



GLUTATHIONE -THE MASTER ANTIOXIDANT - AS VITAL FOR HUMAN LIFE AS OXYGEN.

Biological Science

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ABSTRACT

Glutathione also known as GSH is the body's essential health AID-Antioxidant, Immune booster and Detoxifier. This small protein, produced naturally in the body, maintain these three crucial protective functions. In fact your life depends on glutathione. Without it, your cells would disintegrate from unrestrained oxidation, your body would have little resistance to bacteria, viruses and cancer, and your liver would shrivel up from the eventual accumulation of toxins. Glutathione is not yet household word. Even doctors have only a vague idea of it. However, everyone will soon be talking about this critical supplement. There was a time when scientists had heard of cholesterol and vitamins, but today everyone knows about them. Now it's glutathione turn in the last five years over twenty-five thousand medical articles about this substance have been published, and this scientific understanding is gradually becoming common knowledge. Each and every cell in the body is responsible for its own supply of glutathione and must have the necessary raw material to make it. Glutathione is always in great demand and is rapidly consumed when we experience any sort of pressure – illness, stress, fatigue and even exercise. Glutathione level also diminish as we age and many disease normally associated with aging have been linked to glutathione deficiency.

KEYWORDS

Glutathione, Immune system enhancer, Detoxifier, Antioxidant, oxidative stress, cystic fibrosis, Parkinson disease

Introduction

Glutathione is a small protein produced naturally in body and plays three important functions i.e. Antioxidant, Immune booster and detoxifier thus also knows as the body's essential health AID^[1]. Glutathione is produced naturally in each and every cell in the body^[1]. Glutathione is the body's antioxidant present within cell and referred as "The Master Antioxidant". It protects our health naturally by reducing the negative impact of stress hormone, proper cell oxygenation, inhibits cellular mutagens and also warding off hazardous cellular invaders. Glutathione neutralize overactive and dangerous free radicals by roaming through our body^[3]. Glutathione is also useful in cellular reactions like glyoxalase system, reduction of ribonucleotides to doxyribonucleotide, regulation of proteins and gene expression^[4]. It is a water soluble substance that protects our body against infection by performing detoxification reactions^[5]. It neutralizes toxic peroxides thus provide antioxidant defense mechanism in all mammalian cells. Ingestion of certain medications, environmental toxins, chronic liver infection and HIV infection results in rapid consumption and depletion of glutathione^[6,7,8]. Glutathione is an endogenous antioxidant but also as essential factor in energy utilization as it protects the cell and mitochondria from oxidative and peroxidative damage^[2]. Glutathione is a tripeptide, consists of three amino acids i.e. glycine, glutamic acid and cysteine. Cysteine is most important amino acid as it determines the production of glutathione in body^[2]. Deficiency of cysteine leads to inadequate production of glutathione which further results in accelerated aging, toxins accumulation, less protection from disease, decline in health and greater degree of cellular oxidation^[2]. Glutathione is poorly absorbed through GLT thus tissue level and serum concentration of glutathione can be increased by co-administration of N-acetyl cysteine, α -lipoic acid, silymarin flavonoid and l-glutamine^[9]. "No other antioxidant is as important to overall health as glutathione. It is the regulator and regenerator of immune cells and the most valuable detoxifying agent in the human body"

-Patrick J.D. Bouic, Ph.D. in the immune system cure-

Antioxidant

Antioxidants are valuable in the treatment and prevention of that disease which involves oxidative attack by free radicals. Free radicals play causative role in all shots of illness like heart disease, cancer, diabetes and aging. Vitamin C, vitamin E and selenium are naturally occurring antioxidants acts by neutralizing free radicals.

Glutathione is an important antioxidant generated in body itself^[1]. Effectiveness of other antioxidants like vitamin c, vitamin E, lipoic acid and selenium depends upon presence of glutathione and these antioxidants works synergistically with glutathione^[2]. Glutathione is referred as the master antioxidant as its presence increases the effectiveness of other antioxidants^[1]. There are two states of glutathione i.e. reduced glutathione and oxidized glutathione.

Glutathione reductase is responsible for regeneration of reduced glutathione. In healthy cell and tissue the % of reduced glutathione and oxidized glutathione is 90% and 10% respectively. Oxidized stress can be indicated by activity of glutathione reductase. Glutathione is a cofactor for enzyme glutathione peroxide which maintains ascorbate and tocopherol level by acting as a reducing agent^[5,6,7,8,10,11,12,13,16].

Detoxifier

Liver is the primary organ for the detoxification. Poor liver functions leads to increased toxin load. Glutathione in liver eliminate toxins like pollutants, heavy metals, carcinogens, and radiation damage and drug metabolites^[2]. Primary mechanism of eliminating free radicals is glutathione conjugation^[30]. Impaired liver's detoxification capacity leads to depletion of glutathione level in liver which in turn results in accumulation of toxins and potentially dangerous byproducts of metabolism^[14, 15, 16, 17, 18]. Glutathione also helps in safe and efficient elimination of fat soluble toxins by converting them into water soluble forms^[15,12].

