

Oxidative Stress

Protocols

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Ingredients Dosage Rationale Reference
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Carcinogenesis is a complex process. In order to fully address cancer, one needs to consider a minimum of four functional areas: oxidative damage, immune system function, chronic inflammation, and detoxification. Hormonal balance must also be addressed for hormone-related cancers.

Integrative cancer support is available to address each of these areas and can be used as an adjunct to conventional therapies.

Coenzyme Q10 (CoQ10) (ubiquinone) Natural form High purity	300 mg, twice daily Under doctor's supervision, may be used concurrent with conventional therapies.	Reduced CoQ10 levels have been linked to many chronic disease states. Cancer patients demonstrate significant CoQ10 deficiency (clinical data) ¹ Well-documented antioxidant and free radical scavenger Protects mitochondrial DNA, protein, and lipids from oxidative damage Slows tumor growth in cancer patients ² Significantly increases levels of IgG and T4-lymphocytes (clinical study) ³ Increased cancer patient survival on an exploratory basis for periods of 5-15 years ⁴ To be effective, supplemental CoQ10 must cross the blood-brain barrier and increase cellular CoQ10 concentrations	 3. 4. 	Portakal O, et al. Coenzyme Q10 concentrations and antioxidant status in tissues of breast cancer patients. Clin Biochem. 2000 Jun; 33(4):279-84. Lockwood K, et al. Partial and complete regression of breast cancer in patients in relation to dosage of coenzyme Q10. Biochem Biophys Res Commun.1994 Mar30; 199(3):1504-8. Folkers K, et al. The activities of coenzyme Q10 and vitamin B6 for immune response. Biochem Biophys Res Commun. 1993 May 28; 193(1):88-92. Folkers K, et al. Survival of cancer patients on therapy with coenzyme Q10. Biochem Biophys Res Commun. 1993 Apr 15; 192(1):241-5.
Reduced Glutathione (GSH) 10% Anthocyanins Blend: Beet Bilberry Black Currant European Elder L-Cysteine	Take with water on an empty stomach, 1-3 times daily. 400 mg 200 mg 80 mg Under doctor's supervision, may be used concurrent with conventional therapies.	 Reduced glutathione¹ Powerful antioxidant Essential to cellular detoxification and production of coenzymes Recycles antioxidant vitamins E and C Anthocyanins² Involved in free radical scavenging, anticarcinogenesis, and induce of apoptosis of tumor cells² Blend³ Enhances glutathione levels (clinical study) Protects against the toxic effects of cytotoxic agents and multi-drug resistance Inhibits tumor growth (in colon cancer patients and <i>in vitro</i>) Causes tumor regression May reverse weight loss (cachexia) Statistically significant improvements in Karnofsky's scale 	 3. 	Sung JH, et al. Protective effect of glutathione in HIV-1 lytic peptide 1-induced cell death in human neuronal cells. <i>J Neurovirol</i> . 2001 Oct;7(5):454-65. Hou DX. Potential mechanisms of cancer chemoprevention by anthocyanins. <i>Curr Mol Med</i> . 2003 Mar;3(2):149-59. Garcia-Giralt E, et al. Preliminary study of GSH L-cysteine anthocyane [brand name] in metastatic colorectal carcinoma with relative denutrition. Presented at the European Cancer Conference. September 14-18, 1997. <i>Eur J Cancer</i> . 1997:33(sup 8).



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Fermented Papaya Preparation (FPP)	6-9 g daily, for the first 2-3 days, then 3 g daily thereafter. Take in between meals. Dissolve in mouth. Do not take with water. Do not eat or drink anything 5 minutes before or after.	Additional Oxidative Stress Reduction for Maximum support • Potent antioxidant and free radical scavenger (laboratory study) ¹ • Decreases lipid peroxide levels and increases superoxide dimutase (SOD) activity ¹ • Increases immunostimulatory activity in macrophages ² • In the presence of infection, enhances nitric oxide synthesis, thereby improving host immune defenses ²	1. Imao K, et al. Free radical scavenging activity of fermented papaya preparation and its effect on lipid peroxide level and superoxide dismutase activity in iron-induced epileptic foci of rats. Biochem Mol Biol Int. 1998 Jun;45(1):11-23. 2. Rimbach G, et al. Nitric oxide synthesis and TNF-alpha secretion in RAW 264.7 macrophages: mode of action of a fermented papaya preparation. Life Sci. 2000 Jun 30; 67(6):679-94.



