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Therapeutic Benefits of Whey Protein: a review

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Abstract

Whey, a milk-based protein complex, is being promoted as a functional food with several health advantages. Alpha-lactalbumin, betalactoglobulin, lactoferrin, glycomacropeptide, and immunoglobulins are among the biological components of whey that exhibit a variety of immune-boosting characteristics. Whey can also function as a chelating agent, antiviral, antibacterial, hypolipidemic, antihypertensive, anticancer, and antioxidant. The conversion of the amino acid cysteine into glutathione, a strong intracellular antioxidant, is believed to be the main way that whey works. Whey has been successfully used in several clinical trials as an antibacterial agent and to treat cancer, HIV, hepatitis B, cardiovascular disease, and osteoporosis. Additionally, whey protein has shown promise in improving workout performance.

I. Introduction

In recent years, milk constituents have become recognized as functional foods, suggesting their use has a direct and measurable effect on health outcomes(1). Whey, a by-product of cheese and curd manufacturing, was once considered a waste product. The discovery of whey as a functional food with nutritional applications elevated whey to a co-product in the manufacturing of cheese.(2). Milk contains two primary sources of protein, the caseins and whey. After processing occurs, the caseins are the proteins responsible for making curds, while whey remains in an aqueous environment. The components of whey include beta-lactoglobulin, alpha-lactalbumin, bovine serum albumin, lactoferrin, immunoglobulins, lactoperoxidase enzymes, glycomacropeptides, lactose and minerals.(2). In additional, whey derived from buttermilk versus cheese contains the lipid sphingomyelin. Several cultures consider fermented foods part of a healthful diet. Historically, whey was considered a cure-all used to heal ailments ranging from gastrointestinal complaints to joint and ligament problems. Nanna Rognvaldardottir, an Icelandic food expert, describes how whey, called syra by the Icelandic people, is fermented and stored in barrels. Syra is diluted with water and ingested or used as a marinade or preservative for meat and other food. Syra was the most common beverage of Icelandic people and is thought to have replaced ale, due to lack of grains in the region.(3). Today, whey is a popular dietary protein supplement purported to provide antimicrobial activity, immune modulation, improved muscle strength and body composition, and to prevent cardiovascular disease and osteoporosis. Advances in processing technology, including ultrafiltration, microfiltration, reverse osmosis, and ion-exchange, have resulted in development of several different finished whey products. Whey protein concentrates (ranging from 80-95 percent protein), reduced lactose whey, whey protein isolate, demineralized whey, and hydrolyzed whey are now available commercially(4). Each whey product varies in the amount of protein, carbohydrates, immunoglobulins, lactose, minerals, and fat in the finished product. These variables are important factors in the selection of whey fractions for specific nutritional applications.(5).

Biological Components
Amino Acid Content
When compared to different vegetable protein sources like soy, maize, and wheat gluten, whey proteins provide higher amounts of all the essential amino acids.(6) Whey contains a complete range of amino acids and, in comparison to free amino acid solutions, the amino acids are effectively absorbed and used.7.
The branched-chain amino acids (BCAAs) leucine, isoleucine, and valine are more abundant in whey

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than in other protein sources. Leucine in particular is a crucial component of BCAAs for tissue growth and repair.

During the translation-initiation route of protein synthesis, leucine has been found to be an essential amino acid for protein metabolism.(8). The sulfur-containing amino acids cysteine and methionine are also abundant in whey proteins. Through intracellular conversion to glutathione, immunological function is improved when these amino acids are present in high concentrations.

Lactoferrin

The whey portion of milk and colostrums include lactoferrin, an iron-binding glycoprotein that functions as a non-enzymatic antioxidant. Whereas human lactoferrin has 691 amino acid residues, the lactoferrin component of whey has roughly 689 residues.(9) A single polypeptide chain with two ferric ion binding sites makes up whey lactoferrin. Bovine lactoferrin is only 15–25% iron-saturated prior to processing. Apolactoferrin, or iron-depleted lactoferrin, is defined as having less than five percent iron. Apolactoferrin is found in human breast milk.(10).

Approximately 2 mg/mL and 7 mg/mL of lactoferrin are found in human milk and colostrum, respectively, whereas 0.2 mg/mL and 1.5 mg/mL are found in bovine milk and colostrum, respectively.(11) Although lactoferrin makes up a large portion of whey protein in human breast milk, it only makes up 0.35–2.0 percent of total proteins in the majority of commercial whey protein powders.

