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Whey Proteins: A Novel Source of Bioceuticals

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Abstract: An increasing interest is being focused on whey proteins and its products particularly as functional ingredients in food and pharmaceutical applications and as nutrients in dietetic supplements and health foods. It is obtained from cheese whey that was considered as waste material. The biological components of whey, including lactoferrin, beta-lactoglobulin, alpha-lactalbumin, glycomacropeptide and immunoglobulins, demonstrate a range of immune-enhancing properties. In addition, whey has the ability to act as an antioxidant, antihypertensive, antitumor, hypolipidemic, antiviral, antibacterial and chelating agent. The nutritional value of this product as animal feed has already been appreciated for a long time. The demand for whey products have increased faster in the food as well as in the feed sector and forecasts indicate that human applications of whey (products) may surpass the utilization of other nutraceuticals in the near future. In the present article, an attempt has been made to provide an insight view on the use of whey proteins as a complete bioceutical.

Key words: Nutraceutical · Byproduct · Health · Immune Enhancing · Antimicrobial

INTRODUCTION

Caseins and whey proteins are the 2 major protein fractions of cow milk, comprising about 20% of total milk protein. Whey proteins are separated from casein curds during the cheese-making process. It is obtained by following acid, heat or rennet driven coagulation [1]. It is well known that cheese whey is rich in nutrients but it is discharged directly into the environment that constitutes a significant loss of protein and energy source. Whey proteins, which refer to a group of individual proteins, contain water, lactose, protein, minerals (calcium, phosphorus, magnesium) and fat.

The major proteins present in bovine whey come from the mammary gland that secretes ß-lactoglobulin (ß-LG), 7 a-lactalbumin (a-LA) and glycomacropeptide (GMP) and from serum, like IgG1 and IgG2, IgA, IgE and IgM and albumin. In addition, whey derived from buttermilk versus cheese contains the lipid sphingomyelin [2].

Historically, whey was considered a cure-all used to heal ailments ranging from gastrointestinal complaints to joint and ligament problems. According to Nanna Rognvaldardottir [3], an Icelandic food expert, 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 is the most common beverage of Icelandic people and is thought to have replaced ale, due to lack of grains in the region [3].

Whey protein is an excellent protein choice for individuals of all ages who value the role of a healthy diet in helping to maintain and improve their health. Whey protein isolate is unsurpassed as a source of the essential amino acids required in the daily diet [4]. In the present article, an attempt has been made to provide an insight view on the use of whey proteins as a complete bioceutical.

Benefits of Whey Protein: The best known effects of whey protein are its ability to help to promote weight loss, increase lean muscle mass and boost the immune system. 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 [2]. Advances in processing technology, including ultra-

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filtration, 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, de-mineralized whey and hydrolyzed whey are now commercially available. It contains the full spectrum of amino acids including essential amino acids and branched-chain amino acids (BCAA) which are important in tissue growth and repair. Leucine is a key branched-chain amino acid in protein synthesis and has recently been identified as playing a critical role in insulin and glucose metabolism. The essential amino acids and branched-chain amino acids in whey protein are not only present in higher concentrations than in other protein sources such as soy, corn and wheat; they are also efficiently absorbed and utilized [5].

Market Potential of Whey Protein: According to Sloan Trends' Trend Sense model, whey protein is projected to reach mass market status commercialization in 2013-14. Medical Counts have shown strong and steady growth during the past decade increasing almost 50% reflecting a large and growing body of scientific support. Although a flattening of Medical Counts may cause whey protein to flirt with crossing over into Commercialization over the next few months or temporarily remain a very high level popularization market, it still represents a grossly overlooked opportunity in the specialty and health food channels and among very health conscious and condition-specific consumers, beyond its sports nutrition connection [6].

There are mainly two types of whey: sweet whey and acid whey [7].

Sweet whey is produced by precipitation of casein by proteolytic enzymes such as chymosine and pepsin or microbial enzymes produced from *Mucor miehei* and *M. pusilus*. It comes from the production of cheddar, Swiss and Italian varieties of cheese. It contains approximately 93% water and 6.35% solids, with about 76% of the solids being lactose.

Acid whey is produced by precipitation of caseins during cheese making. It comes from soft cheese with cottage cheese as a predominant product. Precipitation is achieved by acidification not above pH 5.1. Acid whey is rich in minerals due to solubilization of colloidal calcium phosphate of casein micelles that occurs concomitantly with acidification. Its composition is similar to sweet whey except that it has higher lactic acid and ash contents.