Immune system enhancer

White blood cells are the front line of the immune system. High level of glutathione increases W.B.C. production. Glutathione level regulates the healthy growth and development of immune cells thus glutathione serves as food for the immune system. Glutathione is one of the most important components of overall health as it fights off illness. Sufficient or high level of glutathione produces better ability to prevent illness, disease as well as degenerative process of aging^[2].

Food that best promote glutathione production and preservation

Whey protein of fresh, raw milk is natural food source that promotes glutathione production. It provides all key amino acids for glutathione production i.e. cysteine, glycine and glutamate. Glutamyl cysteine is a unique cysteine residue found in whey and has greater affinity to convert in glutathione. denaturation of whey proteins (via mechanical stress, high heat pasteurization and other processes that involves ion exchange, hydrolyzation and use of acidic bathes) decreases its ability of glutathione production^[2]. Cheese, fish, eggs, germs, nuts, roots, vegetables and fruits are the other sources which act as cofactor for glutathione production.

Glutathione in health and disease

Glutathione plays important role in the treatment and prevention of hundreds of disease thus considered as important to health as a well-rounded diet, exercise and good lifestyle. Raised glutathione level decreases the risk of heart disease, stroke, diabetes, high cholesterol. Asthma, cigrate smoking, hepatitis, AIDS and enhance the ability to fight toxins, infectious disease, precancerous cells and aging process. Also responsible for greater strength, endurance, decreased recovery time from injury, less muscles pain, fatigue and muscles promoting activity^[1].

Deficiency of glutathione results in^[3]

1. Disturbed multiplication of white blood cells from immune system.
2. Insufficient production of antibodies.
3. Proliferation of viral cells and cancer cells.
4. Magnification of associated disorders such as AIDS, cancer, intestinal disorders, lung disease, trauma, over trained athlete's syndrome.
5. compromised function of lung, intestinal tract and nervous system "Glutathione promotes longevity, it protects the body against over 60 disease, including arthritis, diabetes, Alzheimer's disease and Parkinson's disease. It boosts the immune system strengths and is useful autoimmune disease and other health problems"

-Dr. gutman MD-

Some possible clinical Applications of Elevated glutathione level Aging

- Parkinson's disease
- Alzheimer's disease
- Cataract formation
- Muscular degeneration
- Cancers of aging
- Prostate problems
- Osteoarthritis

Cardiovascular

- Prevents heart disease
- Prevent stroke
- Prevent atherosclerosis
- Reverses atherosclerosis
- Prevents reperfusion therapy

Digestive system

- Inflammatory bowel disease
- Hepatitis
- Malnutrition
- Pancreatitis
- Peptic ulcer

Toxicology

- Detoxifier certain drug overdose
- Detoxifies substances in cigarette smoke, auto exhaust
- Detoxifies pollutants including heavy metals, pesticides
- Prevents hearing loss from noise pollution
- Detoxifies many well-known carcinogens, Infectious disease and immunology
- Anti-viral (AIDS, hepatitis, herpes, common cold, etc.)
- Bacterial infection
- Certain autoimmune dysfunction
- Chronic fatigue syndrome
- Immuno-suppression

Cancer

- Cancer prevention
- Suppression tumor growth
- Eliminates carcinogens, mutagens
- Retards oxidative damage to DNA
- Prevents wasting disease
- Eases side effect of chemotherapy and radiotherapy

Pulmonary

- Break up mucous
- Cystic fibrosis
- Asthma
- Chronic bronchitis Emphysema pulmonary fibrosis

Metabolic

- Athletic enhancement
- Decreases recovery time from physical stress
- Decreases cholesterol LDL oxidation
- Supports hemoglobin in kidney failure
- Diabetes

Heart disease, stroke and cholesterol

Atherosclerosis (Cholesterol plaque) in the arteries is the root cause of

heart disease and stroke. High glutathione level fights the oxidation of cholesterol level in the blood stream^[1].

Lung disease

Glutathione used to treat many lung disease including asthma, chronic bronchitis, emphysema, cigarette smoking damage, pulmonary fibrosis and other lung disease^[1].

Digestive system

Glutathione is useful to protect body against inflammation of gastritis, stomach ulcers, pancreatitis, inflammatory bowel disease including ulcerative colitis and crohn;s disease^[1].

Hepatitis

Both alcoholic hepatitis and viral hepatitis (Including A, B and C) leads to impaired glutathione level. High glutathione level restores liver functions^[1].