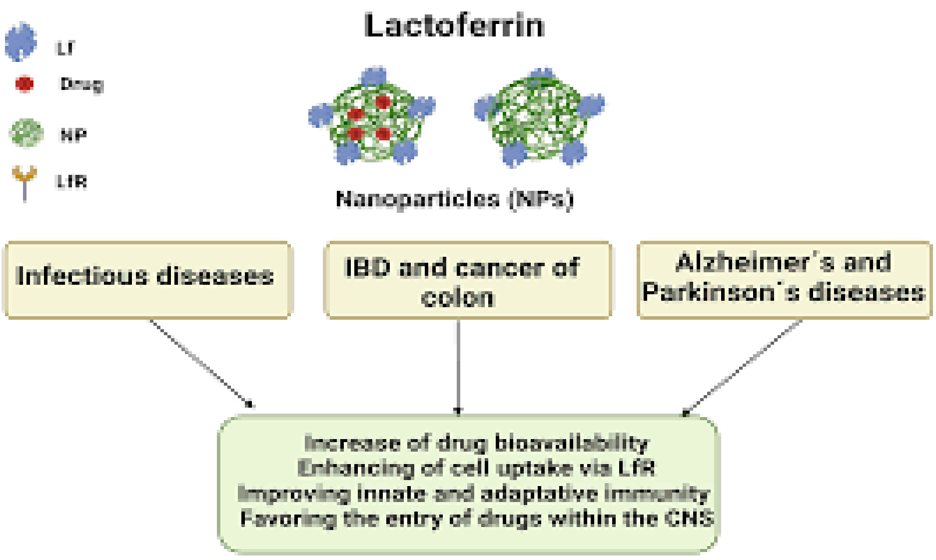

Figure (1)

Therapeutic properties of lactoferrin (39)

Immunoglobulins

An immunoglobulin (Ig) is an antibody or gamma-globulin. There are five classes of antibodies – IgA, IgD, IgE, IgG, and IgM. IgG constitutes approximately 75 percent of the antibodies in an adult. IgG is transferred from mother to child *in utero* via cord blood and by breast-feeding, and serves as a child's first line of immune defense – referred to as "passive immunity." IgA is secreted in breast milk and ultimately transferred to the digestive tract in the newborn infant, providing better immunity than a bottle-fed child.(12). Colostrums contain significantly greater concentrations of immunoglobulins than mature milk. Immunoglobulins reach maximum concentration the first 24-48 hours post-parturition and decline in a time-dependent manner following peak concentration.(13) Similarly, the whey fraction of milk appears to contain a significant amount of immunoglobulins approximately 10-15 percent of total whey

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proteins. An *in vitro* study demonstrated bovine milk-derived IgG suppresses human lymphocyte proliferative response to T cells at levels as low as 0.3 mg/mL of IgG. The authors further conclude bovine milk IgG typically ranges between0.6-0.9 mg/mL and is therefore likely to confer immunity that could be carried to humans.(14). Studies show raw milk from non-immunized cows contain specific antibodies to human rotavirus, as well as antibodies to bacteria such as *E. coli*, *Salmonella enteriditis*, *S. typhimurium*, and *Shigella flexneri*.(15,16).

beta-Lactoglobulin

Although human milk does not include beta-lactoglobulin, it makes up around half of the protein in bovine whey. The beta-lactoglobulin structure contains a retinol-binding protein in addition to essential and branched chain amino acids. This protein has the ability to alter lymphatic responses because it carries tiny hydrophobic compounds, such as retinoic acid.(17).

