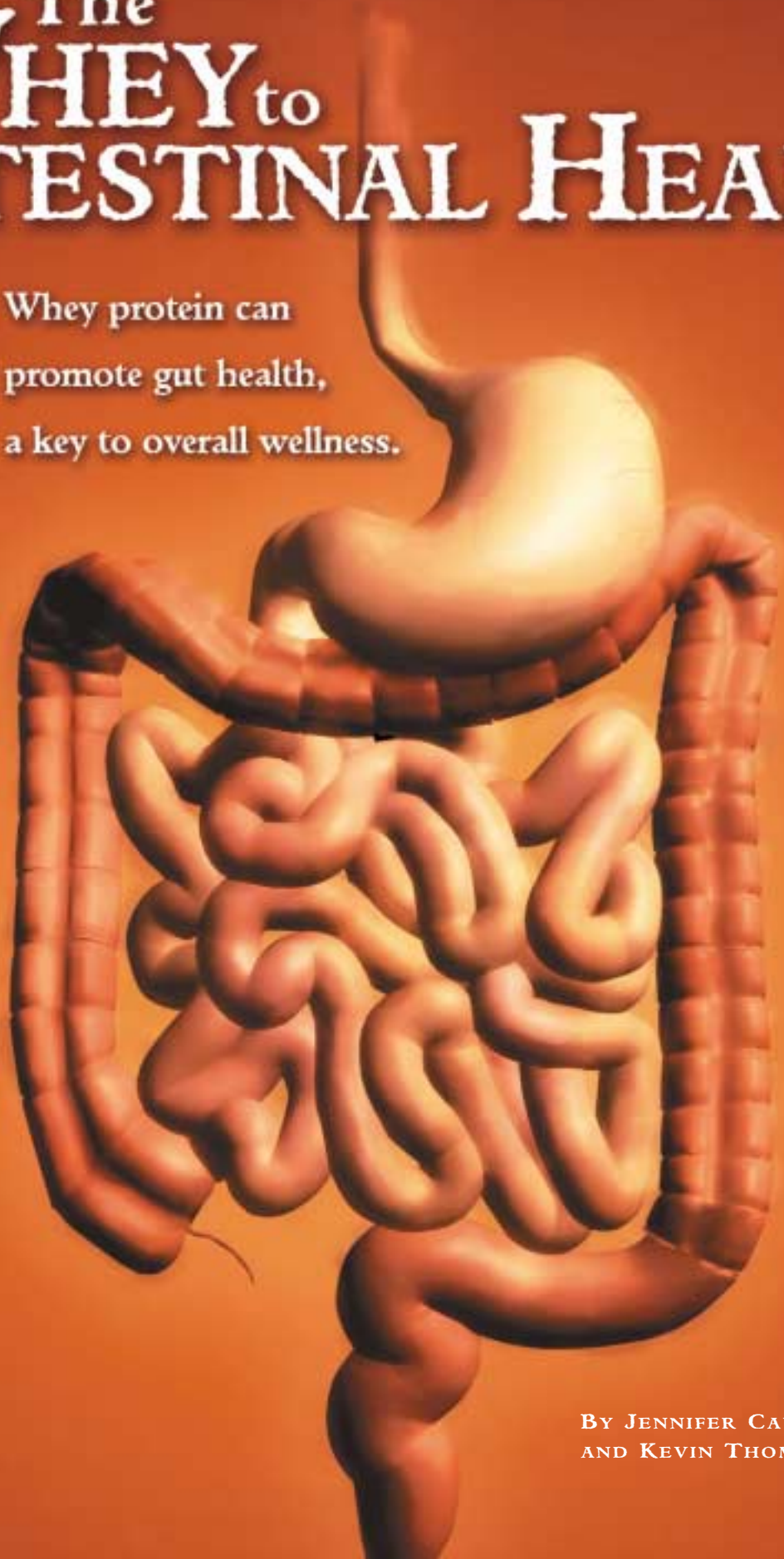
The WHEY to INTESTINAL HEALTH

Whey protein can promote gut health, a key to overall wellness.



By Jennifer Causey, MS, PhD, and Kevin Thomson, RD, MEd

Whey contains excellent-quality protein, carbohydrate, and lipids with specific health benefits. The most recent advances in whey research have discovered a new role for concentrated whey bioactives: enhancing intestinal health. These biologically active components can be selectively concentrated and incorporated into finished products for health promotion.

