



L-Glutathione

- Supports healthy immune system function
- Supports the liver's natural detoxification processes
- Neutralizes free radicals

Glutathione is the master antioxidant in the body and is heavily concentrated in tissues such as the liver, spleen and heart. Therefore, it plays a crucial role in immune function, detoxification capacity and protection against oxidative stress. This L-Glutathione formulation is preformed, reduced glutathione (GSH) and provides a 250 mg dose in a one-capsule serving.

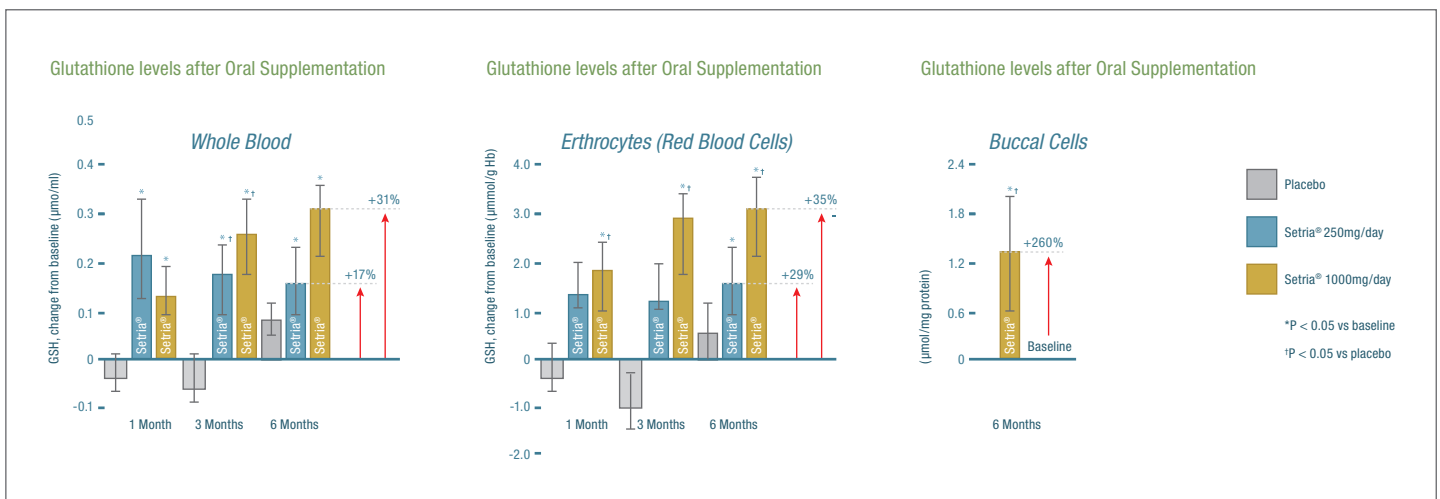
Overview

Modern lifestyle habits like poor dietary choices, lack of sleep, abundance of stress, exposure to chemicals, and exercise extremes can incur physiologic changes. Our bodies were designed to handle stress, detoxify chemicals and preserve cell function, but when the burden increases, those naturally built-in systems can't keep up with demand. One of the most common physiological changes seen is the depletion of the body's most powerful antioxidant, reduced glutathione. Glutathione has been termed "the master antioxidant" because of its ability to quench free radicals and protect cells from damage. It has long been thought that humans were unable to utilize preformed glutathione, but recent research proves otherwise. Setria®, a

unique tri-peptide form of glutathione, has a molecular structure that effectively increases glutathione blood levels when taken orally.¹ It is the only supplemental glutathione backed by a recently published human clinical trial that shows significant uptake of this critical nutrient.¹

Oral Supplementation and Bioavailability[†]

