



## From the 2001 Edition of the Official Physicians Desk Reference

### **Immunocal®** **GLUTATHIONE PRECURSOR** *(Undenatured whey protein isolate)* Powder Sachets

#### **DESCRIPTION**

**Immunocal®** is a U.S. patented natural food supplement which assists the body in maintaining optimal concentrations of glutathione (GSH) by supplying the precursors required for intracellular glutathione synthesis. These precursors are derived from a specially prepared bovine whey protein isolate. Glutathione (L-gamma-glutamyl-L-cysteinylglycine) is the major endogenous antioxidant produced by the cell. Glutathione participates directly in the neutralization of free radicals, reactive oxygen compounds, and maintains exogenous antioxidants such as vitamins C and E in their reduced (active) forms. In addition, through direct conjugation, glutathione plays a role in the detoxification of many xenobiotics (foreign compounds) both organic and inorganic. Glutathione availability is an essential component of the humoral immune response by offsetting oxidative damage resulting from the clonal expansion and inherent metabolism of lymphocytes.

#### **CLINICAL PHARMACOLOGY**

The systemic availability of oral glutathione is negligible, the vast majority of it must be manufactured intracellularly. Glutathione (GSH) is a tripeptide made up of the three amino acids cysteine, glycine and glutamate. Glutamate and glycine are readily available in most North American diets, but the availability of cysteine tends to be the rate-limiting event for the synthesis of glutathione within the cell. It is the sulfhydryl (thiol) group (SH) of cysteine that serves as protein-donor and is responsible for the biochemical activity of glutathione. The free amino acid cysteine does not represent an ideal delivery system to the cell. It is potentially toxic and is spontaneously catabolized in the gastrointestinal tract and blood serum. Conversely, cysteine present as cystine (two cysteine molecules linked by a disulfide bond) released during digestion in the gastrointestinal tract is more stable than the free amino acid cysteine: the disulfide bond is pepsin- and trypsin-resistant, but may be split by heat and mechanical stress. In this way, cystine travels safely through the GI tract and blood serum and is promptly reduced to the two cysteine molecules on cell entry. Immunocal can thus be viewed as a cysteine delivery vehicle.

Specially prepared whey protein isolates contain the thermolabile proteins serum albumin, alpha lactalbumin and lactoferrin. These proteins contain high levels of cystine residues that could be denatured by heat or mechanical stress (unfortunately inherent to most extraction processes). Hence, in serum albumin there are 17 cysteine residues and 6 glutamylcystine (Glu-Cys) dipeptides; in lactoferrin 17 cystine residues and 4 Glu-Cys dipeptides; and in alpha-lactalbumin 4 cystine residues. In particular, the Glu-Cys dipeptides very readily enter the cell to be synthesized into GSH. Of interest, the Glu-Cys dipeptide is an exclusive feature of the only obligatory foods in the early life of mammals and oviparous species, those being milk and egg white respectively. When subject to heat or shearing forces, the fragile disulfide bonds within these peptides are broken and the bioavailability of the glutathione precursors is greatly diminished.

As an antioxidant, glutathione is essential for allowing lymphocytes to express their full potential, without being hampered by oxyradical accumulation during the oxygen-requiring development of the immune response. In a similar fashion, GSH delays the muscular fatigue induced by oxyradicals during the aerobic phase of strenuous muscular contraction.

As a detoxification agent, glutathione has been demonstrated to be effective against chemical pollutants, various carcinogens and ultraviolet radiation.

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.

## **INDICATIONS AND USAGE**

**Immunocal®** being a natural food supplement and as such is limited from stating medical claims per se. Statements have not been evaluated by the FDA. This product is thus not intended to diagnose, cure, prevent or treat any disease.

Glutathione augmentation is a clinical strategy to address states of glutathione deficiency, antioxidant deficiency, high oxidative stress, and certain toxic overloads in which glutathione plays a part in the detoxification of the xenobiotic in question. Glutathione deficiency states include, but are not limited to: AIDS and cancer cachexia, chemical and infectious hepatitis, radiation poisoning, malnutritive states, arduous physical stress, and acetaminophen toxicity. Many pathologies are associated with oxidative stress and are elaborated upon in numerous medical references.

## **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.

Heating or adding **Immunocal®** to a hot liquid, or use of a high-speed blender to reconstitute it will significantly decrease the effectiveness of the product.

## **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. Unless hypersensitive to the constituents, no toxicity of milk proteins has been described.

## **DOSAGE AND ADMINISTRATION**

Maintenance dose is one sachet (10 grams) per day. For mild to moderate health challenges, higher doses are recommended. Clinical trials in patients with AIDS, cancer and chronic fatigue syndrome have used 30 – 50 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. If left standing too long after rehydration, activity of the product may be reduced. Times vary depending on temperature and pH of the liquid used. It is generally recommended to ingest the product within 30 minutes of reconstitution. **DO NOT** heat or use a hot liquid to rehydrate the product or use a high-speed blender for reconstitution. These methods will decrease the activity of the product. Special low-speed blenders or mixing cups can be made available through Immunotec Research Ltd. distribution networks.

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.

US Patent no.'s: 5,230,902 – 5,290,571 – 5,456,924 – 5,451,412 – 5,888,552

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