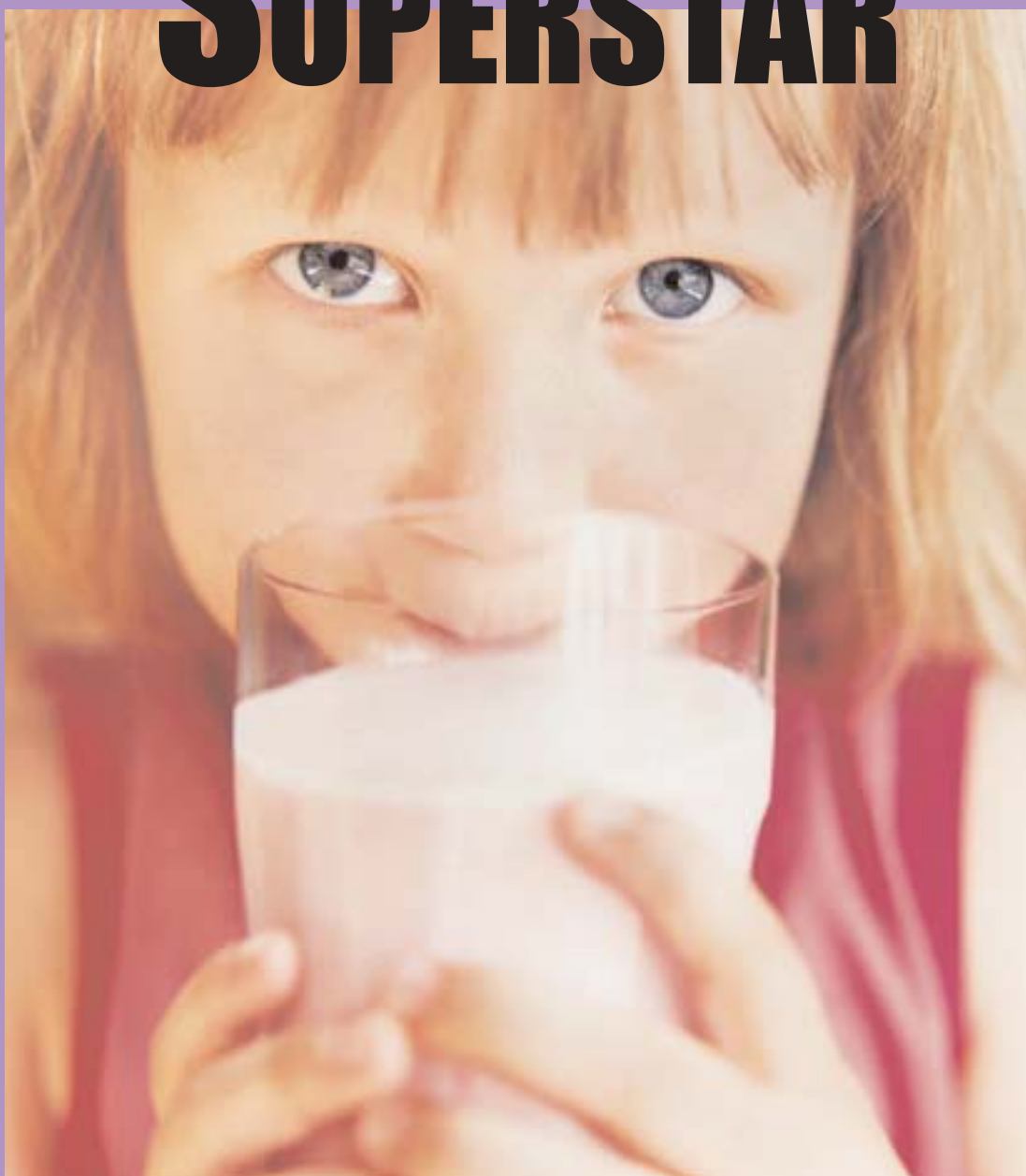


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## SHOWCASING A NUTRITION SUPERSTAR



By Amanda Archibald, RD

**Y**ou are appearing on a talk show as a food and nutrition expert. The topic: Nutrition

Superstars. The goal: to name the most value-added, health-beneficial food or ingredient in the marketplace. What would your answer be? The past 2 decades have revealed a number of nutrition superstar candidates, but how many of you would have said whey protein?