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.

Production of Whey Protein: Milk is pasteurized by HTST (High temperature short time) method at 72.7°C for 30 seconds and held overnight at 40°C. The mixture is cooled to 30°C and inoculated with lactic acid culture and incubated for 20 minutes. The mixture is coagulated by addition of rennet extract followed by stirring. Chymosin, the active enzyme ingredient of rennet, aids in the coagulation of milk by separating it into curds and whey [8]. The liquid whey is drained through a stainless steel screen and the remaining curd is cut and cooked at 30°C. Whey liquid is then filtered at 45°C and brought to a pH of 3 by adding citric acid. The liquid is filtered to one fifth its original volume, resulting in whey concentrate that is approximately 80% protein [2].

This can be additionally micro-filtered to increase protein concentration to as high as 95% [9]. The final whey protein concentrate is warmed and spray-dried to achieve whey protein powder. Whey protein concentrates can then be put through an ion-exchange process to remove fat and lactose. In addition, some manufacturers hydrolyze (cleaving peptide bonds via enzymes or heat) the whey to provide more peptides and free amino acids in the final product [10].

The variation in composition in different types of whey protein is due to the difference in extent and method of processing.

Whey powder is produced by taking the whey directly from cheese production. It is then clarified, pasteurized and dried to provide a fine white powder known as whey powder [1].

Whey concentrate typically uses ultra-filtration membrane technology to filter or concentrate whey components based on the membrane pore size and/ or molecular wt. The fluid whey is allowed to pass through a semi-permeable membrane thereby removing lactose and ash and concentrating the protein content [11].

Whey protein isolate have a protein content of 90% or greater and is produced through a variety of processes like microfiltration and ion exchange. Microfiltration removes additional lactose and fat to increase protein concentration to up to 90% or higher. This process maintains the naturally occurring bioactive components in whey. Advanced chromatography technology can be

used to further separate the individual protein components such as lactoferrin (Lf) and lactoperoxidase (Lp) from the main whey proteins (α-lactalbumin, β-lactglobulin and bovine serum albumin). Advanced membrane technology is used for the enrichment of whey concentrate with whey bioactive components such as sphingolipids, Lf, immunoglobulins (Igs), glycomacropeptide (GMP) and transforming growth factor-beta (TGF-β) [12].

Whey proteins can be separated from the cheese milk permeate (native whey) prior to cheese manufacture by microfiltration (MF) that allows whey proteins to be further processed into value-added whey products such as a native whey protein concentrate as a liquid [13].

Enzymes in Whey Protein: Whey contains many types of enzymes, including hydrolases, transferases, lyases, proteases and lipases.

Lactoperoxidase, an important enzyme in the whey fraction of milk, is the most abundant enzyme and the majority of it ends up in whey following the curding process. Lactoperoxidase accounts for 0.25-0.5% of total protein found in whey. It has the ability to catalyze certain molecules, including the reduction of hydrogen peroxide [14]. This enzyme system catalyzes peroxidation of thiocyanate and some halides (such as iodine and bromium), which ultimately generates products that inhibit and/or kill a range of bacterial species [15]. During the pasteurization process, lactoperoxidase is not inactivated, suggesting its stability as a preservative.

Lactoperoxidase system is a naturally occurring antibacterial system in milk, that is activated by means of increasing the concentrations of two components or activators (hydrogen peroxide and thiocyanate), reacting with each other [16]. This reaction is catalyzed by enzyme lactoperoxidase which is naturally present in milk and leads to the formation of antimicrobial compounds [17].

Glycomacropeptide (GMP) is also known as casein macropeptide. GMP is a protein present in whey at 10-15%, due to the action of chymosin on casein during the cheese making process. GMP is only present when chymosin is used during processing; therefore, cheeses such as cottage cheese not made with chymosin do not produce GMP in the curding process [18]. GMP is high in branched chain amino acids and lacks the aromatic amino acids including phenylalanine, tryptophan and tyrosine. It is one of the few naturally occurring proteins that lack phenylalanine, making it safe for individuals suffering with phenylketonuria (PKU).

GMP can be used to produce "high protein-reduced sugar" drinks, which are beneficial to general health in terms of providing the body with nutrients and helping it to fight viral and bacterial infections [19]. Glycomacropeptide is a carbohydrate-containing peptide, formed from rennin digestion of k-casein that has a large negative charge [20]. This negative charge may have a positive effect on mineral and trace element absorption by assisting the chelation and transport of minerals into the intestinal epithelium, thereby improving trace element status.

