



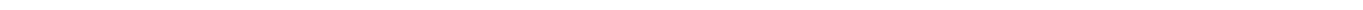
Immunotec

*Clinical
Foundations*

*The Fascinating Story Behind
a Health-Promoting Product -
Patented Milk Serum (Whey)
Protein Concentrate*

by Gustavo Bounous, MD

Notes



SOME BACKGROUND INFORMATION

- In 1978, Dr. Gustavo Bounous in association with Dr. Patricia Kongshavn from McGill University, in Montréal, Québec, Canada, initiated studies on dietary proteins such as casein, soy, wheat, corn, beef, fish, egg albumin and algae, testing for their effects on the immune system.
 - This research led to the discovery of a milk serum (whey) protein isolate that contains unusually high amounts of glutathione (GSH) precursors—notably cystine and glutamylcystine. Experimental research and clinical trials have demonstrated the role of this protein mixture in maintaining cellular glutathione levels allowing for support of the immune response.
 - Analysis of preliminary data effected by scientists of the Canada HIV Trial Network has led to the funding of a Phase III Clinical Trial on adult AIDS patients with Wasting Syndrome. In addition, the Nova Scotia Cancer Center has undertaken a Phase II Trial on breast cancer patients based on a pilot study from the Department of Surgery at Dalhousie University, Halifax, Nova Scotia, Canada.
 - Clinical trials are currently ongoing at the University of Munich, Germany, on patients following major surgery and multiple trauma.
 - A trial is now underway at the King Khalid Hospital, Jeddah, Saudi Arabia, involving children during the course of chemotherapy for the treatment of leukemia.
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INTRODUCTION

This publication is meant to provide a user-friendly yet fully documented overview of the role, relevance and effectiveness of our product, patented milk serum (whey) protein concentrate (WPC), in today's world.

Firstly, a brief review of common causes of glutathione (GSH) depletion and of GSH's role in increasing the body's resistance to these challenges will be presented. Secondly, an article by Dr. Gustavo Bounous will provide the reader with the opportunity to take a closer look at the following:

- how GSH is formed and its role in maintaining optimal function of the immune system;
- the role of the patented WPC, including its effect on the immune system and its benefits similar to those of human milk, as well as its potential role in cancer prevention and the diseases of aging;
- the limits of other strategies aimed at increasing tissue concentration of GSH; and
- finally, the success of our milk serum protein concentrate in sustaining GSH levels, including discussion of its potency and bioactivity.

COMMON CAUSES OF GLUTATHIONE (GSH) DEPLETION

A number of conditions may coexist, each of which places on the body a demand for GSH. Such conditions include:

- production of endogenous oxiradicals during immune activity and strenuous muscular exercise;
- detoxification of foreign pollutants; and
- protection against radiation.

It is conceivable that, during severe challenge, competition for GSH precursors may lead to single or multiple functional deficiencies. Global warming empowers microbes which are now expanding both in number and diversity. Thus, to make matters worse, the GSH-requiring immune system must now compete for GSH precursors with organs increasingly involved in the body's defense against pollutants and ultraviolet radiation resulting from ozone depletion.

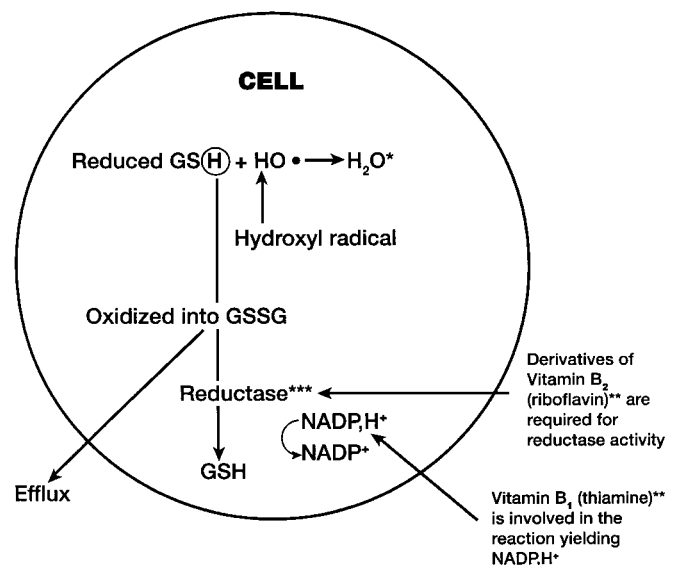
CRUCIAL ROLE OF CELL GSH

Cell GSH is involved in increasing body resistance to challenges in many ways.

Role as Antioxidant

Figure A illustrates the antioxidant properties of cell GSH. As shown in the figure, reduced GSH is oxidized into GSSG in the process of destroying oxiradicals. GSSG is then reduced back to GSH by the action of GSH reductase.