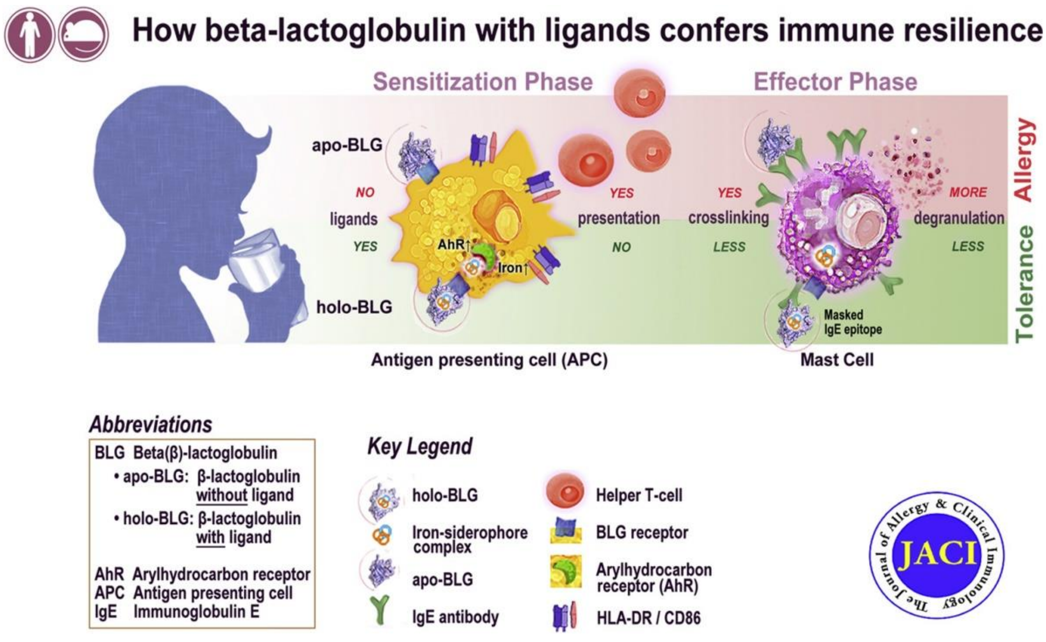

Figure (2) beta-Lactoglobulin(40)

alpha-Lactalbumin

One of the primary proteins in both human and cow's milk is alpha-lactalbumin. It contains a broad range of amino acids, including an easily accessible supply of essential and branched chain amino acids, and makes up around 20–25 percent of whey proteins. Because it has the most structurally similar protein profile to breast milk, purified alpha-lactalbumin is most commonly employed in the production of infant formula. The majority of dairy-based infant formulae, however, contain substances like demineralized whey with increased quantities of beta-lactoglobulin due to cost-effective methods, which makes them less comparable to human milk.

Alpha-lactalbumin, both in its natural and hydrolyzed forms, improved the antibody response to systematic antigen stimulation in a research conducted on mice (18). The same group demonstrated that alpha-lactalbumin suppresses both T cell-dependent and -independent responses and directly affects B-lymphocyte activity.(19).

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Lactoperoxidase

Numerous enzymes, such as hydrolases, transferases, lyases, proteases, and lipases, are found in whey. The most prevalent enzyme, lactoperoxidase, is crucial to the whey portion of milk; after the curdling process, most of it ends up in the whey. Lactoperoxidase makes up 0.25–0.5 percent of whey total protein content. It has the capacity to catalyze the reduction of hydrogen peroxide and other compounds.(20) Thiocyanate and certain halides (including iodine and bromium) undergo peroxidation, which is catalyzed by this enzyme system. The resultant chemicals inhibit and/or kill a variety of bacterial species.(21). Lactoperoxidase is not rendered inactive during the pasteurization process, indicating that it remains stable as a preservative.

Glycomacropeptide

Another name for glycomacropeptide (GMP) is casein macropeptide. Because of the way chymosin interacts with casein during the cheesemaking process, whey contains 10–15% GMP. Cheeses like cottage cheese that aren't prepared with chymosin don't produce GMP during the curdling process since GMP is only present when chymosin is employed during processing. (22) GMP is deficient in the aromatic amino acids phenylalanine, tryptophan, and tyrosine and abundant in branched chain amino acids. It is safe for those with phenylketonuria (PKU) because it is one of the few naturally occurring proteins that does not include phenylalanine.

Bovine Serum Albumin

About 10–15% of the total whey protein is composed of the big protein known as bovine serum albumin (BSA). Even though BSA is a source of vital amino acids, not much is known about its possible medicinal uses.