Colon and rectal cancer make up the second-leading cause of cancer death in the United States.[1] In 2000, abdominal pain and stomach discomfort were the leading emergency department complaints and the focus of more than 45 million physician visits.[2] Clearly, intestinal health is a key to overall wellness and quality of life. This article will focus on four beneficial areas of intestinal health modification with whey components: prebiotic effects, antimicrobial and antiviral properties, anticancer properties, and influences on site-specific and whole-body immunity.

Prebiotic Properties of Whey Components

The concept of intestinal health stretches far beyond the alleviation of constipation or diarrhea. In the early 1990s, with the coining of the term "prebiotic" by Gibson and Roberfroid, recognition of the importance of intestinal health was on the move. According to their definition, a prebiotic is "a nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon."[3]

Bifidobacteria and lactobacilli are two groups of bacteria capable of utilizing prebiotics. They are considered to be beneficial bacteria due in part to their antimicrobial effects against pathogenic bacteria, the production of essential B vitamins, and the inhibition of intestinal enzymes considered to be potential precarcinogens. Collectively, these positive attributes are considered to enhance intestinal health.[4]

Whey-derived carbohydrate components with prebiotic activity have also been found. Lactose has been shown to support lactic acid bacteria (such as bifidobacteria and lactobacilli). Sialic acids (types of oligosaccharides), which are typically attached to proteins commonly found in whey, have also been shown to have prebiotic effects.[4]

Interestingly, three noncarbohydrate prebiotics from whey have also been found. The first is a protein called glycomacropeptide (GMP). GMP is derived from the partial enzymatic breakdown of kappa-casein during cheese production, becoming a component of whey. GMP has been shown to support the growth of bifidobacteria.[5] The second whey-derived prebiotic is lactoferrin (Lf), which has been shown to support the growth of bifidobacteria and lactobacilli.[5]

The third whey component with prebiotic potential is actually a mineral. Dietary calcium, in the form of calcium phosphate (one of the forms found in dairy calcium), has been shown to selectively stimulate the growth of intestinal lactobacilli and decrease the severity of salmonella infections in rats.[6] Further studies in humans are needed to confirm this exciting new role for dairy calcium for the promotion of intestinal health.

Antimicrobial and Antiviral Properties of Whey Components

The intestinal tract can be viewed as a long tube with a continuum of microorganisms inhabiting its inner surface. It is the balance of this complex ecosystem of microorganisms that helps to determine health and disease. Through bacterial attachment to intestinal epithelial cells, these organisms become an integral part of nutrient digestion and uptake. As part of their metabolism, numerous species of microorganisms—such as bifidobacterium, lactobacillus, and bacteroides species—provide the intestinal cells with vital energy sources, such as short-chain fatty acids from the fermentation of fibers and oligosaccharides. The production of broad-spectrum antimicrobials (bacteriocins) by many of these lactic acid bacteria (excluding bifidobacteria) also helps to maintain a healthy intestinal tract through their negative impact on potentially pathogenic organisms.

Whey contains several unique components with broad antibacterial properties, including immunoglobulins (Igs), Lf, lactoperoxidase (Lp), GMP, and sphingolipids. Significant levels of these compounds have been shown to survive passage through the stomach and small intestine and arrive as intact proteins in the large intestine, where they exert their biological effects.[7]

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Perhaps the best-known of the whey components that provide antimicrobial action in the intestinal tract are the Igs. Igs fall into several subclasses, including IgG, IgM, and IgA. IgGs predominate in milk-derived sources, such as whey, and can traditionally comprise up to 1% of the total weight of whey proteins. Specialized whey-protein ingredients are now available with selectively concentrated IgG levels as high as 8%. IgG has been shown to bind the toxin produced by clostridium difficile, thereby reducing much of the deleterious effects of infection—including diarrhea, dehydration, and muscle aches.[7] GMP has also been shown to inhibit cholera toxin binding to receptors in the intestinal tract.[8,18]

Lf, an iron-binding protein, is a whey-derived compound that has gained recognition for its antibacterial properties. Studies have shown that most Lf survives passage through the stomach and small intestine and arrives in the lower bowel, where it can sequester iron from bacteria.[9] Since pathogens in particular have high iron requirements for metabolism and growth, this property of Lf makes it broadly antimicrobial in nature. Lactobacilli can utilize Lf-bound iron, allowing Lf to both inhibit pathogenic bacteria and support growth of lactobacilli.

