

BE SICK, OR "Be Well"

Talk to anyone and they will tell you that one of the most important aspects to their overall physical health is their ability to fight off microbiological invaders. Our immune system being one of our most precious commodities, and the first and last line of defense in our bodies, cannot afford to be compromised. Just like soldiers on the battlefield, the cells of our immune system need rations, weapons, and signals from their commanding officers to optimize the defense of *their* territory. Within the lush greenery of the earth we live in lies an abundance of these military components to be used by the immune cells that defend our bodies . Introducing " Be Well".

Vitamins & Minerals for the Immune System

Vitamin A is a fat-soluble vitamin that belongs to a family of retinoids known for the roles they play in vision and antioxidation. What is more fascinating about vitamin A is the role it plays in the immune system of humans. Recent research explores the potential of vitamin A in immune system regulation including the activation and proliferation of lymphocytes, supercharged differentiation of helper T cells, chemiosmosis and lymphocyte homing of tissue-specific targets, antibody isotype production, reducing inflammation, and/or treating autoimmunity (Mora JR et al., 2008). Vitamin C is a sugar acid that possesses an almost unmatched array of antioxidant characteristics. Along with the myriads of other health benefits that it yields, immune system enhancing is just another attribute to give it a round of applause for. It is known that a plethora of cells of the immune system can accumulate ascorbic acid and in fact require it to perform normal immunological tasks. This is commonly seen in macrophages and T-cells (Ströhle A, Hahn A, 2009). It appears that a diet deficient in vitamin C can result in reduced resistance against certain pathogens, at the same time diets high in the vitamin increases several immune function parameters.

Vitamin E is a class of phyto nutrients called *tocopherols and tocotrienols*. This class of compounds consists of four tocopherols and four tocotrienols, each existing in the alpha, beta, gamma and delta isoforms. Research suggests that the alpha isoform of tocopherol is the most biologically active in higher mammals (Rigotti A, 2007). This is why Be Well uses the alpha form of the tocopherols. One of

the interesting techniques vitamin E uses to protect the immune system via its antioxidant properties is to be the bodyguard of macrophages (the major phagocytes of the body). It does this by hanging out within the membrane of macrophages (the most important part of the macrophage) and protecting them against oxidative stressors, especially peroxidative agents (Kaur G et al., 2009). Zinc, a transition element on the periodic table, is responsible for numerous aspects of human physiology. It is a cofactor for hundreds of enzymes and plays a substantial role in immune function. It appears to be a very involved modulator for the production of immunocytes as well as managing the proper actions of leukocytes, namely neutrophils, macrophages, B and T lymphocytes, and monocytes (Veverka DV et al., 2009).

Immune Enhancing Blend

The citrus bioflavonoids include: quercitrin, tangeritin, hesperidin, and rutin (a cousin to quercitrin). In addition to their antioxidant properties, citrus bioflavonoids exhibit substantial effects on reducing proliferation of cancer cells and reducing heart disease (Stauth, 2007, Ververidis F et al., 2007). Cancer and inflammation have been shown to be greatly reduced via reduction in NF-kappa B expression in humans (Yamamoto et al., 2001) as well as possessing anti-microbial properties (Cushnie TPT et al., 2005). Bee propolis is considered a powerful natural anti-inflammatory by influencing different types of immune-responses, most notably by its immunoregulation of T lymphocytes. This can be seen in the concentrations of serum cytokines before and after supplementation (Ansorge S et al, 2003).

The balance and regulation of T helper 1 (Th1) and Th2-type cytokines are important in the effective immune response to different diseases. Oral garlic has been demonstrated in recent studies to favor the regulation of these cytokines in humoral immune responses (Zamani A et al., 2009). This is why garlic extract is one of the front line men in immune enhancing supplements. Extracts of Yarrow (alkaloids, terpenoids, and flavanoids) have been used in the natural medicine realm for the treatment of fever, inflammation, asthma, and liver diseases. Recent studies show that these constituents of Yarrow increase humoral antibody responses resulting in the reduction of these conditions (Rezaeipoor R et al., 1999).

Echinacea extracts are used in the production of standardized herbal medicines for the prevention and treatment of various infectious diseases. Preparations of the constituents of this herb have been shown to be capable of activating certain receptor types, playing a role as a potential anti-inflammatory and immunomodulator. In particular, studies show that expression of the anti-inflammatory cytokine IL-10 is significantly superstimulated, while the expression of the pro-inflammatory TNF-alpha protein gets inhibited by supplementation with Echinacea (Chicca A et al., 2009).

