WHEY PROTEINS & GLUTATHIONE

A growing amount of scientific evidence reveals that whey contains various bioactive components that are capable of improving health and preventing disease. Whey is a reliable source of high quality and biologically active proteins, carbohydrates and minerals. Individual whey proteins contain a variety of functional and nutritional attributes, which are related to the structure and biological functions of these proteins. Several physiological roles have been defined or suggested for whey proteins or peptides. This brief reviews and highlights the immune enhancing, antioxidant and anticarcinogenic properties of whey proteins, with specific emphasis on the tripeptide glutathione (L-γ-glutamyl-L-cysteinyl-glycine), which is synthesized intracellularly by all mammals, and is essential for metabolic and cell-cycle related functions in virtually all cells.

❑ WHEY PROTEINS & IMMUNE ENHANCEMENT

The immune system plays an important role in protection against bacterial, viral, parasitic and fungal infections, as well as cancers. Deficiencies in any aspect of the immune system can predispose an individual to a greater risk of infection and may enhance the severity of disease. While, there is no adequate knowledge about the effect of whey components on the human immune system, it seems that an important feature of whey proteins is their high concentration of cysteine, which is thought to be rate limiting for glutathione (GSH) synthesis.[1] Whey proteins are rich in the amino acid cysteine, which occurs in its primary sequence as cystine linked to glutamic acid. The sequence glutamyl-cystine (Glu-Cys) seems to be unbreakable by the proteolytic enzyme of the monogastric digestive system. Therefore, peptides with the sequence glutamic acid-cystine are released and absorbed, serving as a substrate for GSH synthesis.[2]

The GSH-modulating effect of whey proteins is believed to underlie both immuno-enhancing and antioxidant actions of whey proteins. Animal studies have shown that dietary whey protein concentrate elevates humoral and cell-mediated responses.[3,4] It has also been reported that several amino acids and peptides they form may stimulate antibody production and the process of phagocytosis.[5]

A study demonstrated that the enhancement of humoral immune response in WPC-fed mice, compared to mice fed casein and cysteine supplemented casein diets, was associated with a greater and more sustained production of glutathione in the spleen during the antigen-driven clonal expansion of lymphocytes. This study indicated that the efficiency of dietary cysteine in inducing supernormal glutathione levels is greater when it is delivered in the whey protein than as free cysteine.[2]

❑ WHEY PROTEINS & ANTIOXIDANT ACTIVITY

Accumulation of intracellular reactive oxygen species (ROS) during extended periods of oxidative stress is associated with the development of chronic diseases. Glutathione functions as an antioxidant; therefore, maintaining a high intracellular concentration of GSH is critical for cellular defense against oxidative stress.[6] In addition to direct scavenging of ROS, GSH is an excellent trap for reactive products of lipid peroxidation, which can inhibit enzyme activity after covalent binding to the protein. A study showed that whey protein isolate, compared with casein, suppressed peroxidation stress in rats fed a low vitamin E-containing diet. The dietary supply of cysteine or Glu-Cys residue in whey proteins can be efficiently used as a precursor to GSH in mammalian organs.[7]

❑ WHEY PROTEINS & ANTICARCINOGENIC ACTIVITY

Since it is considered that oxygen radical generation is frequently a critical step in carcinogenesis, the effect of GSH on free radical detoxification could be important in inhibiting carcinogenesis induced by a number of different mechanisms.[8] Whey proteins have been

reported to provide protection against cancer. Epidemiological studies and experimental

studies suggest that dietary milk products may exert an inhibitory effect on the development of several types of tumors. Experiments in rodents indicate that the antitumor activity of the dairy products is in the protein fraction and more specifically in the whey protein component of milk.[2, 9, 10]