The subject of whey inevitably brings up nostalgic images of Miss Muffett sitting on her tuffett eating something nebulously referred to as “curds and whey.” Many of us sang the rhyme with no thought to the nutritional benefits of whey or, more importantly, the protein component of whey. Not surprisingly, the food industry also sang the same rhyme, using the cheese (or curds) and discarding the remaining liquid whey by spraying it on agricultural fields. In the early 1980’s, this practice was found to be both environmentally and financially unsound when research revealed both nutritional and functional values of whey protein. Over the past decade whey protein has been shown to be a serious candidate in the superstar arena.

## WHAT IS WHEY PROTEIN?

In the United States the most common method of producing whey protein is in conjunction with the cheese-making process. It takes 100 pounds of milk to yield approximately 10 pounds of cheese and 90 pounds of residual liquid known as “whey.” Whey is

comprised of water, lactose, protein, minerals (calcium, phosphorus, magnesium) and fat.<sup>1</sup> By far, the most nutritionally valuable component of whey is its protein, whose attributes and applications have significant interest in a number of arenas including health, infant nutrition, athletic performance and food processing.

## MAKING THE CASE FOR A SUPERSTAR

So, how do you attain nutrition superstar status? This is a question that would undoubtedly yield much debate among nutrition professionals. Regardless of opinions, nutrition professionals may currently be challenged to find a food whose nutritional value, benefits and functionality is as broad and far-reaching as whey protein. That being said, let’s begin looking at the case for whey protein.

To qualify as a nutrition superstar, a product requires a solid case with plenty of evidence. The case for whey protein will focus on its quality and diversity aspects.

## QUALITY

Beginning with the most compelling evidence first, whey protein is a noted complete, high biological value (HBV) protein with a rich amino acid profile. The amino acid profile comprises good quantities of essential, sulfur-containing and branched-chain amino acids (BCAAs), which collectively constitute whey protein’s excellent protein efficiency ratio (PER), as well as its broad scope of applications. *Table 1* compares the quality of

whey protein with various reference proteins.

## DIVERSITY

The evidence for diversity is equally attractive. A plethora of research indicates both existing and emerging applications for whey protein in preventive health, health maintenance and recovery. Whey protein’s spectrum of established and suggested health benefits extend a lifecycle - from infant nutrition to older adults. And, in between, science and research is showing that this dynamic food is a key player in health issues as diverse as gut integrity and motility, immune function and support, cancer, cardiovascular health and performance enhancement. To fully appreciate this wide range of benefits, *Table 2* identifies whey protein’s primary components, and summarizes the key characteristics for each in nutrition and health management.

## CLINICAL PERSPECTIVES

A brief glance at the scope of whey protein’s reported biological activity may be premise alone for backing this superstar. For nutrition professionals, however, an examination of the scientific literature, which supports current and prospective applications for whey protein, is a prerequisite for acceptance.

Nutrition professionals may be familiar with whey protein as an ingredient in both infant formulas and enteral formulas. Beyond its HBV attribute, other reasons for its incorporation are perhaps less commonly known. Whey protein is comprised of 20-25% alpha-

lactalbumin, the primary whey protein found in human milk. It is, therefore frequently referred to as the “humanizing” component of infant formulas. The whey protein profile also comprises serum albumin and immunoglobulins. Immunoglobulins include IgG1, IgG2, IgA and IgM, all of which provide passive immunity to the infant.<sup>2</sup> Another whey protein component, lactoferrin, is a transport protein with iron binding properties. Lactoferrin is widely used in infant formula in various Asian countries since it appears to enhance iron absorption, without causing the constipation commonly associated with inorganic iron supplements.<sup>3, 4</sup>

