

DNA Repair, Glutathione and Immunocal

As listed in the PDR (Physicians' Desk Reference)

I have added a few notations to clarify some of the medical jargon.

IMMUNOCAL® PDR® 2008

NUTRACEUTICAL (Bonded cysteine supplement) glutathione precursor Powder Sachets

DESCRIPTION and CLINICAL PHARMACOLOGY

[IMMUNOCAL®](#) is a U.S. patented natural food protein concentrate in the FDA category of GRAS (generally recognized as safe) which assists the body in maintaining optimal concentrations of glutathione (GSH) by supplying the precursors required for intracellular glutathione synthesis.

It is clinically proven to raise glutathione values.

Glutathione is a tripeptide made intracellularly from its constituent amino acids L-glutamate, L-cysteine and glycine. The sulfhydryl (thiol) group (SH) of cysteine is responsible for the biological activity of glutathione. Provision of this amino acid is the rate-limiting factor in glutathione synthesis by the cells since cysteine is relatively rare in foodstuffs.

[Immunocal®](#) is a bovine whey protein isolate specially prepared so as to provide a rich source of bioavailable cysteine. Immunocal® can thus be viewed as a cysteine delivery system.

The disulphide bond in cystine is pepsin and trypsin resistant but may be split by heat, low pH or mechanical stress releasing free cysteine.

When subject to heat or shearing forces (inherent in most extraction processes), the fragile disulfide bonds within the peptides are broken and the bioavailability of cysteine is greatly diminished.

Glutathione is a tightly regulated intracellular constituent and is limited in its production by negative feedback inhibition of its own synthesis through the enzyme gamma-glutamylcysteine synthetase, thus greatly minimizing any possibility of overdosage.

Glutathione has multiple functions:

1. It is the major endogenous antioxidant produced by the cells, participating directly in the neutralization of free radicals and reactive oxygen compounds, as well as maintaining exogenous antioxidants such as vitamins C and E in their reduced (active) forms.
2. Through direct **conjugation**, it detoxifies many xenobiotics (foreign compounds) and carcinogens, both organic and inorganic.

Notation

Conjugation:

any of a group of enzymes found in blood or in certain organs (as kidney and pancreas) and in some vegetables (as potatoes) that bring about the breakdown of conjugates of pteroylglutamic acid or folic acid.... a water-soluble vitamin belonging to the B-complex group of [vitamins](#). These vitamins help the body break down complex carbohydrates into simple sugars to be used for energy. Excess B vitamins are excreted from the body rather than stored for later use. This is why sufficient daily intake of folic acid is necessary.

3. It is essential for the immune system to exert its full potential, e.g. (1) modulating antigen presentation to lymphocytes, thereby influencing cytokine production and 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 **apoptosis**, thereby maintaining control of the immune response.

Notation

Apoptosis

Simply put cell suicide. Cells may also commit suicide in times of distress, for the good of the organism as a whole. For example, in the case of a viral infection, certain cells of the immune system, called cytotoxic [T lymphocytes](#), bind to infected cells and trigger them to undergo apoptosis. Also, cells that have suffered damage to their DNA, which can make them prone to becoming cancerous, are induced to commit apoptosis.

4. It plays a fundamental role in numerous 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.

Notation

DNA Synthesis and Repair

DNA repair refers to a collection of processes by which a [cell](#) identifies and corrects damage to the [DNA](#) molecules that encode its [genome](#). In human cells, both normal [metabolic](#) activities and environmental factors such as [UV](#) light and [Radiation](#) can cause DNA damage, resulting in as many as 1 [million](#) individual [molecular lesions](#) per cell per day.^[1] Many of these lesions cause structural damage to the DNA molecule and can alter or eliminate the cell's ability to [transcribe](#) the [gene](#) that the affected DNA encodes. Other lesions induce potentially harmful [mutations](#) in the cell's genome, which affect the survival of its daughter cells after it undergoes [mitosis](#). Consequently, the DNA repair process is constantly active as it responds to damage in the DNA

structure.

The rate of DNA repair is dependent on many factors, including the cell type, the age of the cell, and the extracellular environment. A cell that has accumulated a large amount of DNA damage, or one that no longer effectively repairs damage incurred to its DNA, can enter **one of three possible states**:

1. an irreversible state of dormancy, known as [senescence](#)
2. cell suicide, also known as [apoptosis](#) or [programmed cell death](#)
3. **unregulated cell division, which can lead to the formation of a tumor that is cancerous**

The DNA repair ability of a cell is vital to the integrity of its genome and thus to its normal functioning and that of the organism. Many genes that were initially shown to influence [lifespan](#) have turned out to be involved in DNA damage repair and protection.^[2] Failure to correct molecular lesions in cells that form [gametes](#) can introduce mutations into the genomes of the offspring and thus influence the rate of [evolution](#).

INDICATIONS AND USAGE

[IMMUNOCAL®](#) is a natural food supplement and as such is limited from stating medical claims per se. Statements have not been evaluated by the FDA. As such, this product is thus not intended to diagnose, cure, prevent or treat any disease.

Glutathione augmentation is a strategy developed to address states of glutathione deficiency, high oxidative stress, immune deficiency, and xenobiotic overload in which glutathione plays a part in the detoxification of the xenobiotic in question.

Glutathione deficiency states include, but are not limited to: HIV/AIDS, infectious hepatitis, certain types of cancers, cataracts, Alzheimer's Disease, Parkinsons, chronic obstructive pulmonary disease, asthma, radiation, poisoning by acetaminophen and related agents, malnutritive states, arduous physical stress, aging, and has been associated with sub-optimal immune response. Many clinical pathologies are associated with oxidative stress and are elaborated upon in numerous medical references.