Figure A: Cell GSH Acting as Antioxidant

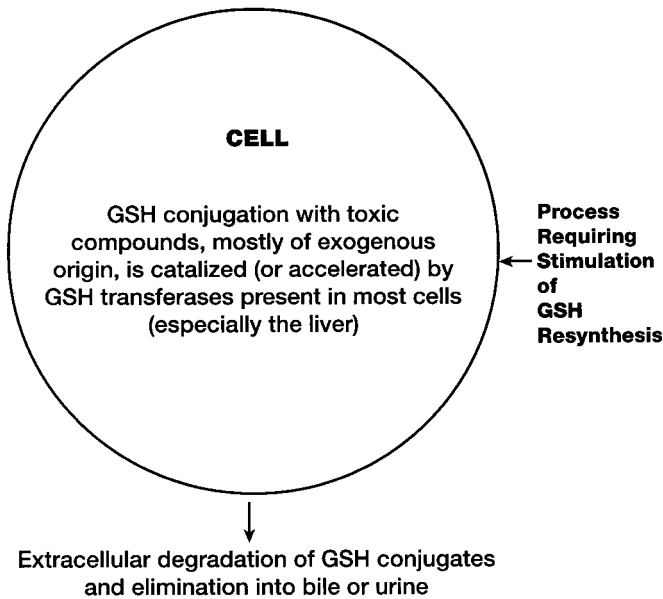


* Water
 ** Both vitamins naturally occurring in whey
 ***An enzyme involved in reducing oxidized glutathione (GSSG) into reduced glutathione (GSH)

Role as Detoxifying Agent

Figure B summarizes the role of GSH in detoxification. This process requires resynthesis of GSH, as indicated in the figure.

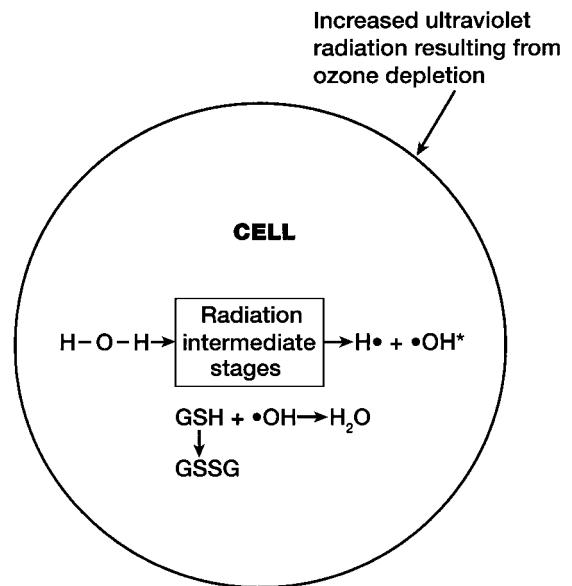
Figure B: Cell GSH Acting as Detoxifying Agent of Chemical Pollutants (Carcinogens, etc.)



Role as Protection against Ultraviolet Radiation

Figure C illustrates the role of GSH in fighting increased ultraviolet radiation resulting from ozone depletion. Here again, GSH reductase reconstitutes oxidized GSH to its functional status.

Figure C: Cell GSH Acting as Protection Against Ultraviolet Radiation



$\cdot OH$ is the most reactive radical known to chemistry

EVIDENCE

A Closer Look at the Central Protective Role of Glutathione (GSH) against Free Radicals, Infections and Chemical Pollutants, and at Milk Serum (Whey) Protein Concentrate, a Natural Source of GSH Precursors

Gustavo Bounous, MD

Mammalian cells have evolved numerous mechanisms to prevent or treat injurious events that can result from normal oxidative byproducts of cellular metabolism. **The “glutathione (GSH) antioxidant system” is foremost among these endogenous protective systems because GSH participates directly in the destruction of reactive oxygen compounds and maintains in reduced active form vitamins C and E, which also exert an antioxidant effect.**¹ In addition, **GSH detoxifies foreign compounds.**² For these reasons, cellular GSH plays a central role in body defense against infection, free radicals and carcinogens. It is not surprising that the liver, which is the major organ involved in the detoxification and elimination of toxic materials, has the greatest concentration of GSH.³

How GSH is Formed

The sulfhydryl (thiol) group (SH) of cysteine is responsible for the chemical properties of the whole GSH molecule (L-gamma-glutamyl-L-cysteinylglycine). As systemic availability of oral GSH is negligible in man⁴ and because there is no evidence for transport of GSH into cells,^{2,3} **GSH has to be synthesized intracellularly.** Though the inflow of cysteine, glutamate, and glycine (components of GSH) may prove somewhat limiting under selected circumstances, **numerous observations have shown that cysteine tends to be the rate-limiting event in GSH synthesis.**

However, free cysteine does not represent an ideal delivery system: it is toxic⁵ and spontaneously oxidized.

