>14</sup>

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### GRAPE SEED EXTRACT

Proanthocyanidin derivative of plant flavonoids. Has been found to improve the toxic

effects of chemotherapeutic agents on normal cells through upregulation of anti-apoptotic protein Bcl-2 expression.<sup>1</sup> Experiments have shown that it provides significant protection against free radicals, lipid peroxidation, and DNA damage. It has been shown to exhibit substantial anti-tumor properties against human breast, lung, and gastric adenocarcinoma cells,<sup>2</sup> as well as carcinogen-induced epidermal tumors.<sup>3</sup>

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## GREEN TEA EXTRACT

Catechin type of polyphenol which acts as a potent antioxidant in combination with vitamin E to prevent oxidative damage to cellular membranes.<sup>1</sup> It has been shown to mediate the cell-signaling processes leading to cell proliferation, by inhibiting the S-phase entry of epidermal growth factor in breast cells.<sup>2</sup> Mice implanted with non-Hodgkins Lymphoma were 50% less likely to experience growth of this tumor if GTE was administered concurrently.<sup>3</sup> GTE reduces tumor-induced inflammation by inhibiting both TNF-alpha and PGE2.<sup>4</sup> Glutathione S-Transferase activity was increased 27 times subsequent to GTE supplementation in liver detoxification of chemotherapeutic agents.<sup>5</sup>

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## INOSITOL

Carbohydrate found in both plant and animal tissues. Phosphorylated derivatives are synthesized and hydrolyzed in the nucleus and participate in cellular signaling mechanisms.<sup>1</sup> It has been shown to exhibit anti-tumor and anti-cell proliferative effects in several experimental models.<sup>2</sup> Dietary myo-inositol intake reduced lung tumor formation by 79%.<sup>3</sup>

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## IODINE

Trace mineral component of thyroid hormones which influence a multitude of metabolic processes. A higher incidence of gastric cancer has been observed in iodine-deficient populations,<sup>1</sup> and thyroid autoimmune diseases were markedly increased in children with poor iodine intake, who were exposed to low level radiation.<sup>2</sup> In rats, chronic iodine deficiency leads to thyroid cancer within 18 months.<sup>3</sup> Iodine has an antioxidant function in the stomach, breast, and thyroid, where these tissues share an iodide concentrating ability combined with a peroxidase activity, which transfers electrons from iodides to the oxygen of hydrogen peroxide. This process in turn protects the cells from damage caused by lipid

peroxidation.<sup>1</sup> Iodine administration has been shown to be preventive against stomach, breast, and thyroid cancers.<sup>1,2,4</sup> Lower T3 levels have been found in breast cancer patients, and these correlate to selenium status. Selenium is thought to act synergistically with iodine through the activity of the selenoenzyme iodothyronine deiodinase<sup>4,5</sup>. Iodine deficiency has also been linked to goiters both in humans and animals. There is a higher risk of thyroid cancer in humans with goiter. Low dietary iodine apparently leads to a hypersecretion of thyroid-stimulating hormone, resulting in goiter, and subsequent development of thyroid carcinoma.<sup>3,6,7</sup> Iodine also protects from radiation injury to the thyroid gland. In mice, a significant decrease in 125 I uptake by the thyroid occurred following dietary iodine supplementation. The degree of suppression was dosage-dependent.<sup>8</sup> Similar protective effects were seen in rats<sup>9</sup> and humans.<sup>10</sup>

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the accidental uptake of radioiodine]. *Radiobiologia.* 1992 Jan-Feb;32(1):30-4. Russian.

## VITAMIN K (PHYTONADIONE)

Coenzyme which plays key role in the synthesis of blood clotting components. In combination with Vitamin C, has been shown to inhibit tumor growth, enhanced the effects of both chemo and radiotherapy.<sup>1,2</sup> Studies have shown that it induces tumor cell death.<sup>3,4</sup>

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## LACTOFERRIN

An iron-binding glycoprotein implicated in the control of immune functions and cell proliferation, apparently exerts its effects depending on target cell phenotype<sup>1</sup> by selectively binding to various glycosaminoglycans.<sup>2</sup> These effects occur independently from its iron-binding role.<sup>3</sup> Several studies show a strong chemopreventive action of lactoferrin on colon carcinoma development.<sup>3,4,5,6,7</sup> T,B, and NK cell levels were all found to increase, and an enhanced production of cytokines was noted.<sup>4</sup> In addition, a significant reduction in small intestine polyps was seen in mice.<sup>7</sup> Other results show an enhancement of GI wound healing, as well as antitumor effects against esophageal, lung, breast, and pancreatic cancers.<sup>1,2,3,6,8</sup>

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## MAGNESIUM

Macromineral functions in conjunction with calcium to maintain bone health. Along with potassium, it is the main intracellular cation, and is crucial for maintaining cellular integrity. It is used in conjunction with cisplatin chemotherapy in order to neutralize the substantial hypomagnesemia caused by cisplatin's nephrotoxic side-effect.<sup>1</sup> In animal studies, its intake is reported to inversely correlate with cancer incidence and mortality.<sup>2</sup> Mg depletion has been shown to be present in about 50% of ICU patients, who also have higher morbidity and mortality rates than patients with normal Mg levels.<sup>[3]</sup> Its deficiency may also result in hypokalemia and hypocalcemia.