The Immune Enhancing Blend also contains mushroom extracts from Maitake, Shiitake, and Reishi. Extracts from the Maitake mushroom have been touted for its cancer preventative properties via activation of macrophages, NK (natural killer) cells, T cells, increasing serum concentrations of interleukin 1, and the superoxide radical in cancer cells (Masuda Y et al., 2008). Maitake also works its anti-cancer actions by inducing apoptosis (programmed cell suicide) within the cancerous cells (Lee JS et al., 2008, Cui Li Xu, 2007). Shiitake contains a β -glucan that is used as an approved clinical drug in various countries for its anti-cancer properties as well (Terakawa N et al., 2008). It has been shown to increase phagocytosis in macrophages, marked decreases in tumor formation, and increases in gamma interferon (Zheng R et al., 2005). Reishi is known for some of its polysaccharide and terpene components to inhibit cytokine-mediated angiogenesis around neoplastic tissue, cancer cell migration, and to induce apoptosis within cancer cells (Stanley G et al., 2005, Jian J et al., 2004). Some extracts of the astragalus genus show immune system boosting properties via increasing phagocytosis in macrophages, and increasing concentrations in lysozyme and plasma antibodies (Guobin Z et al., 2009). Goldenseal contains alkaloids from the genus *Hydrastis* which is thought to increase the production of mucous membranes rich

in IgA (Bergner P, 1996-1997), thus charging up one of the body's first lines of defense. The berberine found in goldenseal has been shown to contribute to the enhancing of the body's immune system by inducing production of interleukin 12 in macrophages and increasing their ability to produce gamma interferon (Tae S et al., 2003).

Several diterpenoids from *Marrubium velutinum* (Horehound) are known for their cytotoxic effects against various cancer cell lines and immunomodulating role in human mononuclear cells, as well as their ability to improve selected lymphocyte function (Karioti A et al., 2007). In this sense, Horehound packs a one-two punch serving as an anti-cancer agent as well as an immune system regulator. β -lapachone, a quinone compound obtained from the bark of the lapacho tree (Pau D'Arco), is reported to possess beautiful anti-inflammatory and anti-cancer properties. One study shows its anti-metastasis and anti-invasion abilities of human hepatocarcinoma cell lines, inhibiting cancer cell viability and migration (Kim SO et al., 2007).

Adaptogenic Blend

An adaptogen is a term used for natural supplements that increase the human body's resistance to stress, trauma, anxiety, and fatigue. Of these adaptogens, *Eleutherococcus* extract has been added to the Adaptogenic Blend due to recent findings regarding its immunomodulatory effects. Research indicates *Eleutherococcus*' ability to greatly enhance production of helper T cells, inducer cells, cytotoxic and NK cells, and B lymphocytes (Bohn B et al., 1987).

Capsaicin is an alkaloid found in the extracts of cayenne peppers that has demonstrated its immune priming effects by boosting helper T cell production of cytokines such as Interleukin 1,2, and 4 as well as gamma-interferon (Takano F et al., 2007). The proanthocyanadins from grapeseed extract show a magnificent array of biological benefits. In particular to the Be Well formula, proanthocyanadins demonstrate prevention of photocarcinogenesis, immunoprotective characteristics, and greatly reduce oxidative stress, especially in our skin (Katarivar SK, 2008).

Purpose

Be Well is an immune system boosting formula designed for those who take seriously the everyday threats of foreign microbial invaders. Utilizing the best phytonutrients our planet has to offer, Be Well has combined these key components into a self-

defense team that pulls no punches against the defenders of our bodies, that is, the human immune system.

References

Mora JR, Iwata M, von Andrian UH; *Vitamin effects on the immune system: vitamins A and D take centre stage*. Nat Rev Immunol. 2008 Aug 8.

Ströhle A, Hahn A; *Vitamin C and immune function*. Med Monatsschr Pharm. 2009 Feb;32(2):49-54

Rigotti A (2007). *Absorption, transport, and tissue delivery of vitamin E*. Mol. Aspects Med. 28 (5-6): 423–36.

Kaur G, Alam MS, Athar M; *Cumene hydroperoxide debilitates macrophage physiology by inducing oxidative stress: possible protection by alpha-tocopherol*. Chem Biol Interact. 2009 May 15;179(2-3):94-102

Veverka DV, Wilson C, Martinez MA, Wenger R, Tamosuinas A; *Use of zinc supplements to reduce upper respiratory infections in United States Air Force Academy cadets*. Complement Ther Clin Pract. 2009 May;15(2):91-5.

Studies force new view on biology of flavonoids, by David Stauth, EurekAlert!. Adapted from a news release issued by Oregon State University. Mar. 2007.

Ververidis Filippou; Trantas Emmanouil, Douglas Carl, Vollmer Guenter, Kretzschmar Georg, Panopoulos Nickolas (October 2007). *Biotechnology of flavonoids and other phenylpropanoid-derived natural products. Part I: Chemical diversity, impacts on plant biology and human health*. Biotechnology Journal 2 (10).

Therapeutic potential of inhibition of the NF- κ B pathway in the treatment of inflammation and cancer. Yamamoto and Gaynor 107 (2): 135 -- Journal of Clinical Investigation.