Cysteine present as cystine—a natural delivery system

On the other hand, **cysteine present as cystine** (two cysteines linked by a disulfide bond) released during digestion in the gastrointestinal tract is more stable than the free amino acid: the disulfide bond is pepsin- and trypsin-resistant, but may be split by heat and mechanical stress.⁶

Thus, cystine travels safely in the body and is promptly reduced to the two cysteine molecules on cell entry.⁷

GSH and the Immune System

It has been demonstrated that **the ability of lymphocytes to offset oxidative damage (during their oxygen-requiring clonal expansion and following that expansion in the production of antibodies, and helper-CD4 and cytolytic-CD8 T lymphocytes) is measured by determining the capacity of these cells to regenerate intracellular stores of GSH, therefore allowing them to respond more fully to the antigenic stimulus.**^{8,9}

Evidence from studies related to HIV infection

More evidence for the involvement of GSH in the modulation of immune function comes from studies related to HIV infection. Staal et al showed that HIV-infected individuals have lower GSH concentrations in their blood lymphocytes.¹⁰ Moreover, a recent study indicates that the more GSH the patients carry in their CD4 helper T-cells—the cells primarily targeted by the HIV virus—the longer these patients are likely to survive.¹¹

Conditions which facilitate cellular GSH replenishment or maintenance are thus expected to optimize the activity of the immune system.

Milk Serum (Whey) Protein Concentrate

In the early 1980s,¹²⁻¹⁴ it was discovered that normal mice fed a **whey protein concentrate (WPC), especially prepared under mild nondenaturing conditions, exhibited a marked increase in antibody production in response to a T cell dependent antigen.** This product (hereafter designated as “the patented WPC”) was patented in recognition of its immunosustaining and GSH-promoting activity. The immunosustaining effect of the protein mixture, unrelated to its nutritional efficiency, was further confirmed by the demonstration of the protective effect of this dietary treatment against pneumococcal infection.¹⁵ This unique property has been defined as the “bioactivity” of the product.

Cellular GSH is a tightly regulated system; hence, substantially increased values are not anticipated in normal animals. There is, however, an increased demand for GSH during the proliferation of lymphocytes in the development of an immune response and, following that expansion, in the production of antibodies, and helper and cytolytic T lymphocytes.

When GSH stores are “used up,” or depleted, the bioactive proteins present in the patented WPC help maintain GSH levels, thus supporting an optimal immune response.

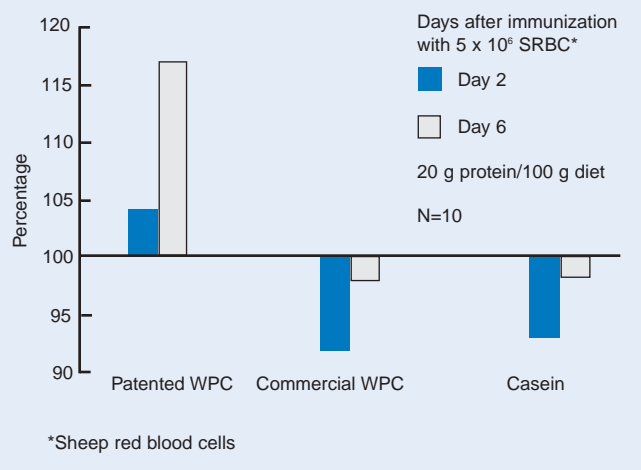
Effect on the immune response

The patented WPC differs from other proteins, including most commercial WPCs, in the following way.

Under normal conditions, at a 20% concentration in the diet, all proteins have been found to exhibit similar nutritional efficiency as measured by body weight, serum protein, circulating lymphocytes¹²⁻¹⁶ and, more specifically, genesis of B lymphocytes in bone marrow.¹⁷ **However, our milk serum (whey) protein concentrate was shown to differ from other proteins in its effect upon the immune response.**

As illustrated in Figure 1, optimization of the immune response in animals fed the patented WPC is attributed to a greater production of GSH in their lymphocytes through continuous dietary provision of supplementary doses of GSH precursors.¹⁶ In addition, when lymphocytes are taken from normal animals which have been fed the patented WPC for a long period of time, and cultured *in vitro*, these cells retain the ability to provide an increased response to an immune stimulus. Thus, this product not only increases intracellular levels of GSH or GSH precursors at the time of ingestion, but also builds up a store of these substances inside the cells, which lasts for considerable periods thereafter.¹⁸

Figure 1: Lymphocyte GSH as Percentage of Values in Unimmunized C3H/HeN Mice Fed the Corresponding Diet (Patented WPC, Commercial WPC or Casein) for Three Weeks



Cysteine/cystine, crucial GSH-promoting components

In the early years of our studies, this newly discovered property was found on a sporadic basis, varying from batch to batch of whey (milk serum) protein concentrates. **It was subsequently realized that the product’s bioactivity was dependent upon a critical concentration of three bioactive proteins contained in the milk serum: i.e., the thermolabiles—serum albumin, alpha lactalbumin and lactoferrin.**