Additionally, Lf has been shown to have important antiviral properties. Through direct interaction with select viral pathogens,

Figure 1 Typical Whey Protein Ingredient Composition

Whey Components	Whey Powder	Whey Protein Concentrate	Whey Protein Isolate
Protein	11% to 14.5%	34% to 89%	90% +
Lactose	63% to 75%	10% to 55%	.5%
Milk Fat	1% to 1.5%	2% to 10%	.5%

Lf inhibits virus replication and ability to attach to colonic epithelial cells. Viral inhibition also results through immune-modulation benefits of Lf.

Another whey-derived protein with potent antimicrobial properties is Lp. Lp catalyzes the oxidation of thiocyanite into hypothiocyanate ion, which is a strong oxidizing agent.[4] Hypothiocyanate ions cause damage to bacterial cell membranes as one of the primary modes of action. This "Lp system" has also been used as a milk-preservative system in countries with inadequate refrigeration.[10]

Whey-derived phospholipids, such as the sphingolipids, are metabolized in the gastrointestinal (GI) tract and produce sphingosine and lysosphingomyelin. These compounds have been shown to be powerful bactericidal agents in vitro.[11] Further research is needed to confirm the potential antimicrobial actions of whey lipids.

Anticancer Properties of Whey Components

Whey is a source of specific components that animal and cell culture studies suggest have anticancer properties. The first are the sulphur amino acids (cysteine and methionine), which are found in high levels in whey protein. Cysteine and methionine are utilized in glutathione synthesis. Glutathione is widely distributed and is a substrate for two classes of enzymes that catalyze detoxification compounds and bind mutagens and carcinogens, facilitating their elimination from the body.[12]

Lf's ability to bind iron is another benefit in the area of colon cancer. Iron is certainly a necessary ingredient, but it also has pro-oxidant properties that create lipid peroxidation and associated DNA damage.[12] Lf fragments have also been shown to have strong bioactive properties. In cultures, they have been shown to induce apoptosis (programmed cell death) to tumor cells and may be a useful adjunct in colon cancer therapy.

Sphingolipids are long-chain fatty acids with various side chains. More than 60 known sphingolipids have been isolated with unique, as well as overlapping biological functions. Integrated into all membranes, they serve numerous roles, including anchoring membrane structures, modulating the activity of growth-factor receptors, and inducing cell death in tumor cells. One of the most abundant whey-derived sphingolipids is sphingomyelin. Sphingomyelins are converted in a cascade requiring three different enzyme systems to ceramide, sphingosine, and sphingosine-1 phosphate.[13] These secondary metabolites of sphingomyelin have diverse roles in cell biology, such as the induction of cell death in tumor cells and the regulation of growth factors involved in cell differentiation.

Sphingomyelins have been investigated for their potential to inhibit colon cancer in animal models. Since intestinal cells undergo rapid turnover, tumor cells resulting from altered cell-cycle regulation may be forced into programmed cell death through the use of dietary sphingomyelins as precursors. Furthermore, sphingomyelins have been found to regulate growth-factor receptors, such as the transforming growth factor-beta family (TGF-ß). TGF-ßs are a multifunctional family of growth factors that regulate cell growth in a variety of normal and tumor cells by suppressing proliferation, inducing differentiation and apoptosis. TGF-ßs are unaffected by passage through the stomach and maintain bioactivity in the colon by withstanding enzymatic proteolysis.[12]

Immune-Enhancing Properties of Whey Components

The human GI tract houses the largest portion of the immune system——the gut-associated lymphoid tissue and mucosal-associated lymphoid tissue. Together, these tissues help to preserve and promote the integrity and function of the GI tract, thus contributing to the maintenance of overall health. These tissues, as well as the colonic epithelial cells, are the initial interface between bacteria, nutrient uptake, and the rest of the body. These tissues are one of the major sites for potential intervention with whey-derived ingredients for the promotion of host immunity.

Igs, Lp, and Lf concentrated from whey have been shown to participate in host immunity. For example, IgGs have been shown to bind bacterial toxins and lower bacterial load in the large bowel. Ridding the intestinal tract of pathogenic organisms has a prominent role in improving passive host immunity. Dietary Lp and Lf also may play important roles in host immunity through their antibacterial action on pathogenic microorganisms. Once again, using whey-derived adjuncts to shift the balance of the intestinal microflora is an important dietary technique to aid in immune enhancement.