Cancer Treatment Adjuvant Immune System Enhancement

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Immune System Enhancement

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Ingredients	Dosage	Rationale	Reference
Blend of: Pancreatic enzymes 10X (full strength, undiluted) Protease 81,250 USP Amylase 81,250 USP Lipase 6500 USP Trypsin Papain Bromelain Amylase Lipase Lysozyme Chymotrypsin	Take 3 times daily. 325 mg 75 mg 50 mg 10 mg 10 mg 10 mg 2 mg	 Improves cancer patient immune system function by breaking down abnormal proteins generated during the course of disease¹ Significantly reduces disease symptoms (e.g., nausea, vomiting, changes in appetite, stomach pain or stomach disorder, tiredness, depression, memory or concentration disorder, sleep disturbance, dizziness, irritability, dyspnea at rest, dyspnea during activity, headache, tumor pain, cachexia, skin disorders and infections)² May prolong survival (epidemiological study)^{2,3} Associated with reduced adverse reactions to chemotherapy and radiation treatment² 	 Sakalova A, et al. Density of adhesive proteins after oral administration of proteolytic enzymes in multiple myeloma. <i>Vnitr Lek.</i> 1995 Dec;41(12):822-6. Popiela T, et al. Influence of a complementary treatment with oral enzymes on patients with colorectal cancers – an epidemiological retrolective cohort study. <i>Cancer Chemother Pharmacol.</i> 2001 Jul;47 Suppl:S55-63. Wald M, et al. Polyenzyme preparation [brand name] inhibits growth of solid tumors and development of experimental metastases in mice. <i>Life Sci.</i> 1998; 62(3):PL43-8.
Clinically Studied Blend: Wild indigo Echinacea purpurea and pallid (coneflower) Thuja (white cedar leaf)	Take 3 times daily. 58.5 mg fixed combination Studied for intermittent use after chemo/ radiation to increase white blood cell counts and limit duration of nadir	 Reduces toxicity associated with intermittent radiotherapy¹⁻⁴ Stimulates T-cell proliferation and increases differentiation into fully functional helper T-cells Also increases phagocytosis In cases where chemotherapy and/or radiation is not interrupted, or there is severe bone marrow depression, the combination did not provide significant results. 	 Bendel R, et al. Additional treatment with [Echinacea herbal blend] in patients with chemo-radiotherapy treatment of advanced breast cancer. <i>Onkologie</i>. 1989 Jun;12 Suppl 3:32-38. Bendel R, et al. Supplementary treatment with [Echinacea herbal blend } of female patients undergoing curative adjuvant irradiation following breast cancer. Strahlenther Onkol. 1988 May;164(5):278-283. Pohl P. Treatment of radiation-induced leukopenia with [Echinacea herbal blend]. Ther Ggw. 1970 Jun;109(6):901. Pohl P. On the therapy of irradiation-induced leucopenia with [Echinacea herbal blend]. Med Klin. 1969; 64(35):1546-7.



Inflammation

acids to augment cancer therapy. *J Nutr.* 2002 Nov; 132(11 Suppl):3508S-3512S.

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Ingredients	Dosage	Rationale	Reference
Omega-3 Fatty Acids 14-18% EPA* 8.3-11.7% DHA* Pharmaceutical grade High purity Naturally stable *EPA=eicosapentaenoic acid *DHA=docosahexaenoic acid	1.5 – 5 g daily	 Possesses anti-inflammatory and immunomodulatory properties Regulates macrophage activity and TNF-alpha and interleukin production¹⁻³ Decreases proliferation and induces differentiation of cancer cells Possesses anti-proliferative and anti-cachectic actions in malignancy (laboratory and <i>in vitro</i> studies)⁴ Slows the growth of experimental cancer in scientific studies, increases the efficacy of chemotherapy, and reduces the side effects of the chemotherapy or of the disease itself ⁵ May slow or stop the growth of metastatic cancer cells, increase longevity of cancer patients and improve their quality of life⁵ 	 Erickson KL, et al. Dietary fish oil modulation of macrophage tumoricidal activity. <i>Nutrition</i>. 1996 Jan;12(1 Suppl):S34-8. Lo CJ, et al. Fish oil modulates macrophage P44/P42 mitogenactivated protein kinase activity induced by lipopolysaccharide. <i>JPEN J Parenter Enteral Nutr</i>. 2000 May-Jun;24(3):159-63. Caughey GE, et al. The effect on human tumor necrosis factor alpha and interleukin beta production of diets enriched in n-3 fatty acids from vegetable oil or fish oil. <i>Am J Clin Nutr</i>. 1996 Jan;63(1):116-22. Jho DH, et al. Role of omega-3 fatty acid supplementation in inflammation and malignancy. <i>Integr Cancer Ther</i>. 2004