Diabetes

Role of glutathione in diabetes is as following^[31]

Protects cells from oxidation – Diabetes patients have many free radicals in their body. Thus high level of glutathione is essential for diabetics to neutralize the harmful free radicals.

Helps in weight control- Overweight peoples are more prone to develop type 2 diabetes mellitus. In diabetes, cells are always hungry because glucose (food for body cells) is unable to enter in cells. Glutathione plays important role in manage and control weight and also prevents accumulation of oxidized fat in blood vessels.

Increased energy level- Diabetes patients tired easily because cells do not get glucose to generate energy. Thus glutathione provides energy and makes patient able to participate in all kind of activities.

Kidney disease

High glutathione level prevents anemia in kidney failure or dialysis patients who suffers from hyper oxidative stress^[1].

Pregnancy, lactation and childbirth

Glutathione acts on placenta to detoxify pollutants and prevents complications^[1].

Boost your glutathione level and revolutionize overall health

Glutathione can be taken orally, IV, inhalational or as a cream. Glutathione intake can be increased by taking cysteine rich diet like poultry yoghurt, egg yolk, red peppers, garlic, onions, oats and wheat germ^[5] Newly developed glutathione patches can increase the production of glutathione n your body by 300% as little as 24 hours^[3].

Disease associated with altered glutathione level

Defects in enzyme of the γ glutamyl cycle- In approximately 50% of patient, mental retardation and neuropsychiatric dysfunction are due to recessive mutation of GSH syntheses. This deficiency accompanied by metabolic acidosis and hemolytic anemia. These patients are associated with excess of 5-loxoprine in blood stream which leads to feedback inhibition by GSH on γ -GCS^[21].

Parkinson disease- Glutathione found in mill molar concentration in brain^[22]. Brain is more involved in oxidative damage than other tissues^[23]. Alteration in glutathione homeostasis results in oxidative stress which in turn leads to neurodegenerative disease like Parkinson disease^[24].

HIV – Immune dysfunction is a hallmark of AIDS. Low GSH level may cause immune dysfunctioning. AIDS patients are associated with low level of glutathione in plasma, epithelial lining fluid (ELF), peripheral blood mononuclear cells and monocytes^[25].

Liver disease- The main function of glutathione in liver is detoxification. Thus inherited disorder in glutathione synthesis and metabolism can alter liver's detoxification function^[26].

Cystic fibrosis - Progression of glutathione deficiency is a characteristic of cystic fibrosis^[27]. NF α B transcription participates in the regulation of inflammatory cytokine. Cellular deficiency leads to an increase in NF α B transcription^[26]. GSH deficiency may cause inflammation (hall mark of cystic fibrosis) and oxidative stress that in

turn leads to damage of cell membrane, cellular protein and DNA^[28,29].

Dosage considerations^[30]

General health support- 1 capsule per day

Liver ailments – 2to 4 capsules par day

Chronic kidney disease- 2 to 4 capsules per day

Regular acetaminophen or alcohol use- 1 to 2 capsule per day

HIV infection- 3 to 4 capsules per day

Bronchitis (to break up mucus) - 3 to 4 capsules per day

Diabetes (to improve glucose tolerance and antioxidant function) -2 capsules per day

Amyotrophic lateral sclerosis, Multiple sclerosis, Parkinson disease- 4 capsules per day

To help reverse buildup of mercury, cadmium, arsenic and other heavy metals- 1to 4 capsules per day

Cataracts – 2 capsules per day

Polycystic ovarian disease- 2 capsules per day.

Adjunctive nutritional cancer management - 3to 4 capsules per day

Conclusion

The many different environmental toxins, medications and other xenobiotic that are common place in our world today have been shown to more rapidly use up the body's pool of glutathione as per glutathione involvement in quenching electrophiles (free radicals), neutralizing peroxides, and detoxifies numerous chemicals via phase I and phase II (Conjugation reactions) pathways. The evidence is strong and consistent that glutathione depletion renders liver cells susceptible to the damaging effects of various drugs and other toxins, contributing to advancing liver disease. Striving to ensure more optimal glutathione nutritional status appears to be a prudent strategy to help the body defend itself against liver damage and reduce concentration of circulating carcinogens in the system. Boosting glutathione levels also helps to support immune function and provide important antioxidant protection to all body cells. Maintaining glutathione status is also providing important antioxidant protection to all body cells. Maintaining glutathione is also important in the nutritional management of chronic liver infections and diseases and HIV infection.