When undenatured, these proteins contain almost the same number of cystine residues per total amino acid.^{19,20} Hence, in serum albumin, there are 17 cystine residues per 66,000 MW molecule, and six glutamylcystine (Glu-Cys) dipeptides;¹⁹ in lactoferrin, 17 cystine residues per 77,000 MW, and four Glu-Cys dipeptides;²⁰ and in alpha-lactalbumin, four cystine residues per 14,000 MW molecule.¹⁹ Conversely, beta-lactoglobulin has only two cystine residues per 18,400 MW molecule¹⁹, and IgG1, the predominant immunoglobulin in cow's milk serum, only four disulphide bridges (cystine) per 166,000 MW molecule. In addition, it has been demonstrated that the Glu-Cys precursors of GSH can easily enter the cell to be synthesized into GSH. Interestingly, the Glu-Cys dipeptide is an exclusive feature of the only obligatory foods in the early life of mammals and oviparous species, i.e., milk and egg white respectively.⁶

Throughout the digestive-absorptive process, the other coexisting protein fractions of whey (milk serum) influence the rate of release of the GSH precursors to the blood, thus affecting the bioavailability of these crucial ingredients.

Figure 2 (page 8) summarizes results obtained in studies serving to clarify the role of cysteine/cystine as GSH precursors in the immunosustaining activity of specially prepared dietary WPCs, and illustrates the higher potency of our product, the patented WPC. As shown in the figure, peak antibody production by spleen lymphocytes (number of plaque-forming cells) is measured after challenge with sheep red blood cells in C3H mice fed different protein-type diets of similar nutritional efficiency. **A higher immune response is exhibited in animals fed WPC, the response being highest with WPC containing more cystine (the patented WPC).**

Benefits similar to those of human milk

Using modern technology, we have succeeded in obtaining and consistently preserving, in

their native form, the specific cow's milk proteins which share with the predominant human milk proteins the same extremely rare GSH-promoting components, as illustrated in Table 1 (page 8).

The patented WPC may thus be considered as a humanized native milk serum protein isolate; the natural benefits of mother's milk for the human baby are now available to the adult population by the oral administration of this health-promoting protein mixture. Breast-feeding is known to be superior to cow's milk-based formulas of similar nutritional efficiency with regard to the health of human babies; for example, it protects against otitis media and pneumonia.^{21,22} Mother's milk also has a protective effect on the incidence of several types of childhood cancers including leukemia, lymphomas, bone tumors and brain tumors.²³ Children who are artificially fed or breast-fed for only a short time are at increasing risk for developing several types of cancers before age 15 as compared to long-term breast-feeders.²⁴

GSH in Cancer Prevention

The search for the potential mechanism of immunoenhancement by milk serum (whey) protein dietary supplementation has revealed the provocative possibility that whey protein may contribute to a broader biological effect of a protective nature with regard to susceptibility to cancer and diseases of aging, as well as general detoxification of environmental agents. Cancer and diseases of aging all appear to be somehow related to a drop in GSH—an ubiquitous element exerting a protective action against oxiradicals and other toxic agents.

The two major theories on the origin of cancer both implicate GSH as a putative protective factor owing to its dual function as antioxidant and detoxifying agent. It has been suggested that the underlying mechanisms of aging and carcinogenesis are closely related, since the incidence of cancer increases progressively with age in humans

Figure 2: Results of Studies Demonstrating the Immunosustaining Role of Specially Prepared Dietary WPCs