Detoxification

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Ingredients	Dosage	Rationale	Reference			
Dietary fiber Fiber blend containing: Psyllium husk Oat bran Guar gum Pectin (from citrus fruit) Marshmallow root	2 g daily 1727 mg daily	 General Detoxification Support Absorbs toxins and carcinogens, such as secondary bile acids and diacylclycerol, while in the intestinal tract¹ Augments the immune system by enhancing natural killer cell activity¹ To be effective, encapsulated fiber products must adequately disperse following ingestion (<i>in vitro</i> study)² 	Reddy BS. Prevention of colon carcinogenesis by components of dietary fiber. Anticancer Res. 1999 Sep-Oct;19(5A):3681-3. Study on the comparative dispersion of encapsulated fiber blends. Unpublished data. June 2003.			
Silybin (from milk thistle extract) bound to phosphatidylcholine for enhanced absorption and bioavailability	120 mg, 1-2 times daily	 Additional Liver Detoxification Support. Improves body's detoxification and cleansing processes by increasing bile production and flow Silymarin increases glutathione production, reducing free radical damage to liver¹ Also increases hepatocyte protein synthesis, which promotes regeneration of the liver¹ Prevents cancer angiogenesis² Silybin bound to fat-soluble phosphatidylcholine is more easily absorbed than unbound forms (clinical study)³ 	 Gonzalez-Correa JA, et al. Effects of silymarin MZ-80 on hepatic oxidative stress in rats with biliary obstruction. Pharmacology. 2002 Jan;64(1):18-27. Singh RP, et al. Silibinin strongly inhibits growth and survival of human endothelial cells via cell cycle arrest and downregulation of survivin, Akt and NF-kappaB: implications for angioprevention and antiangiogenic therapy. Oncogene. 2005 Feb 10;24(7):1188-202 Barzaghi N, et al. Pharmacokinetic studies on IdB 1016, a silybin-phosphatidylcholine complex, in healthy human subjects. Eur J Drug Metab Pharmacokinet. 1990 Oct-Dec;15(4):333-8. 			
Stable, Gastric- Protected Probiotic blend of: Lactobacillus acidophilus and Bifidobacterium longum	1 billion CFU daily	Restoration of Healthy Intestinal Flora Acid-stable probiotics have been shown to balance the intestinal flora in immune compromised individuals • Enhance detoxification of DNA-toxic substances in intestines; associated with anti-carcinogenic effects ^{1,2} • To provide full health benefits, supplement must survive gastric conditions and be released in the intestine (<i>in vitro</i> study) ³	1. Goossens D, et al. Probiotics in gastroenterology: indications and future perspectives. Scand J Gastroenterol Suppl. 2003(239):15-23. 2. Wollowski I, et al. Protective role of probiotics and prebiotics in colon cancer. Am J Clin Nutr. 2001 Feb;73(2 Suppl_:451S-455S. 3. Probiotic Comparison Testing. Unpublished data. June 3, 2002.			