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## MANGANESE

Trace mineral component of many enzyme systems involved in energy production,

as well as SOD, which is a potent free radical scavenger. MnSOD is the predominant intracellular inhibitor of free radicals and superoxide, and as such, reduces oxidative stress, resulting in decreased DNA damage, carcinogenesis, hepatotoxicity and cytotoxicity.<sup>1,2,3,4</sup> Acting synergistically with a variety of antioxidants, it may act paradoxically to potentiate the intracellular oxidizing effects of anticancer drugs such as adriamycin.<sup>5,6,7,8,9,10,11</sup> Therefore, it may act either as an oxidant or antioxidant, which may explain its protective effects on normal cells, and cytotoxic effects on cancer cells.

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## MOLYBDENUM

Essential ubiquitous trace mineral required for purine metabolism. In a 6 year human trial of multiple vitamin and mineral supplementation in 3318 patients with esophageal dysplasia, an 8% reduction in esophageal/gastric cancer mortality was observed.<sup>1</sup> In rats, it was found to decrease the incidence of carcinomas and papillomas of the stomach and esophagus.<sup>2,3</sup> Its derivatives have been shown to exhibit antitumor activity,<sup>4</sup> and the Mb enzyme xanthine dehydrogenase plays a palliative role in chemotherapy.<sup>5</sup>

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## N-ACETYLCYSTEINE (NAC)

An aminothioli precursor of cysteine and glutathione which has been shown to possess substantial antioxidant and chemopreventive properties in the prevention of lung cancer.<sup>1</sup> Its antimutagenic and anticarcinogenic effects are thought to stem from multiple mechanisms, including its nucleophilic and antioxidant activities, intracellular reduced GSH precursor, detoxification modulation, and DNA repair processes.<sup>2</sup> These effects have also been demonstrated to prevent cellular apoptosis.<sup>3</sup> Its administration has been found to reduce the toxicity of anticancer drugs without interfering with their therapeutic benefits,<sup>4,5,6</sup> and its topical

application may protect from the adverse effects of radiation therapy.<sup>7</sup>

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## NT FACTOR™

Proprietary tableting base and nutrient delivery system of Propax™. It has been shown in clinical settings to exhibit therapeutic effects which are far greater than those which could be attributed to the sum of the effects of the individual components.<sup>1</sup> The combined effect is thought to stem primarily from synergistic interactions between the various ingredients in enhancing immune and mitochondrial functions, both directly, and through repairing and improving the function of the colonic mucosa.<sup>2</sup>

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## PANTETHINE

Coenzyme derivative of pantothenic acid, and precursor of cysteamine forms the active thiol component of the CoA molecule. Cysteamine derivatives have been shown to have antimelanoma properties,<sup>1</sup> which are manifested through initial cytostatic inhibition of DNA

synthesis, and subsequent cytotoxic effects.<sup>2,3</sup> Cysteamine itself crosses the blood-brain barrier, and was found to arrest cell proliferation in all phases of the cell cycle in neural cell lines.<sup>4</sup> A portion of the cells succumbed to early apoptosis. Its anti-proliferative effects are thought to result from thiol-induced H<sub>2</sub>O<sub>2</sub> production.<sup>5</sup> Ethylol, a cysteamine analog, has demonstrated broad-spectrum cytoprotection of normal tissues against the toxic effects associated with chemotherapy and radiotherapy, while preserving the antitumor effects of these treatment modalities.<sup>6,7</sup> Pantethine itself was shown to provide the greatest protection against the hepatotoxic effect of CCl<sub>4</sub>.<sup>4,8</sup>

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## PANTOTHENIC ACID

B-group vitamin and precursor of pantethine and CoA, is significantly decreased in the livers of tumor-bearing mice.<sup>1</sup> Irradiation

inhibits mitochondrial electron transport by causing oxidative damage. In Ehrlich ascites tumor cells, the damage was reversed by pre-incubation with pantothenate, which increases their glutathione content by 40%. This increase results from higher cellular CoA levels which protect against cellular damage by removing free radicals and diminishing lipid peroxidation through the activity of glutathione peroxidase and phospholipid hydroperoxide glutathione peroxidase,<sup>2</sup> as well as promoting repair mechanisms, such as phospholipid synthesis.<sup>3</sup> Pantothenic acid protects from the toxic effects of chemotherapy. In guinea pigs, it was observed that it prevents deafness induced by cisplatin.<sup>4</sup>