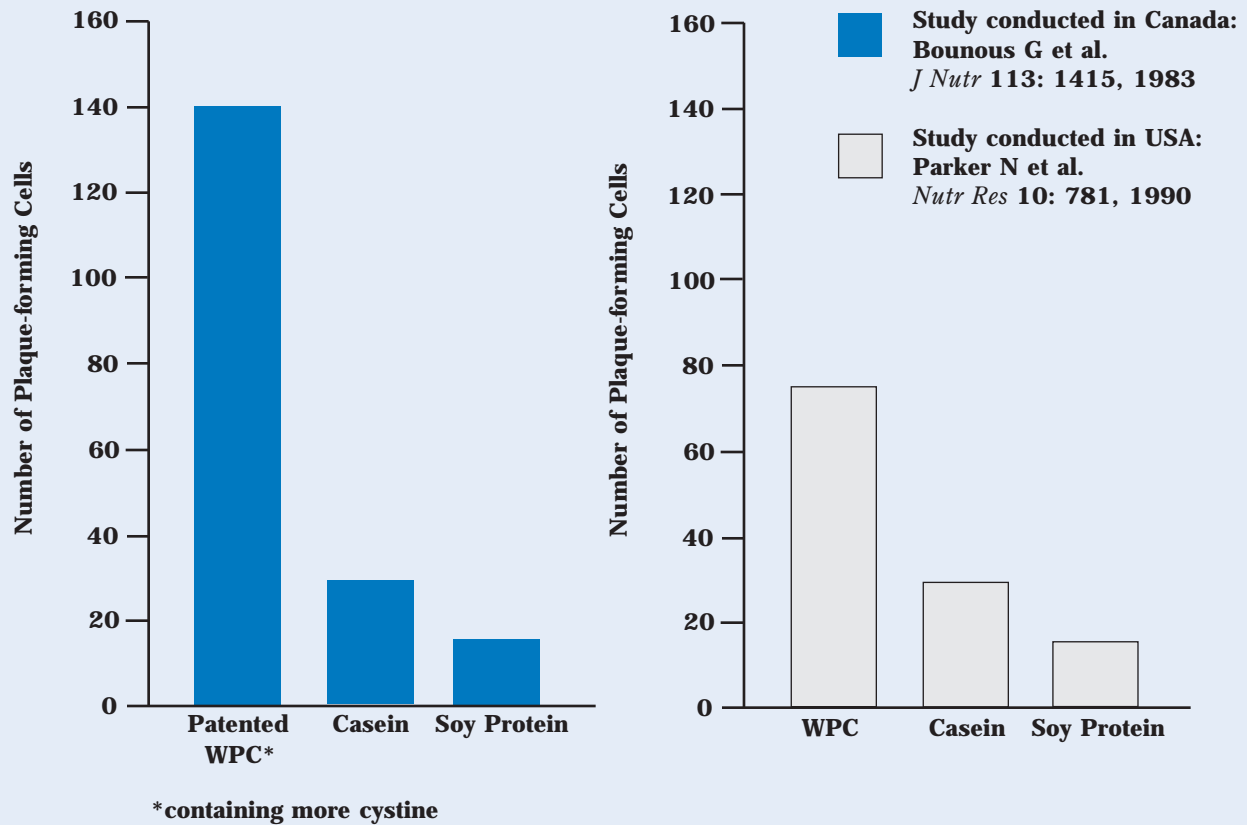


Table 1: Protein Composition of Cow's and Human Milk

Protein	Composition (g/L)		
	Cow's Milk	Human Milk	Cystine/ Molecule
Casein	26	3.2	0*
Beta-lactoglobulin	3.2	Negligible	2
Alpha-lactalbumin	1.2	2.8	4
Serum albumin	0.4	0.6	17
Lactoferrin	0.14	2.0	17
Total cystine (mol/L)	8.19×10^{-4}	13.87×10^{-4}	
Total cystine (mg/g of proteins)	6.4	38.7	

*Casein has 0 to 2 cysteine/molecule.

Adapted from: Jennes R. Inter-species comparison of milk proteins. In: *Developments in Dairy Chemistry-1*. Fox W. (Ed.). 4ASP NY: 87, 1982; and Eigel WN, Butler JE, Ernstrom CA, Farrell HM et al. Nomenclature of proteins of cow's milk. Fifth revision. *J Dairy Sci* 67: 1599-631, 1984

and experimental animals. Indeed, theories of aging based on the accumulation of nonrepairable lesions over time—such as the free radical theory—are similar to theories explaining the origin of certain tumors. Others attribute the aging-associated increase in cancers to accumulation of carcinogens and increased exposure to the action of carcinogens with time.²⁵ In fact, at least 12 carcinogens have been shown to be detoxified by GSH conjugation. These are: aflatoxin B₁, N-acetyl-2-aminofluorene, benz(a)anthracene, benz(a)pyrene, benzdine, dimethylhydrazine, dimethylnitrosamine, ethylmethane sulfonate, N-methyl-4-aminoazobenzene, 7-methylbenzanthracene, 3-methyl-cholanthracene, and 1-nitropyrene.²⁶⁻³⁸

As well, a University of Wisconsin study convincingly showed that physiological levels of androgens are capable of decreasing the GSH content in human prostatic androgen-responsive cells, which could provide a mechanism by which androgen exposure promotes prostate carcinogenesis.³⁹ Conversely, a slightly higher GSH level in the colon, obtained by whey protein feeding, is associated with a lower tumor burden in an experimental model of human colon carcinoma (see Figure 3, page 10), again suggesting that tissue GSH levels modulate tumorigenesis.

A further argument supporting the preventive role of GSH with regard to tumor development is the fact that GSH decreases in aging humans and experimental animals.⁴⁰⁻⁴⁸ Figure 3 summarizes results of studies conducted to illustrate the potential role of WPCs in cancer prevention.