Calcium—by virtue of its prebiotic activity and influence on macrophages—neutrophils, and other white blood cell subtypes may also be classified as immune-modifying minerals.

Human clinical research has shown Lf to provide immune modulation influence on the immune system. Lf is a natural component of the human immune system and is found in the body's mucous substances, including saliva. Lf supplementation has been shown to increase the oral Lf levels in patients with depressed levels.[14,15] Research suggests that Lf supplementation may indeed be a practical approach for immune system enhancement.

TGFs are abundant in milk (1 milligram per liter to 2 milligrams per liter) and colostrum (20 milligrams per liter to 40 milligrams per liter) and serve a major role in GI integrity of newborn animals.[16] TGF-b2 has been shown to reside locally near the tops of the intestinal villi, inhibiting proliferation and signaling neutrophils as a part of innate host immunity.[17]

Whey: Refining the Concept

Whey, produced during cheese manufacturing, continues to evolve from a bulk protein source to a suite of diverse biologically active compounds with unique physiological and functional attributes. Several categories of whey protein ingredients are commonly used in food and nutrition products, including whey powder, whey protein concentrate, and whey protein isolate. They differ in composition as a result of the extent and method of processing. Figure 1 summarizes the typical composition of traditional whey protein ingredients.

Whey powder is produced by taking the whey directly from cheese production. It is then clarified (the fat is removed), pasteurized, and dried to provide a fine white powder ingredient known as whey powder.

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Whey concentrate typically uses ultrafiltration membrane technology to filter or concentrate whey components based on the membrane pore size and/or molecular weight. Passing fluid whey across a semipermeable membrane, lactose and ash are removed, thus concentrating the protein content. The degree to which lactose and ash are removed determines the protein content of the final product.

Whey protein isolate ingredients have a protein content of 90% or greater (dry weight basis) and can utilize a variety of processes, including microfiltration and ion exchange.

Figure 2

Whey Fractions	Bioactive Benefits			
	Immune Enhancement	Prebiotic	Anticancer	Antimicrobial
Lactoferrin	X	X	X	X
Glycomacropeptide		X		X
Immunoglobulins	X			X
TGF-ß2	X		X	
Sphingomyelin			X	X
Calcium	X	X	X	
Lactoperoxidase				X
Lactose		X		
Sialic Acid		X		

To reach the 90% or higher protein level, microfiltration removes additional lactose and fat to increase protein content. This process maintains the naturally occurring bioactive components present in whey. The ion-exchange process utilizes charged resins to bind and separate proteins from other components. Ion exchange allows for the separation of whole protein and protein fractions based on their ionic charge.

As recognition grows with respect to the numerous types of biological components that are known as whey, manufacturing technologies are also becoming more developed. Advanced chromatography technology is in use today to further separate the individual protein components, such as Lf and Lp, from the main whey proteins (alpha-lactalbumin, beta-lactoglobulin, and bovine serum albumin). This process allows for a high degree of purity, but its relatively high cost may be prohibitive in many nutrition markets.

Advanced membrane technology is also in use today. It allows for the enrichment of whey concentrate with whey bioactive components, such as sphingolipids, Lf, Igs, GMP, and TGF-ßs. These new whey ingredients provide an economic delivery system for whey protein with the added health benefits associated with whey bioactive components.

Because separation technologies differ, the makeup of the end products and related health benefits also differ. Dietitians and other healthcare professionals need to be aware of these technological and product-quality differences to provide product-specific education and recommendations on the most nutritionally relevant products for their patients.

Figure 2 provides an overview of the featured components of whey and their corresponding areas of intestinal health promotion. Interestingly, Lf has applications in all four aspects of intestinal health and may provide an important link between whey-derived ingredient consumption and the whey to intestinal health. With advances in whey-manufacturing technology, whey protein ingredients are now available with concentrated bioactive components that are economical solutions for many intestinal health markets.

Conclusion

Whey-derived ingredients such as lactose, Lf, Lp, IgGs, GMP, TGFs, sphingolipids, and calcium are featured in new products appearing in the marketplace as concentrated bioactive whey ingredients for the promotion of intestinal health through action on the intestinal microflora. These compounds also have broad-spectrum antimicrobial, anticancer, and immune-potentiating properties, which provide added benefits over traditional fiber-based prebiotics.

As exciting intestinal health benefits of whey-derived bioactives continue to emerge, companies are stepping up to provide innovative, evidence-based nutritional products to the wellness and medical consumer markets.

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