1. Glutathione, your body's most powerful healing agent by GUTMAN & SCHETTINI @ 2000 G7S health bokks Inc., montreal, Canada.
2. Action-whey-best-for-glutathione.pdf
3. <http://undergroundhealthreporter.com/benefit-of-glutathione-the-master-antioxidant/>
4. Mullinneaux P, Creissen GP. Glutathione reductase: regulation and role in oxidative stress. Oxidative stress and the molecular biology of antioxidant defence. Cold spring harbor laboratory Press[™] 1997.
5. murray RK. Metabolism of xenobiotics. In: Murray RK, Granner DK, Mayes PA et al, eds. Herper's Biochemistry. 24th ed. Stamford, CT: Appleton and lange; 1996.
6. carr A, Cooper DA Penny R. Allergic manifestations of human immunodeficiency virus (HIV) infection. J Clin Immunol 1991;11:55-64.
7. Shriner K, Goetz MB. Severe hepatotoxicity in a patient receiving both acetaminophen and zidovudine. Am J Med 1992; 93: 94-96.
8. Schreck R, Rieder P, Baeuerle P. Reactive oxygen intermediates as apparently wide used messenger in the activation of the NF-kappa B transcription factor and HIV-1. EMBO J.
9. Witshchi A, Reddy S, Stofor B, Lauterburg BH. The systemic availability of oral glutathione. Eur J Clin Pharmacol 1992; 43:667-669.
10. Meister A, Anderson ME. Glutathione. Annu Rev Biochem 1983; 52:7111-760.
11. Meister A. Glutathione-ascorbic acid antioxidant system in animals. J Biol Chem 1994; 269: 9397-9400.
12. hamilos DL, Wedner HJ. The role of glutathione in lymphocyte activation.L.comparison of inhibitory effects of buthioninesulfoximine and 2-cyclohexene-1-one by nuclear size transformation. J Immunol 1985;135:2740-2747.
13. Muller F, Aukrust P, Svardal AM, et al. low serum glutathione, cysteine and homocystein in immunodeficiency virus infecton. In: Watson RR, ed. Nutrition and foods in AIDS. Boca Raton, FL: CRC Press; 1998: 35-39.
14. Marror M, Alcabes P, Titus S, et al. Low serum thiol levels predict shorter times-to-death among HIV infected injecting drug users. AIDS 1997;11:1389-1393.
15. Buhl R, Jaffe HA, Holroyd KJ, et al. Systemic glutathione deficiency in symptom free HIV-seropositive individuals. Lancet 1989;2:1294-1298.
16. Staal FJ, Roederer M, Herzenberg LA, Herzenberg LA. Intracellular thiols regulate activation of nuclear factor KB and transcription of human immunodeficiency virus. ProcNatiAcad Sci USA 1990; 87:9943-9947.
17. Anukrust P, Muller F. glutathione redox disturbances in human immunodeficiency virus infection: immunologic and therapeutic consequences. Nutrition 1999; 15:165-167.
18. Buttker TM, Sandstrom PA. oxidative stress as a mediator of apoptosis. Immunol Today 1994;15:7-10.
19. hamilos DL, Wedner HJ. The role of glutathione in lymphocyte activation.L.comparison of inhibitory effects of buthioninesulfoximine and 2-cyclohexene-1-one by nuclear size transformation. J Immunol 1985;135:2740-2747.
20. Optimize your immunity and wellbeing. www.immunotechGTA.com.
21. Shi ZZ, Habib GM, Rhead WJ Gahl WA, He X, sazer S, et al. Mutations in the glutathione synthetase gene cause 5-oxoprolinuria. Nat Genet 1996;14:361-5.
22. Dringen RGJ, Hirlinger J. Glutathione metabolism in the brain. Eur J Biochem 2000;267:4921-6.
23. Halliwell B, Gutteridge JM, oxygen free radicals and iron in relation to biology and medicine: some problems and concepts. Arch Biochem Biophys 1986;246:501-14.
24. Youdim MB. Understanding parkinson's disease. Sci Am 1997;276:52-9.
25. Buhl R, Jaffe HA, Holroyd KJ, Wells FB, Mastrangeli A, Saltini C, et al. Systemic glutathione deficiency in system –free HIV seropositive immunodeficiency virus. Proc Nati Acad Sci USA 1990;87:9943-7.

26. Hudson V. Rethinking cystic fibrosis pathology: the critical role of abnormal reduced glutathione (GSH) transport caused by CFTR mutation. Free radical Biol MED. 2001;30:1440-61.
27. Roum JH, BUHL R, Mc Elvant NG, Borok Z, Crystal RG, Systemic deficiency of glutathione in cystic fibrosis. JAppl Physiol 1993;75:2419-24.
28. Brown RK, ScBurney A, Lunec J, Kelly FJ. Oxidative damage to DNA in patient with cystic fibrosis. Free radicals Biol Med 1995; 234: 137-46.
29. Brown RK, wyatt H, Price JF, Kelly FJ. Pulmonary dysfunction in cystic fibrosis is associated with oxidative stress. Eur Respir J 1996;9: 334-9.
30. www.adeeva.com/product/vit glutathione.
31. Optimize your immunity and well being. www.immunotechGTA.com