Studies have consistently demonstrated that protein formulas with a higher whey protein:casein ratio are better tolerated because they empty

more rapidly from the stomach. This has significant implications in critical care situations where the availability of nutrition to the gut to aid recovery is critical. Whey protein formulas reduce gastric emptying time and the subsequent potential for gastroesophageal reflux.<sup>5, 6</sup>

Whey protein-based formulas have also demonstrated their ability to assist in modulating bowel movement patterns and stool consistency (diarrhea or constipation) in critical care settings. A study by Graham-Parker et al demonstrated that a diet with a 50:50 whey protein to casein ratio (vs. the 18:82 ratio typical in cows milk) significantly improved bowel movement and consistency patterns in children with severe cerebral palsy.<sup>7</sup> Glauser et al also replicated the role of whey protein in stool

consistency modulation (diarrhea) in HIV-positive adults.<sup>8</sup>

Looking beyond tolerance, absorption and motility, to actual metabolic applications, another application for whey protein comes to light. Whey protein is a rich source of the sulfur-containing amino acids cysteine and methionine. Sulfur amino acids act as precursors to the production of the tripeptide, glutathione (GSH), which, in turn moderates oxidative damage and improves immune function. The role of GSH is vital in critical care settings where patients are under physiological stress, a condition correlated with oxidative damage.<sup>9</sup> A study by Rowe et al investigated the effect of different protein sources (casein or whey) on GSH levels in ICU patients. Rowe’s results indicated that whey protein

Table 1

PROTEIN QUALITY COMPARISON CHART

Protein Type	Protein Digestibility Corrected Amino Acid Score (PDCAAS) <sup>i</sup>	Amino Acid Score	Protein Efficiency Ratio (PER) <sup>ii</sup>	Biological Value (BV)	Protein Digestibility % (PD)
Whey Protein Concentrate	1.00	1.14	3.2	104	99
Whole Egg	1.00	1.21	3.8	100	98
Casein	1.00	1.19	2.9	77	99
Soy Protein Concentrate	0.99	1.04	2.2	74	95
Beef	0.92	0.94	2.9	80	98
Wheat Gluten	0.25	0.47	0.34	54	91

Sources:

i. Protein Quality Evaluation. Report of the Joint FAO/WHO Consultation, 1991.

ii. Reference Manual for U.S. Whey Products, 2nd Edition, U.S. Dairy Export Council. 1999.

formulas (naturally high in cysteine, a rate limiting amino acid in GSH synthesis) positively correlated with increased GSH levels, whereas no change was noted in patients on the casein-based diet.<sup>10</sup>

## IMMUNE SUPPORT

The pivotal role of GSH in mitigating oxidation is particularly relevant to persons with HIV/AIDS. HIV infection is characterized by increased oxidative stress levels, coupled with GSH deficiency. Low GSH levels are associated with higher rates of viral replication. Studies

## A plethora of research indicates both existing and emerging applications for whey protein in preventative health, health maintenance, and recovery.

have consistently indicated that whey protein positively correlates with increased GSH levels.<sup>11, 12, 13</sup> Alan Lee, RD, CDN, CFT, is a nutrition consultant specializing in persons living with HIV/AIDS. Lee extensively recommends whey protein to his HIV/AIDS clients. He bases his recommendations both on whey protein's HBV and its role in increasing GSH levels. Lee feels that whey protein packs a quality nutritional punch for his

clients through its high biological value and antioxidant properties, both critical for his client population.