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## PHOSPHOGLYCOLIPIDS

Structural components of cell membranes found naturally in soy lecithin, composed of EFAs. They have been found to increase the absorption and delivery of antioxidants into cells when they are incorporated with them in nutrient complexes.<sup>1</sup> Their role in strengthening cell membranes may lead to a lower incidence of cancer,<sup>2</sup> and their saponin components have been shown to provide both antioxidant and cell-membrane protective effects on normal cells.<sup>3</sup> Their destructive effects on abnormal cells may be linked to their binding selectively to cancer cells, due to the higher cholesterol content of some cancer cell membranes.<sup>4,5</sup> In addition, they have been shown to provide both humoral and cellular immune enhancement.<sup>6,7,8,9</sup> In a Harvard study report to NTI,<sup>10</sup> it was noted that the rapid cell division and growth seen in many tumors leads to a different membrane phospholipid content from

normal cells.<sup>11,12,13,14,15</sup> Higher phosphatidylcholine transfer rates in tumor cells results in the depletion of phospholipids from normal membranes.<sup>16,17,18,19,20,21</sup> Lower levels of phospholipids in normal cells reduce membrane integrity and transport processes, and enzyme activity.<sup>22,23,24,25,26,27,28,29</sup> This may in turn lead to lower energy levels and increased fatigue.<sup>30,31,32,33,34</sup> NT Factor™ phosphoglycolipid enhances cell maintenance integrity and metabolic functions of normal cells. Rats fed a diet containing NT Factor™ showed a 20% improvement in mitochondrial function over rats fed an identical diet without NT Factor™.<sup>1</sup> The high concentration of lysolecithins in NT Factor™ as compared to soy-derived phosphatidyl-choline may explain the greater biological activity of NT Factor™. Lysolecithin derivatives disrupt cancer cells at concentrations that do not affect normal cells.<sup>35,36,37,38</sup>

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## POTASSIUM

Main intracellular cation electrolyte maintains cellular fluid balance along with extracellular sodium. Electrolyte depletion results from the cytotoxic effects of chemotherapy.<sup>1</sup> Hypokalemia is also caused by ifosfamide and cisplatin-induced renal injury.<sup>2</sup> Potassium supplementation was shown to reverse these conditions, as well as anthracycline-induced cardiac abnormalities observed in the treatment of acute lymphocytic leukemia.<sup>3</sup> Hypokalemia occurs subsequent to magnesium deficiency, which has been determined to be present in approximately half of ICU patients.<sup>4</sup>

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## SELENIUM

An essential trace mineral and an antioxidant component of glutathione peroxidase (GP), it plays an important role in the metabolism of carcinogens, DNA adduct formation, and cellular proliferation.<sup>1</sup> GP is responsible for destroying lipid peroxidation, and acts synergistically with Vitamin E to protect cells and membranes from oxidative stress. It inhibits prostaglandin production through regulation of adenylate cyclase.<sup>2,3,4,5</sup> Various studies establish a correlation between selenium supplementation and favorable outcomes of cancer treatments.<sup>6,7</sup> In clinical trials, overall cancer mortality was reduced 21% and prostate cancer mortality by 65% in selenium treated patients.<sup>8,9</sup> It has also been shown to enhance the effects of chemotherapy<sup>10</sup>. In a randomized controlled trial, a 48% reduction in cancer mortality was observed.<sup>11,12,13</sup>

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## TAURINE

Amino acid and cyteamine derivative modulates calcium ion levels, and parallels the effects of magnesium.<sup>1</sup> It is thought that it acts as an antioxidant in protecting neurons from free radical damage. It has also been shown to reduce inflammation in neurodegenerative processes.<sup>2</sup> A taurine derivative inhibited the growth of rat metastatic colorectal tumor cells in a dose-dependent manner, both *in vitro* and *in vivo*.<sup>3</sup> It reduced the severity of renal dysfunction and lowered the cytotoxicity caused by ifosfamide therapy, while maintaining the antitumor properties of the drug.<sup>4,5,6</sup>

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## VANADIUM

Ubiquitous trace element involved in redox reactions. In synergistic combination with

vitamin D, it provides protection against single strand DNA breaks caused by DEN, in rat liver cells.<sup>1</sup> It also reversed the DEN-induced alterations in hematological indices. Protection against rat liver carcinogenesis was increased, as was survival time.<sup>2</sup> This effect is thought to be mediated an increase in phase II conjugating enzymes which in turn reduce the intracellular concentration of reactive intermediates.<sup>3</sup> A similar protection mechanism was found against DMBA-induced mammary carcinogenesis in rat livers.<sup>4</sup>

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## ZINC

Essential trace mineral component of over 20 enzyme systems, including SOD. In addition to protecting cellular integrity in the same manner as Mn and Cu,<sup>1,2,3,4</sup> it maintains chromosomal integrity through phosphorylation of thymidine, and DNA binding proteins with zinc fingers.<sup>5</sup> It promotes the proper function of p53, which prevents mutations by inhibiting cell division and inducing apoptosis in compromised cells. This zinc protein was observed mutated in 50% of human tumors.<sup>6,7</sup> Zinc deficiency leads to chromosome breaks due to increased oxidative damage, loss of Cu/Zn SOD activity or a DNA repair enzyme.<sup>8,9,10,11</sup> It is also linked to esophageal cancer,<sup>12,13</sup> as well as immune dysfunction.<sup>14,5</sup>

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