

Science

ThionExtra™ Uses VNI's proprietary Prodosome™ technology providing unique and superior synchronized absorption and availability for unrivaled health benefits.

A feature of most, if not all, human disease, including cardiovascular disease, arthritis, and cancer, is increased production and presence of reactive oxygen species (called 'Free Radicals'), which cause oxidative stress, oxidative damage, burdensome immune system challenges and deteriorating health. Free radicals are normally produced as a byproduct of energy production. However, in addition to the 'normal' production of free radicals as a byproduct of energy production, excessive free radicals are also a result of the reduced ability to effectively use oxygen. This inability significantly increases acid burden, promoting excessive oxidative stress and damage. Oxidative damage is involved in almost all aspects of DNA damage, cell destruction, inflammation, and disease. Inflammation is also a characteristic of increased acid burden.

Oxidation is a chemical/energetic reaction that transfers electrons from a substance to an oxidizing agent at a speed like that of electricity. An antioxidant is a molecule that inhibits the oxidation and resulting oxidative damage of other molecules. Antioxidants can play an important role in supporting the immune system by reducing free radical damage to cellular DNA, lipids, and proteins thereby protecting against a breakdown in the structure and function of cells, tissues and organs in the body. It is important to note that not all oxidation is bad, such as that seen in the production of energy, known as oxidative respiration or 'cell respiration'. But, oxidation can, and very often does become excessive, resulting in oxidative damage to DNA, lipids, cellular components, tissue damage and immune distress.

Free radicals are atoms that have unpaired valence electrons. 'Valence' electrons are electrons that exist in pairs in the outer orbit of an atom. Imagine that a wheel on your vehicle loses a portion of its structure. It will not roll in a balanced manner and will cause a very rough ride that results in potentially devastating consequences. Losing one electron disrupts the 'spin' of the atom and makes it very unstable, which creates an imbalance that can start very rapid and potentially dangerous chain reactions. These reactions produce

many more free radicals, basically at the same speed as electricity travels. When these chain reactions occur in a cell, they can cause cellular damage or death and excessive immune system burdens. Antioxidants can terminate these chain reactions by removing or neutralizing free radicals and inhibiting other oxidation reactions. Most often they do this by being completely or partially oxidized themselves so antioxidants are often reducing agents (because they lose electrons that 'reduce' their electrical charge in reduction reactions) such as thiols, ascorbic acid, or polyphenols, all of which are in ThionExtra™.

ThionExtra™ contains ingredients that promote the activity of Super Oxide Dismutase (SOD), an 'antioxidant' enzyme made in the body that transforms the very dangerous superoxide free radical (aka 'hyperoxide') into hydrogen peroxide (H_2O_2) and oxygen (O_2). Superoxide inactivates the production of energy by blocking an enzyme involved in the first step of energy production. Superoxide also can cause the release of potentially toxic iron. SOD is the 5th abundant protein in the body (out of thousands of proteins) and exists in almost every cell in the body. This abundance indicates the importance of its main role of neutralizing the very dangerous superoxide free radicals by creating hydrogen peroxide and water from them in a transformation reaction. SOD has been shown to reduce inflammation and is the most important front line 'first step' of antioxidant defenses against oxygen free radicals (reactive oxygen species [ROS]).

ThionExtra™ contains ingredients that promote the activity of Glutathione (GSH), also an extremely important antioxidant molecule made in the body; and that exists in every cell in the body. GSH is involved in a series of antioxidant transitions that protect important cellular components from damage by reactive oxygen species such as free radicals and peroxides². One of glutathione's important jobs, along with the enzyme catalase, is to convert hydrogen peroxide (H_2O_2) to water (H_2O) and oxygen (O_2). So, it is a very important powerhouse collaborator with SOD.

Glutathione (GSH) has multiple functions:

- It is a major antioxidant made in the body and is produced by the cells participating directly in the neutralization of free radicals and reactive oxygen compounds. It also helps maintain the

functional potential of antioxidants we consume in our foods and supplements, such as vitamins C and E, in their reduced (active) forms.^{3, 4}

- GSH is involved in regulating the Nitric Oxide cycle, which is critical for life and can be problematic if unregulated.⁵ NO is a powerful vasodilator (expands blood vessels), an important biological regulator, and a fundamental component in the fields of neuroscience, physiology, and immunology. Research into its function led to the 1998 Nobel Prize for discovering the role of nitric oxide as a cardiovascular signaling molecule.
- GSH is used in metabolic and biochemical reactions such as DNA synthesis and repair, protein synthesis, prostaglandin synthesis, amino acid transport, and enzyme activation. Thus, every system in the body can be affected by the state of the glutathione system, especially the immune system, the nervous system, the gastrointestinal system and the lungs.
- Through direct conjugation ('joining together'), GSH detoxifies many foreign compounds and carcinogens (xenobiotics - substances coming from outside the body) in the body, both organic and inorganic.
- GSH is essential for the immune system to exert its full potential, e.g.
 - 1 modulating dendritic cell influence on antigen presentation to lymphocytes, thereby influencing cytokine production and the type of response (cellular or humoral) that develops,
 - 2 enhancing proliferation of lymphocytes thereby increasing magnitude of response,
 - 3 enhancing killing activity of cytotoxic T cells and NK cells, and
 - 4 regulating cellular apoptosis (programmed cell suicide), thereby maintaining control of the immune response.