GSH and the Diseases of Aging

The free radical theory of aging⁴⁹ hypothesizes that degenerative changes associated with aging result from toxic effects of free radicals produced during cellular metabolism. Aging is thus considered to be caused by the products of the normal physiological metabolic processes of life. One approach taken to verify the free radical theory of aging has been to

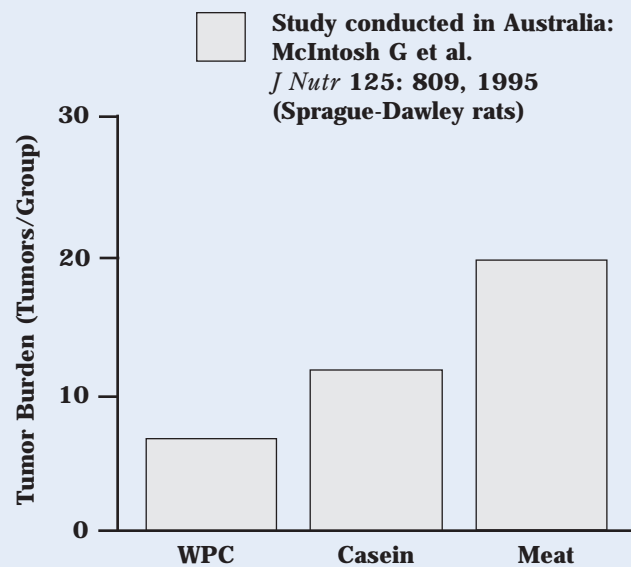
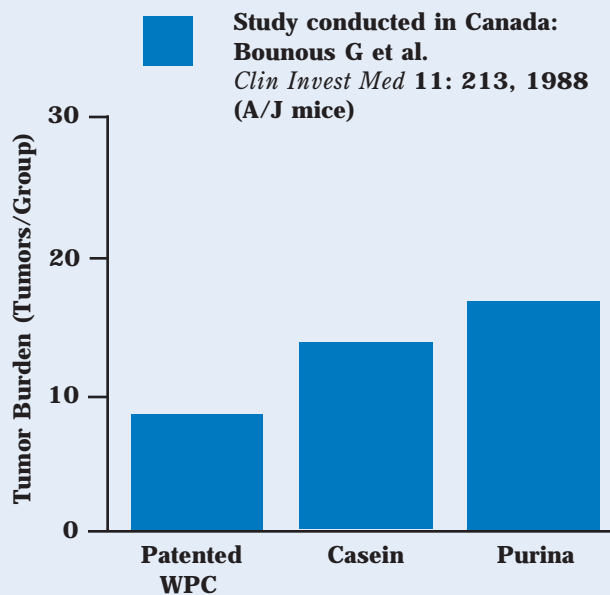
determine whether any age-related changes occur in cellular antioxidative protective mechanisms.

One such principal mechanism is GSH, an ubiquitous cellular constituent and the most abundant thiol-reducing agent in mammalian tissues. It appears that, whereas data on age-related changes in tissue vitamin E and other antioxidants are, at best, contradictory,⁴⁹ reports that tissue GSH levels decline with old age are more consistent. Thus, GSH contents of the liver, kidney,⁴⁰ heart and brain⁴¹ were found to be respectively 30%, 34%, 20% and 30% lower in very old mice as compared to mature mice. Recently, an increased incidence of low blood GSH levels in apparently healthy elderly subjects was reported.⁴² More specifically, some characteristic age-related diseases, such as Alzheimer's disease,⁴³ cataracts,⁴⁴ Parkinson's disease,^{45,46} and arteriosclerosis,⁴⁷ appear to be preceded by or associated with a drop in GSH content in the organ or systems involved.

Our experimental studies have shown that long-term administration of the patented milk serum protein concentrate diet in old mice slightly increases their heart GSH content; it also increases their life span by about 30%⁴⁸ when administered to 21-month-old mice. (The corresponding human age from the survival curves for males in the industrialized world would be 55 years). These data are consistent with two previous studies in hamsters investigating the effect on longevity of dietary milk serum protein in nutritionally adequate and similar diets. In lifetime-feeding studies, survival was reported to be better in hamsters fed 10, 20 or 40 g milk serum protein/100 g diet in comparison with those fed a commercial laboratory diet containing an estimated 24% protein from various sources: hamsters fed the 20% level of milk serum protein survived the longest.⁵⁰ In another study, survival of hamsters during the first 20 weeks was better in animals fed the 20 g milk serum protein/100 g diet than in those fed a corresponding methionine- and cysteine-enriched casein diet.⁵¹

Figure 3: Results of Studies Demonstrating the Role of Specially Prepared Dietary WPCs in Cancer Prevention

Carcinogen was dimethylhydrazine-dihydrochloride (DMH), which induces colon tumors similar to those found in humans (with regard to type of lesions¹ and response to chemotherapy²). The diets were fed before and throughout the 24-weeks DMH-treatment period. No differential effect of diet on body weight was seen.



Colon GSH

WPC	casein	meat
1.01	0.92	0.92

“...These findings confirmed and extended earlier observations of a Canadian research group [Bounous et al, 1991] that also identified dairy proteins, and whey protein in particular, as being protective against the development of intestinal cancers induced by DMH.”