The GMP inhibits the adhesion of cariogenic bacteria such as *Streptococcus* spp. *mutans, sanguis* and *sobrinus* to oral surfaces [21] and it can modify the composition of plaque bacteria to control its acid production and in turn reduce the de-mineralisation of enamel and promote remineralisation [22]. The GMP is a source of N-acetyl-necromantic acid [5] and one study showed that dietary intake of GMP can increase the sialic acid content of saliva, with effects on its viscosity and protective function [22].

Bovine Serum Albumin: Bovine serum albumin (BSA) is a large protein that makes up approximately 10-15% of total whey protein. BSA is a source of essential amino acids, but there is very little available information regarding its potential therapeutic activity.

Mechanism of Action: Whey has a potent antioxidant activity, likely by contributing cysteine-rich proteins that aid in the synthesis of glutathione (GSH), a potent intracellular antioxidant [23]. 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 [24]. As a result of the glutathione/antioxidant component of whey, it is being investigated as an anti-aging agent [25].

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 [26-27] and it has been reported that GSHPx activity in cow's milk and presumably whey, is the same as in human milk [28]. Studies on lactoferrin have demonstrated its ability to activate natural killer (NK) cells and neutrophils, induce colony-stimulating factor activity and enhance macrophage cytotoxicity [29-32].

Lactoferrin also appears to have antiviral, antifungal and antibacterial properties. The antimicrobial effect is likely to be more potent in organisms that require iron to replicate, as lactoferrin has the unique ability to chelate iron in a way that deprives microorganisms of this essential nutrient for growth [33]. In additional, lactoferrin has the ability to release the outer membrane of Gram negative bacteria, the lipo-polysaccharide component, thus acting as an antibiotic [34]. Lactoferrin demonstrates anti-inflammatory properties. A mouse study revealed that lactoferrin has the ability to regulate levels of tumor necrosis factor (TNF) and interleukin 6 (IL-6), thus decreasing inflammation and ultimately mortality [35].

In addition to the above-mentioned properties, alpha-lactalbumin can chelate heavy metals [36]. It reduces oxidative stress because of its iron chelating properties [37].

Whey has been recently touted as a healthful dietary supplement to reduce blood pressure. Antihypertensive peptides have been isolated in the primary sequence of bovine beta-lactoglobulin [38]. These peptides give whey significant angiotensin I converting enzyme (ACE) inhibitory activity, which blocks the conversion of angiotensin I to angiotensin II, a highly potent vasoconstrictor molecule [39]. β-Lactoglobulin has been described by Nagaoka [40] as a cholesterol-lowering agent. In animal studies, beta-lactoglobulin inhibited cholesterol absorption by changing cholesterol solubility in the intestine.

Lactoferrin: Lactoferrin, an iron-binding glycoprotein, is a non-enzymatic antioxidant found in the whey fraction of milk as well as in colostrums. The lactoferrin component of whey consists of approximately 689 amino acid residues, while human lactoferrin consists of 691 residues [41]. Whey lactoferrin is composed of a single polypeptide chain with two binding sites for ferric ions. Before processing, bovine lactoferrin is only 15-20 percent saturated with iron. Iron-depleted lactoferrin, defined as containing less than five percent iron, is referred to as apolactoferrin. Human breast milk contains apolactoferrin [42]. The concentration of lactoferrin in human milk and colostrums is approximately 2 mg/mL and 7 mg/mL, respectively, while in bovine milk and colostrums it is approximately 0.2 mg/mL and 1.5 mg/mL, respectively [43]. Lactoferrin is a dominant component of whey protein in human breast milk; however, the concentration in most commercial whey protein powders is only 0.35-2.0% of total proteins [44]. Lactoferrin has been shown to possess important antibacterial and antiviral properties. It sequesters iron from bacteria [45]. Since pathogens in particular have high iron requirements for metabolism and growth, this property of lactoferrin makes it broadly antimicrobial in nature. It directly interacts with selected viral pathogens, inhibits virus replication and their ability to attach to colonic epithelial cells. Viral inhibition also results through immune modulation benefits of lactoferrin [46].