The whey protein component, lactoferrin, has also exhibited immuno-modulating activity through both antimicrobial and antitoxin activity. Research by Bellamy et al in 1992 suggested that lactoferrin B, a peptide obtained by gastric pepsin digestion of bovine lactoferrin,

Table 2

### PRIMARY WHEY PROTEIN COMPONENTS, NUTRITIONAL CHARACTERISTICS AND REPORTED BIOLOGICAL ACTIVITY<sup>i</sup>

Protein Component	% of Total Whey Protein	Nutritional Characteristics and Reported Biological Activity
Beta-lactoglobulin	50% to 55%	<ul style="list-style-type: none"> <li>• Binds fat-soluble vitamins making them more available to the body</li> <li>• Provides an excellent source of essential and branched chain amino acids (BCAAs), which help prevent muscle breakdown.</li> </ul>
Alpha-lactalbumin	20% to 25%	<ul style="list-style-type: none"> <li>• Primary whey protein found in human breast milk</li> <li>• Preferred whey protein component for infant formulas</li> <li>• Contains higher levels of tryptophan (associated with stress modulation)</li> <li>• Provides all the essential amino acids and BCAAs</li> <li>• Demonstrates potential anticancer activity</li> </ul>
Immunoglobulins	10% to 15%	<ul style="list-style-type: none"> <li>• Exhibits immunity enhancing and disease protection benefits</li> </ul>
Bovine Serum Albumin	5% to 10%	<ul style="list-style-type: none"> <li>• Provides essential amino acids</li> </ul>
Glycomacropeptides (GMP) <sup>ii</sup>	2% to 5% amino acids	<ul style="list-style-type: none"> <li>• Contains high amounts of BCAAs, but only trace amounts of the aromatic</li> <li>• Provides an immuno-modulatory effect and a passive defense mechanism to newborns</li> <li>• Exhibits bacterial antitoxin activity</li> <li>• Stimulates the body to produce cholecystokinin, the hormone that is released after eating to give a sense of satiation</li> <li>• Desirable protein source (in an isolated form) for individuals with phenylketonuria due to the lack of phenylalanine</li> </ul>
Lactoferrin	1% to 2%	<ul style="list-style-type: none"> <li>• Exhibits bacterial antitoxin activity<sup>iii</sup></li> <li>• Promotes the growth of beneficial bacteria, such as Bifidus</li> <li>• Regulates iron absorption and bio-availability</li> <li>• Demonstrates an immuno-modulatory effect along with antiviral, anticancer, and antithrombotic activity</li> </ul>

Sources:

- i. Adapted from information provided by the Whey Protein Institute and the Reference Manual for U.S. Whey and Lactose Products, 2002 Edition.
- ii. Whey protein obtained through the acid separation from casein will not contain any GMP.
- iii. The USDA recently approved the use of lactoferrin on meat to prevent the growth of pathogens, such as e. coli and salmonella.

inhibited a range of gram-positive and gram-negative bacteria by damaging their outer membranes.<sup>14</sup> A number of studies and reviews since 1992 have validated this observation.<sup>15, 16</sup> Additionally, lactoferrin has also been associated with providing protection against viruses such as hepatitis, cytomegalovirus, and influenza.<sup>17</sup>

## WHEY PROTEIN AND CANCER THERAPY

Whey protein may play a role in both protecting against cancer<sup>18</sup> and also in sensitizing cells to chemotherapy.<sup>19</sup> Again, GSH is a major contributor to these observations. Tumor cells contain higher levels of GSH than normal cell tissues. Studies have suggested that an elevated GSH concentration in tumor cells is a useful predictor of resistance or reduced sensitivity to anticancer treatments.<sup>20</sup> In vitro and animal studies have demonstrated a positive correlation between an ingestion of whey protein and a reduction of intracellular GSH activity in cancer cells, a direct contrast to the effect seen in HIV/AIDS patients.

Results of a 1995 study involving 5 patients with metastatic carcinoma of the breast and one with metastatic carcinoma of the liver indicated that ingestion of whey protein might deplete intracellular concentrations of GSH and render them more sensitive to chemotherapy.<sup>21</sup> A 2000 study, conducted by Tsai et al, demonstrated that a whey protein isolate (WPI) had an enhancing effect on the cytotoxicity of baicalein, a potential anticancer drug, when

applied to a human cell line.<sup>19</sup>

A United States Department of Agriculture-funded study at the Arkansas Children's Nutrition Center examined the roles of soy and whey protein in breast cancer in rats.<sup>22</sup> Findings revealed that all rats in the control group (fed a casein protein diet), 77% of the soy-fed rats, and 54% of the whey protein-fed rats developed at least one tumor. The whey protein fed rats who developed mammary tumors had fewer and smaller tumors than the control rats. These observations may further validate the suggested role of whey proteins in tumor prevention or regression.