Mechanism of Action

Whey has potent antioxidant activity, likely by contributing cysteine-rich proteins that aid in the synthesis of glutathione (GSH), a potent intracellular antioxidant.2 GSH is comprised of glycine, glutamate, and cysteine . Cysteine contains a thiol (sulfhydryl) group that serves as an active reducing agent in preventing oxidation and tissue damage. As an antioxidant, glutathione is most effective in its reduced form. Riboflavin, niacinamide, and glutathione reductase are essential cofactors in the reduction of glutathione.(23). As a result of the glutathione/antioxidant component of whey, it is being investigated as an anti-aging agent.(24). As a detoxifying agent, glutathione peroxidase (GSHPx), which is derived from selenium and cysteine, is an endogenous antioxidant enzyme with the ability to convert lipid peroxides into less harmful hydroxy acids. The peroxidases interact with hydrogen peroxide to reduce it to water, negating its oxidative potential. Both glutathione peroxidase activity and selenium concentrations have been shown to decrease as lactation continues, peaking at approximately one month after initiation. Practitioners use whey protein products as a source of cysteine to increase intracellular glutathione levels (25,26). And it has been reported that GSHPx activity in cow's milk, and presumably whey, is the same as in human milk.(27). Studies on lactoferrin have demonstrated its ability to activate natural killer (NK) cells and neutrophils, induce colony-stimulating factor activity, and enhance macrophage cytotoxicity.(28-29).
Lactoferrin also appears to have antiviral, antifungal, and antibacterial properties (30). The antimicrobial effect is likely more potent in organisms that require iron to replicate, (31) as lactoferrin has the unique ability to chelate iron in a way that deprives microorganisms of this essential nutrient for growth.(32). In additional, lactoferrin has the ability to release the outer membrane of gramnegative bacteria, the lipopolysaccharide component, thus acting as an antibiotic.(33)Lactoferrin demonstrates anti-inflammatory properties. A mouse study revealed lactoferrin had the ability to regulate levels of tumor necrosis factor (TNF) and interleukin 6 (IL-6), thus decreasing inflammation and, ultimately, mortality. (34) In addition to the above-mentioned properties, alpha-lactalbumin can chelate heavy metals(35). It reduces oxidative stress because of its ironchelating. properties.(36) Whey has been recently touted as a

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healthful dietary supplement to reduce blood pressure. Antihypertensive peptides have been isolated in the primary sequence of bovine beta-lactoglobulin. (37) These peptides give whey significant angiotensin I converting enzyme (ACE) inhibitory activity, which blocksthe conversion of angiotensin I to angiotensin II, a highly potent vasoconstricto r molecule.(38) beta-Lactoglobulin has been described (39) as a cholesterol-lowering agent. In animal studies, beta-lactoglobulin inhibited cholesterol absorption by changing micellar cholesterol solubility in the intestine. (39).

II. Conclusion

One of the earliest useful nutrients that mammals have access to is milk. Mammals depend on their mothers' milk for sustenance and immunological support from birth. The different components of milk, particularly whey, and their potential effects on health and illness are being better understood by scientists. There is still a lot of good research being published about whey and its biological components. Although a substantial portion of clinical data from Asia was not backed by interest groups with a dairy affiliation, it is interesting that some of the study has been funded by commercial dairy organizations. Whey protein products have not yet been associated with any serious side effects, though some patients report mild gastrointestinal issues.

Whey products might not be appropriate for people with severe milk allergies, while many dairy-sensitive people discover that casein is the cause and can handle whey. Other people with dairy sensitivity are lactose intolerant. Lactose is eliminated from the majority of whey proteins during processing, leaving just trace levels in final whey products. For people who are lactose intolerant, de-lactosed whey—which is made by crystallizing most of the lactose out and recovering the remaining whey—is suitable. Before starting therapeutic quantities, a person with dairy allergies should do a challenge test using a modest amount of a specific whey supplement.

It is anticipated that new functional foods will emerge as researchers continue to examine the components of whey. Glycomacropeptide, lactoperoxidase, whey immunoglobulin, and bovine serum albumin isolated products may be studied in addition to the currently available isolated colostrum, lactoferrin, and alpha-lactalbumin products. The range of whey proteins currently on the market enables customization of their application for particular therapeutic conditions. Athletes and other people seeking a low-allergenic, rapidly absorbed protein source find hydrolyzed whey's easily accessible di- and tri-peptide fractions appealing. For immunological regulation, undenatured whey has the largest amounts of intact natural proteins, including immunoglobulins and lactoferrin.

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