Hormonal Balance

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Ingredients	Dosage	Rationale	Reference
Calcium D-glucarate	1.5 g, 3 times daily	 Elevated beta-glucuronidase activity has been associated with an increased risk for various cancers, particularly hormone-dependent cancers such as breast, prostate, and colon cancers. Calcium D-glucarate inhibits activity of β-glucuronidase^{1,2} It also helps regulate estrogen metabolism¹ 	1. Walaszek Z, et al. Metabolism, uptake, and excretion of a D-glucaric acid salt and its potential use in cancer prevention. Cancer Detect Prev. 1997; 21(2):178-90. 2. Walaszek Z, et al. Antiproliferative effect of dietary glucarate on the Sprague-dawley rat mammary gland. Cancer Lett. 1990 Jan; 49(1):51-7.
Stable, Bioavailable Diindolylmethane (DIM), co-solubilized with vitamin E and phosphatidylcholine, for enhanced absorption and bioavailability	120 mg blend (30 mg DIM) daily	 Acts as a natural hormone detoxifier, helping the body to efficiently and effectively break down and excrete estrogen Increases the ratio of desirable 2-OH estrogen over the undesirable 16-OH estrogen metabolites, thereby preventing estrogen dominance Demonstrated anti-proliferative effects against prostate, breast, and cervical cancer cells (in vitro)^{1,2} Also plays a significant role in the regulation of dihydrotestosterone (DHT), a potent androgen² 30 days supplementation in postmenopausal women with a history of early-stage breast cancer significantly increased the 2-hydroxylation of estrogen urinary metabolites (clinical study)³ 	 Hong C, et al. 3, 3'- Diindolylmethane (DIM) induces a G (1) cell cycle arrest in human breast cancer cells that is accompanied by Sp1- mediated activation of p21 (WAF1/CIP1) expression. Carcinogenesis. 2002 Aug; 23(8):1297-305. Le HT, et al. Plant-derived 3, 3'-Diindolylmethane is a strong androgen antagonist in human prostate cancer cells. J Biol Chem. 2003; 278(23):21146-45. Dalessandri KM, et al. Pilot study: effect of 3, 3'- diindolylmethane supplements on urinary hormone metabolites in postmenopausal women with a history of early-stage breast cancer. Nutr Cancer. 2004; 50(2):161-7.



Breast Cancer

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Ingredients	Dosage	Rationale	Reference
	Dosage Take twice daily. 400 IU 1000 mg 500 mg 200 mg 30 mg 100 mg	·	Reference 1. Weitsman GE, et al. Vitamin D enhances caspase-dependent and independent THF-induces breast cancer cell death: the role of reactive oxygen species. Ann NY Acad Sci. 2003 Dec; 1010:437-40. 2. Tilak JC, et al. Antioxidant availability of turmeric in relation to its medicinal and culinary uses. Phytother Res. 2004; 18(10):798-804. 3. Roy AM, et al. Epigallocatechin-3-gallate induces apoptosis in estrogen receptor-negative human breast carcinoma cells via modulation in protein expression of p53 and Bax and caspase-3 activation. Mol Cancer Ther.
Maitake (<i>Grifola</i> frondosa) (30% pure D-	90 mg	cells Turmeric² Reduces systemic inflammation Inhibits COX-2 preferentially- not inhibiting	estrogen receptor-negative human breast carcinoma cells via modulation in protein expression of p53 and Bax and caspase-3
		 Maitake mushroom D-fraction⁵ Suppresses tumor growth (clinical study) Enhances natural killer cells activity by 1.2 to 2.7 times (clinical study) Calcium D-glucarate – see Rationale and References above. DIM - see Rationale and References above. 	



Protocols

Cancer Treatment Adjuvant

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Prostate Cancer

Ingredients Dosage Rationale Reference Costello LC, et al. The clinical Take twice Additional Prostate Support relevance of the metabolism of daily. Zinc is critical for proper cell growth, prostate cancer; zinc and Zinc 15 mg proliferation, metabolism and migration¹ tumor suppression: connecting Saw Palmetto (Serenoa 160 mg Saw palmetto inhibits prostate cell the dots. Mol Cancer. 2006 May 15;5(1):17 [Epub ahead of repens) growth by up to 20-25% and cancer cell print] Pumpkin (Cucurbita 100 mg growth by up to 50% (in vitro); also Goldmann WH, et al. Saw reduces inflammation (COX-2)² palmetto berry extract inhibits Pygeum (Pygeum 50 mg cell growth and Cox-2 Pumpkin mildly inhibits 5-alpha expression in prostatic cancer africanum) reductase (enzyme which converts cells. Cell Biol Int. Stinging Nettle (Urtica 50 mg testosterone to ihydrotestosterone) (in 2001;25(11):1117-24. dioica) vivo); reduces inflammation; and reduces Zhang X, et al. Effect of the Lycopene 1 mg prostate symptoms³ extracts of pumpkin seeds on the urodynamics of rabbits: an Pygeum improved micturition in 66% experimental study. J Tongji men after two months (clinical study)⁴ Med Univ. 1994;14(4):235-8. Meta analysis of 18 randomized Barlet A, et al. Efficacy of Pygeum africanum extract in controlled trials involving 1,562 men the medical therapy of found that men who received pygeum urination disorders due to extract were more than twice as likely to benign prostatic hyperplasia: report improvements; nocturia was evaluation of objective and reduced by 19%, residual urine volume subjective parameters. A placebo-controlled doubleby 24% and peak urine flow increased by blind multicenter study. Wien 23%⁵ Klin Wochenschr. 1990 Nov 23;102(22):667-73. Stinging nettle improved lower urinary