Whey Proteins for Physical Performance and Sports: Research studies [4] have proved whey protein as the 'gold standard' of proteins especially for athletes. There are several factors:

- Whey protein is a naturally complete protein that contains all of the essential amino acids required in the daily diet. It has the ideal combination of amino acids to help to improve body composition and enhance athletic performance.
- Whey protein is a rich source of branched chain amino acids (BCAAs), containing the highest known levels of any natural food source. BCAAs are important for athletes since unlike the other essential amino acids; they are metabolized directly into muscle tissue and are the first ones used during periods of exercise and resistance training. Whey protein provides the body with BCAAs to replenish depleted levels and start repairing and rebuilding lean muscle tissue.
- Whey protein is an excellent source of the essential amino acid, leucine. Leucine is important for athletes as it plays a key role in promoting muscle protein synthesis and muscle growth. Research has shown that individuals who exercise benefit from diets high in leucine and have more lean muscle tissue and less body fat compared to individuals whose diet contains lower levels of leucine [2]. Whey protein isolate has approximately 50% more leucine than soy protein isolate.

- Whey protein is a soluble, easy to digest protein and is efficiently absorbed into the body. It is often referred to as a "fast" protein for its ability to quickly provide nourishment to muscles.
- Whey protein helps athletes to maintain a healthy immune system by increasing the levels of glutathione in the body. Glutathione is an anti-oxidant required for a healthy immune system and exercise and resistance training may reduce glutathione levels. Whey protein helps keep athletes healthy and strong to perform their best.

Nutritional Value of Whey Proteins: Whey proteins are considered to have the highest nutritional values of all food proteins. They contain all the amino acids required by humans, in the right proportions. Whey proteins are rich in branched chain amino acids, components that provide energy for people undergoing intense or prolonged periods of exercise and help prevent loss of body mass and muscle. They are also readily digestible and completely bio-available. Whey proteins supply additional nutritional benefits, for example, α-lactalbumin, the second most abundant whey protein, has a high content of the amino acid tryptophan, a precursor of the vitamin niacin [10]. The health and nutritional value of the components of whey include (i) high quality nutritional source of amino acids; (ii) anti-microbial action; (iii) growth enhancement of beneficial gut microflora, such as bifidobacteria; (iv) immuno-enhancing properties; (v) control of specific diseases, including cancer; and (vi) antitoxin activity [5].

The composition and applications of different types of whey proteins are given in Table 1.

Functional Properties of Whey Proteins: Whey proteins bring a wide range of valuable functional properties as food ingredients (Table 2). They can modify some or all of the organoleptic, visual, hydration, surfactant, structural, textural and rheological properties of food, resulting in improved consumer acceptance of the food product. Whey proteins in their native state are highly soluble in food and beverage systems and are used for applications such as whipping/foaming. They act at oil/water interfaces to form and stabilize emulsions. In their undenatured form, whey proteins have the ability to form rigid, heat-induced irreversible gels that hold water, fat and provide structural support. In addition, they play an important role in controlling the texture of many food products and are used to modify the rheological properties of foods [47-48].

Table 1: Composition and applications of different types of whey protein (%) (Source: Dairy Council of California, 2004)

Product	Protein	Lactose	Milk fat	Applications
Whey powder	11-14.5%	63-75%	1-1.5%	Used in breads, bakery and snack items and dairy foods.
Whey protein concentrates (WPC)	34-89%	10-55%	2-10%	Used in protein beverages and bars, bakery and confectionary products, dairy foods and other nutritional food products.
Whey protein isolates (WPI)	90%	0.5%	0.5%	Used in protein supplementation products, protein beverages, protein bars, other nutritional food products
Hydrolyzed whey protein concentrate	>80%	<8%	<10% (varies with protein concentration)	Used in sports nutrition products
Hydrolyzed whey protein isolate	>90%	0.5-1%	0.5-1%	Highly digestible form containing easy to- digest peptides that reduce risk for allergic reaction in susceptible individuals. Commonly used in infant formulas and sports nutrition products.