The foods and supplements routinely used to boost endogenous glutathione production offer a variety of health benefits. The challenge for the practitioner becomes prioritizing what supplementation is most critical and most helpful. Depending on a patient's genetics, health status and environmental exposures, even the best efforts to provide precursor molecules and cofactors may not effectively optimize glutathione production. This is because genetic polymorphisms or health challenges can alter enzymatic function in ways that hinder glutathione production or glutathione metabolism, despite excellent nutrient intake. According to a 2015 publication in the *European Journal of Nutrition*, supplementing with Setria® glutathione at doses of 250 mg and 1,000 mg a day for six months increased glutathione levels in whole blood, erythrocytes and buccal cells. This was



[†] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

the first long-term, randomized, placebo-controlled trial of oral glutathione supplementation.¹

L-Glutathione and Detoxification[†]

Because of glutathione's central role in detoxification, about 25% of all glutathione resides in the liver. Glutathione is more than simply an electron donor; glutathione plays an important role in protecting living cells from toxicity by detoxifying the reactive intermediates via enzymatic conjugation. Enzymatic conjugation, catalyzed by the enzyme glutathione-S-transferase, occurs in Phase II liver detoxification and in gastrointestinal mucosal secretions.² Glutathione conjugation provides a mechanism to neutralize reactive toxins before they damage body tissues.

Glutathione can also function as a detoxifying agent within the intestinal lumen, catching harmful toxins before they enter the body and create the necessity for liver detoxification. Glutathione sources in the intestinal mucosa include intracellular synthesis, biliary supply and dietary intake. The intestinal lumen receives a large quantity of hepatic GSH from biliary secretion.³ Studies of oral GSH supplementation in humans and laboratory animals have shown that the enhancement of intestinal mucosal GSH levels by oral GSH supplementation under conditions in which intracellular GSH status is compromised can restore tissue GSH and promote ROS metabolism.⁴ Thus, it has been described that orally administered GSH acts as backup for GSH-deficient tissue. In the intestinal mucosa, this mechanism of action supports the enzymatic activity of glutathione-S-transferase, which plays a role in deconjugation at the site of the mucosa without the necessity for GSH uptake.

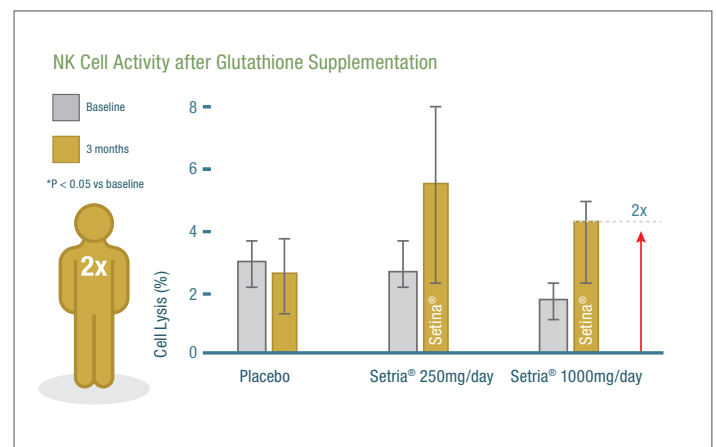
L-Glutathione and Immune Health[†]

It is well known that the gastrointestinal cells, the mitochondria and the efficiency of immune cell function are three major factors in immune function. Glutathione happens to play a role in all three elements. When small intestinal mucosa atrophies, it causes an increase in epithelial permeability and compromised tight junctions, which can lead to translocation of bacteria.⁴ This translocation of bacteria is implicated in immune activation and autoimmunity. Studies have shown that this epithelial damage is in part due to the inability to mitigate reactive oxygen species (ROS).⁴ Supplementing with oral glutathione under conditions in which intracellular glutathione status is compromised can restore tissue glutathione and promote ROS metabolism, thereby mitigating tissue atrophy, according to a 2017 study published in the *World Journal of Gastroenterology*.⁴

The most commonly discussed role of glutathione is in the protection of the mitochondria from free radical damage during the process of ATP production. Glutathione is the master antioxidant to quench the reacted oxygen species produced as byproducts, allowing ATP production without the damaging

impact that can occur in an environment lacking adequate antioxidant capacity. Mitochondrial health plays a crucial role in immune function via its influence on the T-cell surveillance activity, pattern recognition receptor function, and any ATP-dependent immune functions.

