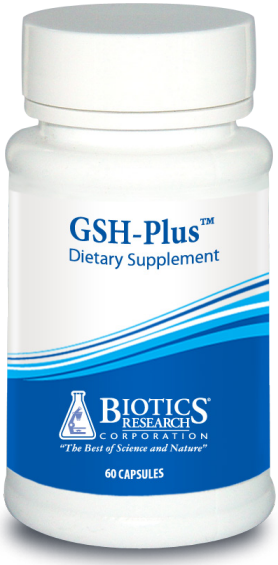
GSH-Plus™



Oxidative stress is defined as the "steady-state level of oxidative damage within a cell, tissue or organism," as the result of reactive oxygen species (ROS).[1] The correlation between oxidative stress and aging, termed the molecular basis of aging, or the oxidative stress theory of aging is one of the most studied, and the most widely accepted hypotheses on the aging process. Given the fact that oxidative stress, and the damage it may ensue, is implicated in many disease processes, particularly in the critically ill,[2] as well as in the aging process, countering its negative effects is one way to achieve positive health benefits.

Antioxidants function to neutralize free radicals by virtue of their ability to donate an electron, thus act to scavenge these radicals, in turn eliminating their volatility towards other cellular components. Their scavenging ability allows them to function in a protective manner to both aide and prevent cellular and tissue damage. Void of this protection, the cellular matrix, including lipids, membranes, proteins, and DNA, is predisposed to injury as a consequence of these volatile, reactive molecules.

GHS-Plus™ supplies Glutathione, N-Acetyl-L-Cysteine (NAC) and Glycine, providing powerful cellular support, via their ability to quench free radicals.

L-Glutathione. Glutathione (GSH) functions as one of the most powerful intracellular antioxidants. It also participates as an important component in detoxification via its reaction with hydrogen peroxide and organic peroxides,[3] or other electrophilic compounds (electron-deficient carbon centers), by means of catalysis by glutathione-S-transferases and glutathione peroxidases.[4] Reactive electrophilic compounds may include peroxides or epoxides, or more noxious compounds such as genotoxic chemical carcinogens, or cytotoxic chemotherapeutic agents.[5] GSH also serves in a protective capacity, as it aids in quenching xeno-biotics and other reactive compounds, produced via the metabolism of both endogenous and exogenous compounds.[6]

Structurally, GSH is made up of a tripeptide, consisting of glutamic acid, cysteine and glycine residues. Besides its function as a major intracellular antioxidant, it also participates in other key functions, which are generally associated with detoxification, protein structure preservation, immune function maintenance, and in the regulation of protein function.

Lower GSH levels correspond to higher oxidative stress. A reduction of plasma GSH is an associated risk factor for cardiovascular disease, with lower glutathione levels correlated to an elevated risk.[7] In addition to age, GSH depletion may also result as a consequence of poor dietary habits or environmental exposure, including pollution, toxins, medications, stress, trauma, aging, infections and radiation. A 'disturbance in homeostasis' of GSH has also been implicated in 'diseases of the aging,'[8] as well as in a wide range of pathologies, including neurodegenerative, cardiovascular, inflammatory, metabolic and immune diseases. Additionally, a depleted level is also indicated in fibrosis, viral infections, diabetes, cancer, and liver disease.[9,10,11] Interestingly, the intake of acetaminophen (Tylenol) is associated with the blockage of glutathione production, which in turn alters the liver's ability to break down and eliminate toxins.[12]

N-acetyl-L-cysteine (NAC) is an antioxidant. Although NAC has numerous functional activities in the body, it is recognized for three primary actions; the modulation of neurotransmitters, the ability to reduce inflammatory cytokines, and cellular protection from oxidative stress. As a precursor to the amino acid cysteine, NAC participates in the general antioxidant activities of the body, while cysteine influences the reward-reinforcement pathway, via its role as a modulator of the glutamatergic system.[13] Its classical medicinal use is in counteracting acetaminophen (Tylenol) overdose, as well as in carbon monoxide poisoning.[14]

NAC functions as an important compound in increasing the cellular concentration of GSH. Moreover, due to the fact that GSH penetration via the blood-brain barrier is relatively poor, NAC functions to assist in this transfer, as unlike GSH, NAC can readily penetrate the blood-brain barrier. An increase in the level of GSH in the brain with NAC use has been demonstrated in both animal[15,16,17] and human studies.[18]

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NAC has been demonstrated to modulate both the gene expression, and the activity of inflammatory cytokines, via its ability to both block NF-KappaB activation,[19,20] and to reduce TNF-α, IL-1β and IL-6.[21] It also possesses the capacity to alter the expression of nitric oxide synthase mRNA, resulting in a modulation of the production of nitric oxide, with a consequential hepatoprotective effect.[22]

NAC use is suggested in situations where GSH deficiency and/or oxidative stress are indicated.

Glycine plays as an important role in GSH synthesis, functions in the conjugation of the aromatic acids, and is a required amino acid for phase II conjugation.[23] It is recognized as a major inhibitory neurotransmitter, at both excitatory and inhibitory synapses,[24] including both the brainstem and spinal cord.[25] As such, glycine functions as a vital component in the performance of the central nervous system.[26]

Glycine has been demonstrated to diminish the secretion of inflammatory cytokines, including TNFα and interleukin (IL)-1, and to enhance the secretion of IL10, an anti-inflammatory cytokine.[27] In addition, it exerts an immunomodulary effect on T-lymphocytes and has demonstrated protective effects in renal ischemia, on hepatocytes and on epithelial cells, specifically in those subjected to hypoxia, or faced with a chemical challenge (ie. cyanide, hydrogen peroxide).[28,29,30,31]

In summary, the combination of the ingredients supplied in **GSH-Plus™** function primarily to increase the cellular glutathione level, principally in the bloodstream and the brain. The combination of these compounds may be particularly valuable in offsetting decifiencies which may result from poor dietary habits, toxin exposure, medications, stress, trauma, and infections. Additionally, due to their antioxidant nature, GSH offers added cellular protection, and can assist in detoxification mechanisms, which may be particularly advantageous in the ill and elderly, as well as with prolonged environmental or toxic stressors.

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