Glutathione concentration is high in most tumor cells and this may be an important factor in resistance to chemotherapy. A number of animal studies show glutathione suppresses tumor development at various sites. The incidence of colon tumors and tumor area in WPC fed mice was reported substantially lower than that in mice fed either the equivalent casein or a Purina diet.[10] In a similar study, animals continuously fed the WPC diet were found to be alive at the end of the experiment, 32% of those on a casein or Purina diet died.[11] Same results were obtained in another study where the impact of different dietary protein sources (whey, casein, soybean, red meat) on the incidence, burden and mass index of induced intestinal tumors in rats was assessed. Whey and casein diets were more protective against the development of intestinal tumors than were the red meat or soybean diets. The intracellular GSH measured in the liver was greatest in whey protein and casein fed rats and lowest in soybean fed animals.[9]

All this evidence from animal, cell culture and clinical trial studies suggests that whey proteins have anticarcinogenic properties, antioxidant activities and that they increase the levels of glutathione. Whey proteins consist of α-lactoalbumin, β-lactoglobulin, immunoglobulins, serum albumin, lactoferrin, lactoperoxidase, and other minor proteins and peptides. β-lactoglobulin, serum albumin and lactoferrin are rich sources of cysteine and glutamylcysteine, thus providing the precursors for the synthesis of glutathione.

The positive health benefits of whey proteins do not end with its effects on immunity, cancer prevention and treatment or its antioxidant activities. The whey protein components can provide passive protection against infection; modulate digestive and metabolic processes; and act as growth factors for different cell types, tissues and organs. Whey proteins and their role in hypertension, lowering of cholesterol, appetite

suppression, bone physiology, muscle growth and fatigue prevention has also been suggested.

REFERENCES:

1. Kaplowitz, N., T.Y. Aw & M. Ookhtens. 1985. The Regulation of Hepatic Glutathione. Ann. Rev. Pharmacol. Toxicol. 25: 715-744.
2. Bounous, G., G. Batist & P. Gold. 1989. Immunoenhancing Property of Dietary Whey Protein in Mice: Role of Glutathione. Clin. & Inv. Medicine. Vol. 12. 3: 154-161.
3. Bounous, G., & P.A.L. Kongshaven. 1982. Influence of Dietary Proteins on the Immune System of Mice. J. Nutr. 112: 1747-1755.
4. Wong, C.W. & D.L. Watson. 1995. Immunomodulatory Effects of Dietary Whey Proteins in Mice. J. Dairy Res. 62: 359-368.
5. Belokrylov, G.A., O. Y. Popova, I.V. Molchanova, E.I. Sorochinskaya & V.V. Anokhima. 1992. Peptides and Their Constituent Amino Acids Influence the Immune Response and Phagocytosis in Different Ways. Int. J. Immunopharmac. 14: 1285-1292.
6. Kent, K.D. W.J. Harper, J.A. Bomser. 2003. Effect of Whey Protein Isolate on Intracellular Glutathione and Oxidant-induced Cell Death in Human Prostate Epithelial Cells. Toxicology in Vitro. 17: 27-33.
7. Zommara, M., H. Toubo, M. Sakono & K. Imaizumi. 1998. Prevention of Peroxidative Stress in Rats Fed on a Low Vitamin E-containing Diet by Supplementing with a Fermented Bovine Milk Whey Preparation: Effect of Lactic Acid and B-Lactoglobulin on the Antiperoxidative Action. Biosci. Biotechnol. Biochem., 62 (4): 710-717.
8. Bounous, G. 2000. Whey Protein Concentrate (WPC) and Glutathione Modulation in Cancer Treatment. Cancer Research. 20: 4785-4792.
9. McIntosh, G.H., G.O. Regester, R.K. LeLue, & P.J. Royle. 1995. Dairy Proteins Protect Against Dimethylhydrazine-induced Intestinal Cancer in Rats. J. Nutr. 125: 809-816.
10. Bounous, G., R. Papenburg, P.A.L. Kongshaven, P. Gold, & D. Fleiszer. 1988. Dietary Whey Protein Inhibits the Development of Dimethylhydrazine Induced Malignancy. Clin. Invest. Med. 11: 213-217.
11. Papenburg, R., G. Bounous, D. Fleiszer & P. Gold. 1990. Dietary Milk Proteins Inhibit the Development of Dimethylhydrazine-induced Malignancy. Tumor Biol. 11: 129-136.