Tumor mass was lower in mice fed patented WPC than in mice fed casein or purina.³

No significant difference in tumor mass was noted among the treatment groups.

1. Enker WE, Jacobitz JL. Experimental carcinogenesis of the colon induced by 1,2-dimethylhydrazine-dl HCL: Value as a model of human disease. *J Surg Res* 21: 291, 1976.
2. Corbett TH, Griswold DP, Roberts GJ, Peckham JC et al. Evaluation of single agents and combinations of chemotherapeutic agents in mouse colon carcinogenesis. *Cancer* 40: 2650, 1977.
3. Rodent chow (purina) containing varying amounts of beef, fish, corn, and whey proteins.

Although cellular GSH is decreased in old age, conditions known to favor GSH replenishment or sustainment—such as feeding of milk serum protein concentrate—are shown to prolong life expectancy. This strongly suggests that aging cells are able to synthesize sufficient amounts of GSH when provided with an increased supply of its natural precursors.

Limits of Other Strategies to Increase Tissue GSH Concentration

As mentioned in the section on GSH synthesis (see page 5), administration of GSH by oral or intravenous routes does not have a sustained effect in increasing tissue GSH concentration even in GSH-depleted cells.⁵² GSH monoethyl ester was found to lead to an approximate doubling of the kidney and liver GSH levels two hours after injection to normal mice, with return to preinjection values eight hours later.⁵³ However, metabolism of GSH monoethyl ester will release ethanol;⁵⁴ ethanol is metabolized to acetaldehyde which, in high concentration, can conjugate and deplete GSH.

Oral supplementation of sulfur amino acids can replete tissue GSH,⁵² but cysteine and methionine are toxic at high doses;⁵⁵ in addition, cysteine is readily catabolized.⁵² The limitations of sulfur amino acid administration can be overcome by cysteine prodrugs that are converted intracellularly to cysteine.

N-acetylcysteine administered to patients by the oral or intravenous routes transiently increases GSH concentrations in plasma and erythrocytes⁵⁶, and is used as an antidote for acetaminophen toxicity in humans.⁵⁷ Oral N-acetylcysteine may however result in nausea and diarrhea; with intravenous administration, some patients may experience anaphylactic reactions⁵⁸ and other unacceptable side effects.⁵⁹

Another cysteine prodrug, oxothiazolidine-4-carboxylate (OTC), was found to restore GSH levels in the liver of mice that had previously been deplet-

ed of GSH.⁶⁰ OTC supplementation, however, does not escape factors such as feedback inhibition and nutritional regulation of GSH synthesis.⁵²

Basically, these methods offer an interesting possibility for short-term intervention—as, for example, in acute liver failure—, but their long-term effectiveness in producing sustained elevation of cellular GSH has not been confirmed, nor has the potential toxicity of their long-term use been disproved.

Conversely, oral administration of natural GSH precursors found in the patented WPC has been shown to produce significant, rapid GSH replenishment in lymphocytes during the GSH-depleting immune response in mice,¹⁶ as well as a moderate but sustained increase in organ GSH of old mice (following long-term administration).⁴⁸

Success of the Patented WPC in Sustaining GSH Levels

Moreover, a Canadian clinical trial with the patented WPC was conducted in children with AIDS and Wasting Syndrome over a six-month period. Patients who started the study with low blood-lymphocyte GSH exhibited a substantial increase in GSH content.⁶¹ A most recent clinical trial showed that a three-month administration of the patented WPC to patients with hepatitis B restores GSH concentrations in lymphocytes to normal values.⁶²

Finally, the success of this form of dietary treatment, using natural GSH precursors and by the previously mentioned methods, clearly indicates that, in most experimental or clinical conditions characterized by GSH depletion, the capacity of the cell to synthesize GSH is maintained. **Hence, optimal concentration of GSH can be obtained through an adequate “cysteine delivery system,” such as the one provided by our patented milk serum protein concentrate.**

Potency and bioactivity of the patented milk serum (whey) protein concentrate (WPC), a key characteristic

In animal studies, WPCs constitute the only protein component of the diet. This is of course not feasible for humans, for whom a protein-free diet is impractical even in a hospital setting. Therefore, WPCs must be taken by humans as a protein supplement.

Here is where the important question of potency comes into play. For example, in a comparative *in vivo* study, we found that commercial WPCs containing substantially less cystine-rich proteins exhibit a marginal bioactivity, or none at all.⁶ Recently, similar results were obtained using an *in vitro* assay of GSH synthesis by normal human lymphocytes.⁶¹ **It is therefore essential to provide a milk serum isolate such as our product in which the ratio of active ingredients—such as cystine—to other amino acids allows biological activity to be obtained without overloading the system with nitrogen.**

Conclusion

This article has addressed the central role of GSH in providing protection against endogenous oxiradicals and foreign pollutants. As an antioxidant, GSH is essential for allowing the lymphocyte to express its full potential, without being hampered by oxiradical accumulation during the oxygen-requiring development of the immune response. In a similar fashion, GSH delays the muscular fatigue induced by oxiradicals during the aerobic phase of strenuous muscular contraction.