tract symptoms for 81% of patients; peak

flow rate increased 2.5 times that of

Research suggests lycopene may

decrease growth of prostate cancer

placebo⁶

- Ishani A, et al. Pygeum africanum for the treatment of patients with benign prostatic hyperplasia: a systematic review and quantitative metaanalysis. Am J Med. 2000 Dec 1:109(8):654-64.
- Safarinejad MR. Urtica dioica for Treatment of Benign Prostatic HyperplasiaA Prospective, Randomized, Double-Blind, Placebo-Controlled, Crossover Study. J Herb Pharmacother. 2005;5(4):1-11.
- 7. Kucuk O, et al. Phase II randomized clinical trial of lycopene supplementation before radical prostatectomy. Cancer Epidemiol Biomarkers Prev. 2001;10:861-868.



Prostate Cancer

Fraction on the carcinoma angiogenesis. *Cancer Lett.* 2001;172:193-198.

Protocols www. protocols.integrativeinc.com Ingredients Rationale Dosage Reference Walaszek Z, et al. Metabolism, Calcium D-glucarate Take twice uptake, and excretion of a daily with Elevated beta-glucuronidase activity has Dglucaric acid salt and its meals. been associated with an increased risk potential use in cancer Calcium D-Glucarate 200 mg for various cancers, particularly prevention. Cancer Detect Prev.1997;21:178-190. Green Tea (Camellia 50 mg hormone-dependent cancers such as Walaszek Z. Potential use of sinensis) breast, prostate, and colon cancers. D-glucaric acid derivatives in Maitake (Grifola 55 mg Calcium D-glucarate inhibits activity of βcancer prevention. Cancer Lett glucuronidase^{1,2} frondosa) Mushroom 1990;54:1-8. Gupta S, et al. Inhibition of Lycopene 2.5 mg Green tea inhibits prostate cancer prostate carcinogenesis in development, progression, and TRAMP mice by oral infusion metastasis^{3,4} of green tea polyphenols. Proc Natl Acad Sci U S A. Maitake mushroom activates immune 2001;98:10350-10355. cells and possesses anti-tumor activities⁵ Chung LY, et al. Induction of apoptosis by green tea catechins in human prostate cancer DU145 cells. Life Sci. 2001;68:1207-1214. Matsui K, et al. Effects of maitake (Grifola frondosa) D-



Prostate Cancer

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	Ingredients	Dosage	Rationale	Reference		

ADDITIONAL SUPPORT Stable, Bioavailable Diindolylmethane (DIM), co-solubilized with vitamin E and phosphatidylcholine, for enhanced absorption and bioavailability	30 mg daily	 EANCER PREVENTION OR ESTROGEN DO Estrogen Balance Shifts estrogen metabolism to C-2 pathway in liver, which increases ratio of 2-hydroxy and 2-methoxy estrogen metabolites over 16-hydroxyestrone estrogen metabolites¹ Exhibits potent antiproliferative and antiandrogenic properties in androgendependent human prostate cancer cells² Also reduces intracellular and secreted PSA levels² 	MIN 1. 2.	ANCE Zeligs MA. Safer estrogen with phytonutrition. <i>Towns Lett.</i> 1999;189:83-88. Le HT, et al. Plant-derived 3,3'-Diindolylmethane is a strong androgen antagonist in human prostate cancer cells. <i>J Biol Chem.</i> 2003 Jun 6;278(23):21136-45.
Calcium D-Glucarate	0.5 – 1.5 g three times daily with meals	 Estrogen Detoxification Detoxifies estrogen and xenoestrogen by inhibiting beta-glucuronidase and preventing hydrolysis of their glucuronides¹ 	1.	Walaszek Z, et al. Metabolism, uptake, and excretion of a D-glucaric acid salt and its potential use in cancer prevention. <i>Cancer Detect Prev.</i> 1997;21(2):178-90.

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