## WHEY PROTEIN AND CARDIOVASCULAR HEALTH

Mounting evidence indicates that certain bioactive compounds of whey protein may have positive effects on cardiovascular health. Specifically, whey proteins have exhibited angiotensin converting enzyme (ACE) inhibitor and antithrombotic activity, as well as cholesterol-reduction activity.

A number of studies conducted around the world since the 1980s, most notably the work of Tokano et al in Japan,<sup>23</sup> have suggested that bioactive whey protein peptides, isolated from fermented milk, demonstrate antihypertensive activity. More recent animal studies have shown that hydrolyzed whey peptides act as inhibitors to the ACE, which is responsible for converting

angiotensin I to angiotensin II, a potent vasoconstrictor. According to Joel J. Pins, MS, MPH, director of the Hypertension and Cholesterol Research Clinic at the University of Minnesota Medical School, "If a full scale clinical trial confirms what we have seen in the pilot, then yes, I think we will see more whey protein dietary products with structure/function claims and we will eventually see a health claim. That would lead to the addition of whey peptides to many food products with the intent of lowering blood pressure. The public health benefits in this area are immense."

A 12-week double blind, prospective and randomized trial, presented at the Institute of Food Technologists conference in 2001, evaluated the effect of whey protein isolate (WPI) and isolated soy protein (ISP) in healthy adults.<sup>24</sup> The study looked at a variety of indicators, including low-density lipoprotein (LDL) cholesterol and total cholesterol. Results from the trial indicated "a significant decrease in LDL cholesterol within each group, specifically 10% for the ISP group and 20% for the WPI group." For total cholesterol, results indicated a 15% drop for WPI compared to a 6% drop for ISP.

The role of whey protein in LDL cholesterol reduction is still emerging; however, lactoferrin is implied as an antiatherogenic agent that inhibits cholesterol esters in macrophages.<sup>25</sup> Similarly, the antithrombotic attributes of whey protein are also emerging with

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lactoferrin and glycomacropeptide as possible inhibitors of platelet-binding activity.

## PERFORMANCE NUTRITION

In the sporting world, where time is literally money, athletes are advised to take a serious look at whey protein. Whey protein contains a high level of BCAAs – isoleucine, leucine, and valine - an attribute of significant interest in the sports performance arena. BCAAs are oxidized directly by skeletal muscle during prolonged activity. Current theory suggests that ingestion of BCAAs may protect/reduce catabolism of muscle mass for energy and also allow more rapid recovery.<sup>26</sup>

BCAAs may help offset fatigue. One theory suggests that this is achieved by altering the ratio of free tryptophan/BCAA across the blood brain barrier. Tryptophan is a precursor to serotonin (5-HT). By decreasing the availability of tryptophan via an increase in circulating BCAAs, the hypothesis suggests that fatigue can be offset.<sup>27</sup> Whey protein is also an excellent source of arginine and lysine. These two amino acids have suggested roles in stimulating growth hormone – an anabolic hormone. This correlation is particularly significant for strength athletes for whom anabolic drugs are prohibited.<sup>28</sup>

## EMERGING AREAS

Additional areas of nutritional interest involving whey protein include the following:

- Inhibition of *Helicobacter pylori* by lactoferrin. *H. pylori* is linked to gastroesophageal reflux

disease and stomach cancer.<sup>29</sup>

- Stress reduction – recent studies showed that a diet including alpha-lactalbumin enriched whey protein was helpful in improving mood levels and in increasing serotonin levels in the brain.<sup>30</sup>
- Potential benefits include bone health, dental health, and appetite suppression.<sup>31, 32, 33</sup>

## APPLICATIONS FOR THE NUTRITION PROFESSIONAL

In the areas of nutrition support, immuno-compromised populations and performance nutrition, whey protein has demonstrated its role and value. Other areas such as hypertension management, cholesterol reduction, cancer prevention and regression, strongly suggest that the nutrition professional keep a close watch on the emerging scientific literature.