It is, however, the second function of GSH—that of detoxification of chemical pollutants, carcinogens and ultraviolet radiation—that may well be of greater concern to medical science today, because of the ever-increasing demand on GSH as the major detoxifying agent. Under normal circumstances, a nutritionally balanced diet should provide sufficient precursors of GSH to allow for intracellular synthe-

sis of adequate amounts of GSH. But in our current polluted environment, trace amounts of precursors found in an otherwise adequate diet may not be sufficient to allow for full GSH replenishment. This results in highly undesirable competition for GSH precursors developing amongst different systems. Cysteine prodrugs have helped clarify the essential role of GSH in athletic performance, immune function, AIDS, etc., but their effect is short-lived and their long-term use is not without adverse effects.

Using modern technology, it has been possible to obtain and consistently preserve, in their native form, the specific cow's milk proteins which share with predominant human milk proteins the same extremely rare GSH-promoting components. This product—the patented WPC—differs from most commercial WPCs in that it contains the active ingredients—notably cystine and glutamylcystine—in undenatured form and an amount sufficient to exhibit its potency when given as a dietary supplement, without overloading the system with excessive nitrogen intake.

It is therefore possible to obtain, with the patented milk serum protein concentrate, long-term moderate but sustained intracellular elevation of GSH and GSH precursors so that, when the challenge occurs, an efficient cellular response can be achieved.

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APPENDIX: SHORT GLOSSARY OF KEY WORDS

ANTIGENIC CHALLENGE:

Challenge with an antigen, a substance usually from microbes (bacteria, viruses, etc.), which induces the immune system to respond by producing antibodies and T lymphocytes that cause destruction of microbes and infected cells.

Maintenance of sufficient glutathione levels in the cell (lymphocyte), assisted by the patented whey protein concentrate (WPC), allows for more efficient human immune response.

CYSTEINE AND CYSTINE:

Cysteine is a crucial and rare precursor of glutathione. Without it, glutathione cannot be synthesized. Other main dietary sources of cysteine include raw eggwhite, milk, and meat, in which traces of it are found. Although cysteine does not represent an ideal delivery system because it is spontaneously inactivated, cysteine present as cystine (two cysteine molecules linked by a disulphide bond, in undenatured form), released during digestion in the gastrointestinal tract, is more stable. Thus, cystine travels well in the body and is promptly reduced to the two cysteine molecules on cell entry.

Cystine, containing cysteine, is found in relatively high concentration in the patented milk serum protein concentrate and determines its effectiveness.

FREE RADICAL:

A free radical is an atom or a molecule that has one or more unpaired electrons. Unpaired oxygen atoms and hydroxyl radicals are examples of naturally-occurring free radicals. A radical might donate its unpaired electron to another molecule, or it might take an electron from another molecule in order to

pair. Thus, a feature of the reactions of free radicals is that they tend to proceed as chain reactions that perpetuate their harmful effect on cells and cell components—including cellular membranes, protein and DNA.

The antioxidant properties of glutathione, as supported by the patented milk serum (whey) protein concentrate, help to defend the body against radical-induced damage.

GLUTATHIONE:

A multifunctional tripeptide composed of three amino acids—glutamate, cysteine, and glycine—, glutathione is ubiquitous, but is found in greater concentration in the liver, which is the major organ involved in detoxification of harmful compounds. Sufficient intracellular stores of glutathione are necessary for the oxygen-requiring optimal multiplication of lymphocytes and antibody production—an essential part of the human immune response process.

The patented WPC, containing the essential glutathione-promoting cystine, thus proves instrumental in supporting the normal functioning of the immune system.

LABILE:

Capable of changing state or becoming inactive when subjected to heat and radiation, as for example the proteins found in cow's milk which contain cystine, the glutathione precursor.

In the preparation of the patented WPC, special care is taken to fully preserve all the labile cystine-rich proteins present in the raw milk and maintain them in their undenatured bioactive form.

OXIDATION:

Normal but damaging result of cellular metabolism involved in the immune response. Reactive oxygen compounds produced by oxidation can cause serious injuries to vital cell constituents.

Antioxidants, such as glutathione derived from the patented milk serum protein concentrate, can act to counter the damaging effects of oxidation, and help to maintain the activity of other antioxidants.

PRECURSOR:

A chemical that is transformed into another compound, thus preceding it in the synthetic pathway. In the absence of such a precursor, the second compound will not be produced.

Cysteine, found as cystine in the patented WPC, is a natural precursor of glutathione.

WPC:

A concentrate of whey (milk serum) proteins which is called "isolate" if the protein content is $\geq 90\%$.

Notes

*Clinic
Foundations*