Bolstering glutathione function and benefits using precursors of glutathione synthesis is a strategy developed to address states of glutathione deficiency; high oxidative stress; damage to DNA, cell membranes and intracellular components; impaired immune response and deficiency; and xenobiotic overload in which glutathione plays a part in the detoxification of the xenobiotic in

question (especially through the hepatic route). Glutathione deficiency states include, but are not limited to, HIV/AIDS, chemical and infectious hepatitis, myalgic encephalomyelitis, chronic fatigue syndrome,^{6, 7} prostate and other cancers, cataracts, Alzheimer's disease, Parkinson's disease, chronic obstructive pulmonary disease, asthma, radiation poisoning, malnutritive states, arduous physical stress, aging, and has been associated with suboptimal immune response. Many clinical pathologies are associated with oxidative stress and are the subject of numerous scientific studies. Low glutathione is also strongly implicated in wasting and negative nitrogen balance,⁸ as seen in cancer, AIDS, sepsis, trauma, burns and even athletic overtraining. Glutathione supplementation can oppose this process, and in AIDS, for example, result in improved survival rates.⁹ However, studies in many of these conditions have not been able to differentiate between low glutathione as a result of acutely (as in septic patients) or chronically (as in HIV) increased oxidative stress, and increased pathology as a result of preexisting deficiencies.

People with atherosclerosis, diabetes, or hypertension (among other problems) often show impaired Nitric Oxide metabolism¹⁰ and low glutathione levels.¹¹

Schizophrenia and bipolar disorder are associated with lowered glutathione as well. Accruing data suggest that oxidative stress may be associated with the pathophysiology of bipolar disorder (BD), major depressive disorder (MDD), and schizophrenia (SCZ).

Glutathione (GSH) is the major free radical scavenger in the brain.¹² Diminished GSH levels elevate cellular vulnerability towards oxidative stress, characterized by accumulating reactive oxygen species. GSH depletion has also been implicated in cellular predisposition to premature 'apoptosis' ('programmed cell suicide').¹³ Replenishment of glutathione using N-acetyl cysteine has been shown to reduce symptoms of both disorders.¹⁴

Free radicals cause excessive wear and tear on the body; overburden the immune system; and reduce energy and quality of life.

Nitric Oxide protects the heart by relaxing and dilating the inner lining (endothelium) of blood vessels, promoting healthy lower blood pressure, increased blood flow, and oxygen utilization.^{10, 15}

Nitric oxide can be secreted as an immune response because it is toxic to bacteria and intracellular parasites.^{16, 17, 18, 19} Nitrogen is also a component of ATP, the primary storage 'battery' in cells that provide energy for reactions such as cellular metabolism/cell respiration.

Nitric oxide therapy has the potential to significantly increase the quality of life and, in some cases, save the lives of infants at risk for pulmonary vascular disease.²⁰ Nitric oxide acts as an important part of the immune mediated inflammation response. It also plays a positive free radical-acting role in immune response, as it is toxic to bacteria and intracellular parasites.^{17, 18, 21}

NO activates NF-KB (nuclear factor kappa-light-chain-enhancer of activated B cells). NF-KB is a protein complex that controls transcription of DNA. NF-KB is found in almost all animal cell types and is involved in cellular responses to stimuli such as stress, cytokines, free radicals, ultraviolet irradiation, oxidized LDL, and bacterial or viral antigens.²² NF-KB plays a key role in regulating the immune response to infection (K light chains are critical components of immunoglobulins). Incorrect regulation of NF-KB has been linked to cancer, inflammatory, and autoimmune diseases, septic shock, viral infection, and improper immune development.

ThionExtra™ is designed to:

- Provide antioxidant and immune support*
- Promote nitric oxide metabolism and nitrogen balance,^{1, 2} which is essential to produce molecules like amino acids - the building blocks of proteins, and nucleic acids, including among other molecules, RNA and DNA - the genetic material that allows cells to grow and replicate.*
- Stabilize gene (DNA) structure*
- Repair, maintain, and protect your genes (DNA); a crucial role for ensuring the healthy structure and function of every cell and system in the body.*

ThionExtra™ is made with evidence-based powerhouse nutraceuticals that nutritionally support:

- DNA Protection*
- Nitrogen Balance*
- Cell Detoxification*
- Anti-oxidant function (promoting **Glutathione and SOD**)*

- Immune Function*
- Cellular Energy Output*
- Improved Mental Clarity*
- Anti-Aging and Life Extension*