Today's marketplace reveals an abundance of clinical and sports performance products incorporating whey protein as one of the primary ingredients. Nutrition professionals can expect to see consistent expansion of whey protein product formulations in both health institution and retail settings.

At the retail level, whey protein powders, bars and beverages can be purchased in grocery stores,

health food outlets or on the Internet. Because these products are abundant, consumers will increasingly ask nutrition professionals about the actual and potential health benefits of whey protein. The role of the nutrition professional remains essential in helping the consumer understand the facts, the health benefits and appropriate dietary choices using whey protein. For further information about products containing whey protein, view the *Whey Protein Institute* website at [www.wheyoflife.org](http://www.wheyoflife.org) or call 1.866.949.9439.

## CONFIRMING THE SUPERSTAR STATUS

So, the case for whey protein has been presented. Imagine a year has passed and you are invited back to the talk show. Would you admit that whey protein is a nutrition superstar, or would you have a compelling case for something else? The jury may deliberate a while longer, but, when the verdict is delivered, the headlines will be big!

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1.866.949.9439 [www.wheyoflife.org](http://www.wheyoflife.org)

## WHEY PROTEIN PRODUCT LIST

MANUFACTURER	PRODUCT NAME	FORM	APPLICATION	CONTACT INFORMATION
Bionexus®	Nutrivir™	P	HIV/Wasting	www.bionxs.com 1.800.835.0869
	Nutri <sup>NSA</sup> (No Sugar)	P		
Block Medical Center	Rebuild Plus™	P	Immune Enhancing & Nutritional Supplement - Rebuild Plus™ contains egg white powder	1.800.834.8787
	Immuno Pro™	P		
Cold Fusion Foods	Frozen Protein Juice Bars and Cups	F	Nutritional Supplement	www.coldfusionfoods.com 1.800.447.9998
Hormel HealthLabs™	NutriMil Plus™	L	Nutritional Beverage	www.hormelhealthlabs.com  1.800.866.7757
	Hi ProCal	P	High protein & calorie supplement	
	ProPass®	P	Elemental or Semi Elemental	
	PRO-Peptide™	L	Elemental or Semi Elemental	
	PRO-Peptide <i>for kids</i>	L	Pediatric version of PRO-Peptide	
Immunotec	Immunocal®	P	Immune Enhancing	www.immunocal.com
Mead Johnson®	Boost Breeze®	L	Nutritional Supplement	www.meadjohnson.com 1.812.429.5000
	Subdue®	L	Elemental or Semi Elemental	
	Subdue Plus®	L	Elemental or Semi Elemental	
Metagenics®	BioPure Protein™	P	Immune Enhancing	www.teamapn.com 1.800.647.6100
Nestle® Clinical Nutrition (NCN)	NuBasics® Complete Nutrition Decaffeinated Coffee	P	Instant Coffee Oral Supplement	www.nestleclinicalnutrition.com  1.877.4NESTLE (1.877.463.7853)
	NuBasics® Clear Liquid Juice Drink	L	Nutritional Supplement	
	Nutren® 1.0	P	Oral or Tube Feeding	
	Nutren® with Fiber	P	Oral or Tube Feeding	
	Nutren® Diabetes	P	Oral or Tube Feeding	
	Nutren Junior®	L, P	Oral or Tube Feeding	
	Nutrihep®	L	Hepatic Diets	
	Peptamen®	L, P	Elemental or Semi Elemental	
	Peptamen® 1.5	L	Elemental or Semi Elemental	
	Peptamen® VHP®	L	Elemental or Semi Elemental	
	Peptamen® with FOS/Inulin	L	Elemental or Semi Elemental	
	Peptamen Junior®	L, P	Elemental or Semi Elemental	
	Reabilan® Diet	L	Small Peptide Elemental	
	Renalcal® Diet	L	Renal Formula	
Novartis	Peptinex™	L	Elemental or Semi Elemental	www.NovartisNutrition.com  1.800.333.3785
	Impact® Recover	P	Immune Enhancing/Wound Healing	
	Resource® Arginaid™ Extra	L	Wound Healing	
	Resource® Fruit Beverage	L	Nutritional Supplement	
	Resource® Instant Protein Powder	P	Nutritional Supplement	
	Resource® Nutritious Juice Drink	L	Nutritional Supplement	
	Resource® Frosty Thick	F	Dessert	
	Resource® Ground Meat Enhancer	L	Nutritional Supplement	
	Resource® Hydration Gelatin	P	Nutritional Supplement	
	Resource® Just For Kids	L	Oral or Tube Feeding	
Pro Health™	ImmunPlex™	P	Immune Enhancing	www.immunesupport.com 1.800.366.6056
Ross	Enlive!	L	Nutritional Supplement	www.ross.com 1.800.986.8510 1.800.231.3330
	Promod®	P	Nutritional Supplement	
	Forta Drink®	L	Nutritional Supplement	
Well Wisdom™	ImmuneProRx™	P	Immune Enhancing	www.immunepro.com 619.469.8196