Table 2: Typical functional properties of whey proteins in food systems [49]

Functional Property	Mode of action	Food System
Solubility	Dissolvable	Beverages
Water absorption	Water binding	Meat/ Bakery
Viscosity	Thickening	Soups/ gravy
Gelation	Structure forming	Meat/ fish
Emulsion properties	Emulsifying	Infant formula
Fat absorption	Binding free fat	Sausages
Foaming properties	Aeration	Whipped topping
Flavour binding	Binding/ release	Formulated foods
Mineral binding	adsorption	Nutritional foods

There Are Numerous Applications of Whey Protein:

In Weight Management: Whey protein can play an important role in weight management. Specific factors in whey protein are being investigated for their ability to promote weight loss by increasing satiety, influencing glucose homeostasis and maintaining lean body mass [2]. Adding whey proteins to the diet tremendously helps in weight management due to the following reasons:

- The body requires more energy to digest protein than other foods (thermic effect) and consequently more calories are burnt after a protein meal.
- Whey protein isolate is pure protein with little or no fat or carbohydrates. It is a perfect complement to any low carbohydrate or low glycemic index diet plan.
- Recent studies have highlighted the role of the essential amino acid leucine in improving body composition. High quality whey protein is rich in leucine to help to preserve lean muscle tissue while promoting fat loss. Whey protein contains more leucine than milk protein, egg protein and soy protein.
- Protein helps to stabilize blood glucose levels by slowing the absorption of glucose into the bloodstream. This in turn reduces hunger by lowering insulin levels and making it easier for the body to burn fat.
- Whey protein contains bioactive components that help to stimulate the release of two appetite-suppressing hormones: cholecystokinin (CCK) and glucagon-like peptide-1 (GLP-1). In support of this, a new study found that whey protein has a greater impact on satiety than casein, the other protein in milk [13].

Immunity Enhancement: The whey fraction of milk appears to contain a significant amount of immunoglobulins, approximately 10-15 percent of total whey proteins. An *in vitro* study demonstrated that 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 concluded that bovine milk IgG typically ranges between 0.6-0.9 mg/mL and is therefore likely to confer immunity that could be carried to humans [50]. Studies show raw milk from non-immunized cows contains specific antibodies to human rotavirus, as well as antibodies to bacteria such as *E. coli, Salmonella enteriditis, S. typhimurium* and *Shigella flexneri* [51]. The following immunoglobulins have been reported in whey proteins.

***β-Lactoglobulin*:** β-Lactoglobulin represents approximately half of the total protein in bovine whey, while human milk contains no β-lactoglobulin. Besides being a source of essential and branched chain amino acids, a retinol-binding protein has been identified within the beta-lactoglobulin structure. This protein, a carrier of small hydrophobic molecules including retinoic acid, has the potential to modulate lymphatic responses [52].

***α-Lactalbumin*:** α-Lactalbumin is one of the main proteins found in human and bovine milk. It comprises approximately 20-25% of whey proteins and contains a wide variety of amino acids, including a readily available supply of essential and branched chain amino acids. In another study α-lactalbumin in both the native and hydrolyzed state enhanced antibody response to systematic antigen stimulation [53]. The same group proved α -lactalbumin has a direct effect on B-lymphocyte function, as well as suppressing T cell-dependent and independent responses [54].

Whey proteins are unique in their ability to optimize a number of aspects of the immune system, primarily by boosting glutathione (GSH) levels in various tissues. GSH, the centerpiece of the body's antioxidant defense system, protects cells against free radical damage, pollution, toxins, infection and UV exposure. GSH levels are typically depressed in individuals with cancer [55], HIV, chronic fatigue syndrome and other immune-compromising conditions. GSH also decreases with age and may be partially responsible for diseases such as Alzheimer's disease, cataracts, Parkinson's disease and arteriosclerosis, e.g. the concentration of immunoglobulins in bovine milk is 0.6-1.0 g/kg [56].

Specific components in whey are thought to play a role in enhancing the immune system which include:

Cysteine - an amino acid found in high levels in whey proteins, is involved in the intracellular production of GSH [4].

Lactoferrin - has been shown to exhibit immune-modulating activity through both antimicrobial and antitoxin activity; it may also provide protection against viruses such as hepatitis, cytomegalovirus and influenza [57].

Immunoglobulins - may confer disease protection to infants through passive immunity and to adults by promoting the activity level of the immune system [56].

Branched chain amino acids (*BCAAs*) - are metabolized in the muscle to manufacture glutamine, a precursor to GSH and another important component of the immune system [58].

Thus, incorporating whey proteins into the diet may protect the health of not just those with a compromised immune system but those of all ages.

In Cardiovascular Health: Research has shown that whey protein may help against hypertension. Both human clinical and animal studies found that a hydrolyzed whey protein isolate assists in reducing the blood pressure of borderline hypertensive individuals [4].