References

- 1 Sies H. Oxidative stress: Oxidants and antioxidants. *Experimental Physiology*, 82 (2): 291-5 1997
- 2 Pompella A, Visvikis A, Paolicchi A, et al. The changing faces of glutathione, a cellular protagonist. *Biochemical Pharmacology*, 66 (8): 1499-503 (2003)
- 3 Scholz RW, Graham KS, Gumprecht E, Reddy CC. Mechanism of interaction of vitamin E and glutathione in the protection against membrane lipid peroxidation. *Ann NY Acad Sci* 570:514-7 (1989)
- 4 Hughes RE. Reduction of dehydroascorbic acid by animal tissues. *Nature* 203:1068-9 (1964)
- 5 Clementi E, Smith GC, Howden M, et al. (1999). Phytochelatin synthase genes from *Arabidopsis* and the yeast *Schizosaccharomyces pombe*. *The Plant Cell* 11 (6): 1153-64
- 6 Bounous G and Molson J. Competition for glutathione precursors between the immune system and the skeletal muscle: Pathogenesis of chronic fatigue syndrome. *Med Hypotheses*. 53(4) (oct): 347-9 (1999)
- 7 Richards RS and Roberts TK. Blood parameters indicative of oxidative stress are associated with symptom expression in chronic fatigue syndrome. *Redox Rep.* 1 (5): 35-41 (2000)
- 8 Dröge W and Eggert H. Role of cysteine and glutathione in HIV infection and other diseases associated with muscle wasting and immunological dysfunction. *FASEB*. 11 (13): 1077-89 (1997)
- 9 Herzenberg LA, et al. Glutathione deficiency is associated with impaired survival in HIV disease. *Proc Natl Acad Sci.* 94 (5): 1967-72 (1997)
- 10 Ghosh SM, Kapil V, Fuentes-Calvo I, et al. Enhanced Vasodilator Activity of Nitrite in Hypertension: Critical Role for Erythrocytic Xanthine Oxidoreductase and Translational Potential. *Hypertension* 61(5): 1091-102 (2013)
- 11 Clementi E, Smith GC, Howden M, et al. (1999). Phytochelatin

- synthase genes from *Arabidopsis* and the yeast *Schizosaccharomyces pombe*. *The Plant Cell* 11 (6): 1153-64
- 12 Gawryluk JW, Wang JF, Andreazza AC, et al. Decreased levels of glutathione, the major brain antioxidant, in post-mortem prefrontal cortex from patients with psychiatric disorders. *Intl J Neuropsychopharmacol.* 14 (1): 123-30 (2011)
- 13 Franco R and Cidlowski JA. Apoptosis and glutathione: beyond an antioxidant. *Cell Death Differ.* 16 (10): 1303-14 (2009)
- 14 Dean O, Giorlando F, Berk M. N-acetylcysteine in psychiatry: current therapeutic evidence and potential mechanisms of action. *J Psychiatry Neurosci.* 36(2):78-86 (2011)
- 15 Webb AJ, Patel N, Loukogeorgakis S, et al. Acute Blood Pressure Lowering, Vasoprotective, and Antiplatelet Properties of Dietary Nitrate via Bioconversion to Nitrite. *Hypertension* 51 (3): 784-90 (2008)
- 16 Green SJ, Crawford RM, Hockmeyer JT, et al. Leishmania major amastigotes initiate the L-arginine-dependent killing mechanism in IFN-gamma-stimulated macrophages by induction of tumor necrosis factor-alpha. *J Immunol.* 145 (12): 4290-7 (1990)
- 17 Seguin MC, Klotz FW, Schneider I, Weir JP, et al. Induction of nitric oxide synthase protects against malaria in mice exposed to irradiated *Plasmodium berghei* infected mosquitoes: Involvement of interferon gamma and CD8+ T cells. *J Exper Med.* 180 (1): 353-8 (1994)
- 18 Mellouk S, Green SJ, Nacy CA, Hoffman SL. IFN-gamma inhibits development of *Plasmodium berghei* exoerythrocytic stages in hepatocytes by an L-arginine-dependent effector mechanism. *J Immunol.* 146 (11): 3971-6 (1991)
- 19 Klotz FW, Scheller LF, Seguin MC, et al. Co-localization of inducible-nitric oxide synthase and *Plasmodium berghei* in hepatocytes from rats immunized with irradiated sporozoites. *J Immunol.* 154(7): 3391-5 (1995)
- 20 Hayward CS, Kelly RP, and MacDonald PS. Inhaled nitric oxide in cardiology practice. *Cardiovascular research* 43 (3): 628-38 (1999)
- 21 Green SJ, Crawford RM, Hockmeyer JT, et al. Leishmania major amastigotes initiate the L-arginine-dependent killing

mechanism in IFN-gamma-stimulated macrophages by induction of tumor necrosis factor-alpha. *Journal of immunology* 145 (12): 4290-7 (1990)

Gilmore TD. Introduction to NF-KB: players, pathways, perspectives. *Oncogene* 25 (51): 6680-4; Brasier AR (2006). The NF-KB regulatory network. *Cardiovasc. Toxicol.* 6 (2): 111-30 (2006)