\* P = Powder, L = Liquid, F = Frozen

## REFERENCES

1. National Dairy Council. Health Enhancing Properties of Dairy Ingredients. *Dairy Council Digest*. 2001;73(2).
2. Walzem RL. Health enhancing properties of whey proteins and whey fractions. USDEC Monograph: Nutritional and Beverage. 1999;1-8.
3. German JB, Dillard CJ, Walzem RL. US Whey Products and Dairy Ingredients for Health: A Review. May 2000. U.S. Dairy Export Council. In press, 2001.
4. Harper WJ. Biological Properties of Whey Components. A Review. Chicago, IL: The American Dairy Products Institute. 2000.
5. Tolia V, Lin CH, Kuhns LR. Gastric emptying using three different formulas in infants with gastroesophageal reflux. *J Pediatric Gastroenterology and Nutr*. 1992;15:297-301.
6. Khoshoo V, Brown S. Gastric emptying of two whey-based formulas of different energy density and its clinical implication in children with volume tolerance. *Eur J Clin Nutr*. 2002;56:1-3.
7. Graham-Parker, et al. Effect of whey-based diet on incidence of vomiting in G-tube fed children with severe neurodevelopmental delay. Presented at the 25<sup>th</sup> ASPEN Clinical Congress in January, 2001.
8. Glauser M, et al. Assessment of the Efficacy of Peptamen Diet in Reducing the Incidence of Diarrhea and Decreasing Stool Fat. Presented at VII International Conference on AIDS in 1993.
9. Bounous G, Gold P. The biological activity of undenatured dietary whey protein: role of glutathione. *Clin Invest Med*. 1991;14:296-309.
10. Rowe B, Kudsk K, Borum P, Madsen D. Effects of whey- and casein-based diets on glutathione and cysteine metabolism in ICU patients. *J Am Coll Nutr*. 1994;254:535-541.
11. Bounous G, Baruchel S, Falutz J, Gold P. Whey Proteins as a food supplement in HIV-seropositive individuals. *Clin Invest Med*. 1993;1(3):204-209.
12. Micke P, Beeh KM, Schlaak JF, Buhl R. Oral supplementation with whey proteins increases plasma glutathione levels of HIV-infected patients. *European J Clin Invest*. 2001;31(2):171-178.
13. Baruchel S, Viau G, Olivier R, et al. Nutraceutical modulation of glutathione with humanized milk serum protein isolate, IMMUNOCAL: Application in AIDS and cancer. In: *Oxidative Stress in Cancer, AIDS and Neurodegenerative Diseases*. Montagnier L, et al, eds. 1998;447-461.
14. Bellamy W, Takase M, Wakabayashi H, et al. Antibacterial spectrum of lactoferricin B, a potent bactericidal peptide derived from the N-Terminal region of bovine lactoferrin. *J Appl Bacteriol*. 1992;73(6):472-479.
15. Naidu AS, ed. *Lactoferrin: Natural, Multifunctional, Antimicrobial*. Boca Raton, FL: CRC Press 2000.
16. Harper WJ. Biological Properties of Whey Components. A Review. Chicago, IL: The American Dairy Products Institute. 2000.
17. Hoerr RA, Bostwick EF. Bioactive proteins and probiotic bacteria: modulators of nutritional health. *Nutrition*. 2000;16(7-8):711-713.