Regarding individual immune cells, decreased glutathione levels in various cells, such as T-lymphocytes, are observed in patients with immune challenges and the decreased glutathione levels are considered to contribute to a compromised immune system. The antioxidant properties of glutathione support healthy immune system function. Intracellular GSH plays a key role in the maintenance and regulation of certain immunological functions, including the activation of lymphocytes and functional activity of natural killer (NK) cells. Within three months of 1,000 mg/day Setria[®] glutathione, NK cell cytotoxicity increased more than twofold from baseline.



Directions

1 capsule per day or as recommended by your health care professional.

Does Not Contain

Gluten, corn, yeast, artificial colors and flavors.

Cautions

If you are pregnant or nursing, consult your health care professional before taking this product.

Supplement Facts^{v1}

Serving Size 1 Capsule
Servings Per Container 60

| 1 capsule contains | Amount Per Serving | % Daily Value |
|--|--------------------|---------------|
| L-Glutathione (Reduced) (Setria [®]) | 250 mg | * |

* Daily Value not established

References

1. Richie JP, Nichenametla S, Neidig W, et al. Randomized controlled trial of oral glutathione supplementation on body stores of glutathione. *Eur J Nutr.* 2015;54(2):251-263.
2. Ketterer B, Coles B, Meyer DJ (1983). The role of glutathione in detoxication. *Environ Health Perspect,* 49:59-69.
3. P. S. Samiec, L. J. Dahm, D. P. Jones, Glutathione S-Transferase in Mucus of Rat Small Intestine, *Toxicological Sciences*, Volume 54, Issue 1, March 2000, Pages 52–59, <https://doi.org/10.1093/toxsci/54.1.52>
4. Uchida H, Nakajima Y, Ohtake K, et al. Protective effects of oral glutathione on fasting-induced intestinal atrophy through oxidative stress. *World J Gastroenterol.* 2017;23(36):6650–6664. doi:10.3748/wjg.v23.i36.6650
5. Morris D, Ly J, Chi PT, et al. Glutathione synthesis is compromised in erythrocytes from individuals with HIV. *Front Pharmacol.* 2014;573.
6. Rushworth GF, Megson IL. Existing and potential therapeutic uses for N-acetylcysteine: the need for conversion to intracellular glutathione for antioxidant benefits. *Pharmacol Ther.* 2014;141(2):150-159.
7. Sido B, Hack V, Hochlehnert A, Lipps H, Herfarth C, Dröge W. Impairment of intestinal glutathione synthesis in patients with inflammatory bowel disease. *Gut.* 1998;42(4):485-492.
8. Witschi A, Reddy S, Stofer B, Lauterburg BH. The systemic availability of oral glutathione. *Eur J Clin Pharmacol.* 1992;43(6):667-669.
9. Allen J, Bradley RD. Effects of oral glutathione supplementation on systemic oxidative stress biomarkers in human volunteers. *J Altern Complement Med.* 2011;17(9):827-833.
10. Ballatori N, Krance SM, Notenboom S, Shi S, Tieu K, Hammond CL. Glutathione dysregulation and the etiology and progression of human diseases. *Biol Chem.* 2009;390(3):191-214.
11. Hunjan MK, Evered DF. Absorption of glutathione from the gastro-intestinal tract. *Biochim Biophys Acta.* 1985;815(2):184-188.
12. Iantomasi T, Favilli F, Marraccini P, Magaldi T, Bruni P, Vincenzini MT. Glutathione transport system in human small intestine epithelial cells. *Biochim Biophys Acta.* 1997;1330(2):274-283.