Low glutathione is also strongly implicated in wasting and negative nitrogen balance, notably as seen in cancer, AIDS, sepsis, trauma, burns and even athletic overtraining. Cysteine supplementation can oppose this process and in AIDS, for example, result in improved survival rates.

CONTRAINDICATIONS

[IMMUNOCAL®](#) is contraindicated in individuals who develop or have known hypersensitivity to specific milk proteins.

PRECAUTIONS

Each sachet of [IMMUNOCAL®](#) contains nine grams of protein. Patients on a protein-restricted diet need to take this into account when calculating their daily protein load. Although a bovine milk derivative,

[IMMUNOCAL®](#) contains less than 1% lactose and therefore is generally well tolerated by lactose-intolerant individuals.

WARNINGS

Patients undergoing immunosuppressive therapy should discuss the use of this product with their health professional.

ADVERSE REACTIONS

Gastrointestinal bloating and cramps **if not sufficiently rehydrated**. Transient urticarial-like rash in rare individuals undergoing severe detoxification reaction. Rash abates when product intake stopped or reduced.

OVERDOSAGE

Overdosing on [IMMUNOCAL®](#) has not been reported.

DOSAGE AND ADMINISTRATION

For mild to moderate health challenges, 20 grams per day is recommended. Clinical trials in patients with AIDS, COPD, cancer and chronic fatigue syndrome have used 30-40 grams per day without ill effect. IMMUNOCAL® is best administered on an empty stomach or with a light meal. Concomitant intake of another high protein load may adversely affect absorption.

RECONSTITUTION

[IMMUNOCAL®](#) is a dehydrated powdered protein isolate. It must be appropriately rehydrated before use. Remains bioactive up to 12 hours after mixing. DO NOT heat or use a hot liquid to rehydrate the product. DO NOT use a high-speed blender for reconstitution. These methods will decrease the activity of the product. Proper mixing is imperative. Consult instructions included in packaging.

HOW SUPPLIED

10 grams of bovine milk protein isolate powder per sachet. 30 sachets per box.

STORAGE

Store in a cool dry environment. Refrigeration is not necessary. Patent no.'s: 5,230,902 - 5,290,571 - 5,456,924 - 5 ,451,412 - 5,888,552

REFERENCES

1. Baruchel S, Viau G, Olivier R. et al. Nutraceutical modulation of glutathione with a humanized native milk serum protein isolate, Immunocal®: application in AIDS and cancer. *In: Oxidative Stress in Cancer, AIDS and Neurodegenerative Diseases*. Ed.; Montagnier L, Olivier R, Pasquier C. Marcel Dekker Inc. New York, 447-461, 1998

2. Bounous G, Kongshavn P. Influence of protein type in nutritionally adequate diets on the development of immunity. *In* Absorption and Utilization of Amino Acids Vol.II. Ed. M. Friedman. CRC Press, Inc., Fla. 2:219-32, 1989
3. Bounous G, Gold P. The biological activity of undenatured whey proteins: role of glutathione. *Clin Invest Med* 14:296-309, 1991
4. Bounous G, Baruchel S, Falutz J. Gold P. Whey proteins as a food supplement in HIV-seropositive individuals. *Clin Invest Med.* 16:3; 204-209, 1992
5. Bounous G. Whey protein concentrate (WPC) and glutathione modulation in cancer treatment. *Anticancer Res.* 20:4785-4792, 2000
6. Bounous G. Immunoenhancing properties of undenatured milk serum protein isolate in HIV patients. *Int. Dairy Fed: Whey:* 293-305, 1998
7. Bray T, Taylor C. Enhancement of tissue glutathione for antioxidant and immune functions in malnutrition. *Biochem. Pharmacol.* 47:2113- 2123, 1994.
8. Droge W, Holm E. Role of cysteine and glutathione in HIV infection and other diseases associated with muscle wasting and immunological dysfunction. *FASEB J:* 11(13):1077-1089, 1997
9. Herzenberg LA, De Rosa SC, Dubs JG et al. Glutathione deficiency is associated with impaired survival in HIV disease. *Proc Natl Acad Sci* 94:1967-72, 1997
10. Kennedy R, Konok G, Bounous G et al.. The use of a whey protein concentrate in the treatment of patients with metastatic carcinoma: A phase I-II clinical study. *Anticancer Res.* 15:2643-50, 1995
11. Lands LC, Grey VL, Smountas AA. Effect of supplementation with a cysteine donor on muscular performance. *J. Appl. Physiol.* 87:1381-1385, 1999
12. Locigno R, Castronovo V. Reduced glutathione system: Role in cancer development, prevention and treatment. *International Journal of Oncology* 19:221-236, 2001
13. Lomaestro B, Malone M. Glutathione in health and disease: pharmacotherapeutic issues. *Ann Pharmacother* 29: 1263-73, 1995
14. Lothian B, Grey V, Kimoff RJ, Lands. Treatment of obstructive airway disease with a cysteine donor protein supplement: a case report. *Chest* 117:914-916, 2000
15. Meister A. Glutathione. *Ann Rev Biochem* 52:711-60, 1983
16. Peterson JD, Herzenberg LA, Vasquez KK, Waltenbaugh C. Glutathione levels in antigen-presenting cells modulate Th1 versus Th2 response patterns. *Proc. Natl. Acad. Sci.* 95:3071-3076, 1998

17. Watanabe A, Higachi K, Yasumura S. et al. Nutritional modulation of glutathione level and cellular immunity in chronic hepatitis B and C. Hepatology. 24:597A, 1996

18. Witschi A, Reddy S, Stofer B, Lauterberg B. The systemic availability of oral glutathione. Eur. J. Clin. Pharmacol. 43:667-669, 1992.

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