Cushnie TPT, Lamb AJ (2005). *Antimicrobial activity of flavonoids*. International Journal of Antimicrobial Agents 26 (5): 343-356

Ansorge S, Reinhold D, Lendeckel U; *Propolis and some of its constituents down-regulate DNA synthesis and inflammatory cytokine production but induce TGF-beta1 production of human immune cells*. Z Naturforsch [C]. 2003 Jul-Aug;58(7-8):580-9

Zamani A, Vahidinia A, Ghannad MS; *The effect of garlic consumption on Th1/Th2 cytokines in phytohemagglutinin (PHA) activated rat spleen lymphocytes*. Phytother Res. 2009 Apr;23(4):579-81.

Rezaeipoor R, Saeidnia S, Kamalinejad M; *Immunosuppressive activity of Achillea talagonica on humoral immune responses in experimental animals*. J Ethnopharmacol. 1999 Jun;65(3):273-6.

Chicca A, Raduner S, Pellati F, Strompen T, Altmann KH, Schoop R, Gertsch J; *Synergistic immunopharmacological effects of N-alkylamides in Echinacea purpurea herbal extracts*. Int Immunopharmacol. 2009 Mar 19.

Masuda Y, Murata Y, Hayashi M, Nanba H. *Inhibitory effect of MD-Fraction on tumor metastasis: involvement of NK cell activation and suppression of intercellular adhesion molecule (ICAM)-1 expression in lung vascular endothelial cells*. Biol Pharm Bull 2008 Jun;31(6):1104-8

Lee JS, Park BC, Ko YJ, (2008), *Grifola frondosa (maitake mushroom) water extract inhibits vascular endothelial growth factor-induced angiogenesis through inhibition of reactive oxygen species and extracellular signal-regulated kinase phosphorylation.*, J Med Food. 11 (4): 643-51

Cui, Li, Xu (April 2007), *Induction of apoptosis in SGC-7901 cells by polysaccharide-peptide GFPS1b from the cultured mycelia of Grifola frondosa GF9801*. Toxicol In Vitro. 21 (3): 417-27

Terakawa N, Matsui Y, Satoi S et al. (2008). *Immunological effect of active hexose correlated compound (AHCC) in healthy volunteers: a double-blind, placebo-controlled study*. Nutr Cancer. 60:643-651

Stanley G, Harvey K, Slivova V, Jiang V and Sliva D. *Ganoderma lucidum suppresses angiogenesis through the inhibition of secretion of VEGF and TGF-beta from prostate cancer cells*. Biochem Biophys Res Commun 2005; 330:46-52

Jian J, Slivova V, Valachivocova T, Harvey K and Sulva D. *Ganoderma lucidum inhibits proliferation and induces apoptosis in human prostate cancer cells PC-3*. Int J Oncol 2004; 24:1093-9

Bergner, Paul Goldenseal and the Antibiotic Myth Medical Herbalism: A Journal for the Clinical Practitioner Volume 8, Number 4, Winter 1996–1997

Zheng,-R; Jie,-S; Hanchuan,-D; Moucheng,-W; *Characterization and immunomodulating activities of polysaccharide from Lentinus edodes*. Int-Immunopharmacol. 2005 May; 5(5): 811-20.

Guobin Zhang Shiyuan Gong, Denghang Yu, Hanwen Yuan; *Propolis and Herba Epimedii extracts enhance the non-specific immune response and disease resistance of Chinese sucker, Myxocyprinus asiaticus*. Fish, Shellfish Immun. March 2009, pp. 467-472

Tae S. Kim, Bok Y. Kang, Daeho Cho & Seung H. Kim; *Induction of interleukin-12 production in mouse macrophages by berberine, a benzodioxoloquinolizine alkaloid, deviates CD4⁺ T cells from a Th2 to a Th1 response*. Immun. 2003, Vol 109 Issue 3, pp. 407 – 414

Katiyar SK; *Grape seed proanthocyanidines and skin cancer prevention: inhibition of oxidative stress and protection of immune system*. Mol Nutr Food Res. 2008 Jun;52 Suppl 1:S71-6.

Karioti A, Skopeliti M, Tsitsilonis O, Heilmann J, Skaltsa H; *Cytotoxicity and immunomodulating characteristics of labdane diterpenes from Marrubium cylleneum and Marrubium velutinum*. Phytochemistry. 2007 Jun;68(11):1587-94

Kim SO, Kwon JI, Jeong YK, Kim GY, Kim ND, Choi YH; *Induction of Egr-1 is associated with anti-metastatic and anti-invasive ability of beta-lapachone in human hepatocarcinoma cells*. Biosci Biotechnol Biochem. 2007 Sep;71(9):2169-76

Bohn B. et al; *Flow Cytometric Studies with Eleutherococcus senticosus Extract as an Immunomodulatory Agent*. Arzneimittel-Forschung Drug Research, vol.37(10), pp.1193-1196, 1987.

Takano F, Yamaguchi M, Takada S, Shoda S, Yahagi N, Takahashi T, Ohta T; *Capsicum ethanol extracts and capsaicin enhance interleukin-2 and interferon-gamma production in cultured murine Peyer's patch cells ex vivo*. Life Sci. 2007 Apr 3;80(17):1553-63.