18. Harper WJ. Biological Properties of Whey Components. A Review. Chicago, IL: The American Dairy Products Institute. 2000.
19. Tsai WY, Chang WH, Chen CH, et al. Enhancing effect of patented whey protein isolate (Immunocal) on cytotoxicity of an anticancer drug. *Nutr and Cancer*. 2000;38(2):200-208.
20. Bounous G. Whey protein concentrate (WPC) and glutathione modulation in cancer treatment. *Anticancer Res*. 2000;20(6C):4785-4792.
21. Kennedy RS, Konok GP, 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*. 1995;15(6B):2643-2649.
22. Hakkak R, Korourian S, Shelnutt SR, Badger TM, et al. Diets containing whey proteins or soy protein isolate protect against 7,12-dimethylbenz(a)anthracene-induced mammary tumors in female rats. *Cancer Epidemiol Biomarkers Prev*. 2000;9(1):113-117.
23. Takano T. Milk derived peptides and hypertension reduction. *Int. Dairy Journal*. 1998;8:375-381.
24. Nelson LA, Colker CM, Kalmer DS, Swain M. Comparative pilot trial evaluating the effect of whey protein isolate and isolated soy protein in healthy adults. Presented at the 2001 IFT Annual Meeting: Institute of Food Technologists, Session 29. Supported by Davisco Foods International, Inc, Eden Prairie, MN, USA.
25. Kajikawa M, Ohta T, Takase M, et al. Lactoferrin inhibits cholesterol accumulation in macrophages mediated by acetylated of oxidized low-density lipoproteins. *Biochimica et Biophysica Acta*. 1994;1213(1):82-90.
26. Blomstrand E, Hassmen P, Ekblom B, Newsholme E. Administration of Branched Chain Amino Acids During Sustained Exercise and Effects on Performance and Plasma Concentrations of Some Amino Acids.
27. Davis JM. Carbohydrates, branched chain amino acids, and endurance: the central fatigue hypothesis. *International Sport Journal* 1995; 5:29-38.
28. Lemon P, Tarnopolsky M, MacDougall J, Atkinson S. Protein requirements and muscle mass/strength changes during intensive training in novice bodybuilders. *J Applied Physiology*. 1992;73:767-775.
29. Dial EJ, LeLichtenberger LM. Effect of lactoferrin on Helicobacter felis induced gastritis. *Biochem. Cell Biol*. 2002;80:113-117.
30. Markus CR, et al. The bovine protein alpha-lactalbumin increases the plasma ratio of tryptophan to the other large neutral amino acids, and in vulnerable subjects raises brain serotonin activity, reduces cortisol concentration, and improves mood under stress. *Am J Clin Nutr*. 2000;71:1536-1544.
31. Takada Y, Aoe S, Kumegawa M. Whey protein stimulates the proliferation and differentiation of osteoblastic MC3T3-E1 cells. *Biochem Biophys Res Commun*. 1996;223(2):445-449.
32. Loimaranta, et al. Effects of bovine immune and non-immune whey preparations on the composition and pH response of human dental plaque. *Eur J Oral Science*, 1999;107:244-250.
33. Beucher S, Levenez F, Yvon M, Corring T. Effects of gastric digestive products from casein on CCK release by intestinal cells in rats. *Journal of Nutritional Biochemistry*, 1994;5:578-584.