Elevated cholesterol is another factor associated with heart disease and whey protein has been shown to reduce cholesterol in a number of animal and clinical studies [4]. Certain bioactive components in whey protein may be responsible for the cholesterol reduction however additional research is needed in this area.

Induces Cell Senescence: Research studies have shown that peptide from water buffalo cheese whey induces senescence cell death in human colon adeno-carcinoma cell line through ceramide secretion. Milk proteins are a source of bioactive peptides. Recent studies have indicated that protein-derived peptides released in buffalo cheese acid whey exert a cyto-modulatory effect in human epithelial colon cancer ($CaCo_2$) cells [59].

In Cancer: Some whey components possess anticancer properties. The first are the sulphur containing amino-acids (cysteine and methionine) that are found in high levels in whey protein. Cysteine and methionine are utilized in glutathione synthesis. Glutathione is a substrate for two classes of enzymes that catalyze detoxification compounds and bind mutagens and carcinogens, facilitating their elimination from the body. Lactoferrin's ability to bind iron is another benefit in the area of colon cancer. They induce apoptosis in tumour cells and so are useful adjunct in colon cancer therapy [60].

Cancer patients undergoing radiation or chemotherapy often have difficulty in meeting their daily nutritional requirements due to nausea and lack of appetite. This may lead to weight loss, muscle loss and protein calorie malnutrition. Whey protein is an excellent protein choice for cancer patients as it is very easy to digest and very gentle to the system. Whey protein may be added to a wide variety of foods and beverages to increase the protein content without affecting taste. Other authors concluded that the iron-binding capacity of whey may also contribute to anticancer potential, as iron may act as a mutagenic agent causing oxidative damage to tissues [61].

As with serious athletes, cancer patients often have reduced glutathione levels and a weakened immune system. Numerous studies have shown that whey protein, rich in the amino acid cysteine, provides an extra boost to the immune system by raising glutathione levels [13]. This may help reduce the risk of infection and improve the responsiveness of the immune system. Also research showed that women with the highest levels of plasma cysteine have a 56% reduction in the risk of breast cancer compared to individuals with the lowest levels of plasma cysteine [5].

Whey protein has been shown through animal and *in vitro* studies to inhibit the growth of several types of cancer tumors. It was found that feeding rats' whey protein resulted in their developing 50% fewer tumors than rats fed casein. The rats fed whey protein also developed fewer tumors than rats fed soy protein and the tumors took longer to develop.

Yoo *et al.* [62] demonstrated that lactoferrin has the ability to inhibit metastasis of primary tumors in mice with cancer. Bovine serum albumin (10-15 percent of total whey protein) has demonstrated inhibition of growth in human breast cancer cells *in vitro* [63].

Sphingomyelin, one of the most abundant whey derived sphingolipids, have the potential to inhibit colon cancer. Sphingomyelins also regulate growth factor receptors, such as transforming growth factor beta family (TGF-β) [64].

TGF-βs are a multifunctional family of growth factors that regulate cell growth in a variety of normal and tumour cells by suppressing proliferation, inducing differentiation and apoptosis. TGF-β passes out unaffected through the stomach and maintains bioactivity in colon by withstanding enzymatic proteolysis [11].

In Diabetes: Whey protein, a high quality, high biological value protein, is a good choice for diabetics who need to carefully managed food intake. Whey protein provides more value than equal amounts of lower quality proteins that are often higher in fat and cholesterol. In addition, whey protein helps to control blood glucose levels and has been shown to be beneficial for weight management, both of which are often a concern for type-2 diabetics [4].

Infant Nutrition: Whey protein contains many of the same components found in human breast milk and for this reason, is a key ingredient in a wide variety of infant formulas, including those for premature infants. Certain types of whey protein based infant formulas have also been shown to help to reduce crying in colicky infants [5].

While breast-feeding is preferred, infant formulas containing whey protein are the next best thing when breast-feeding is not an option. In addition, whey protein is an excellent protein choice for the expectant mother who needs increased amounts of protein [4]. Pregnancy can increase the body's protein needs by up to 33%.

In Healthy Ageing: Good nutrition and adequate amounts of high quality whey protein may help maintaining strong muscles during aging, especially when combined with an exercise and resistance training program [13].

A recent study in Europe compared whey protein to casein, the primary protein in milk. They found that older men who consumed whey protein showed greater protein synthesis, or growth, which helped to limit muscle loss over time [4].

Another benefit of whey protein for seniors is the ability to help prevent bone loss. A recent study conducted at Boston University showed that elderly individuals who consumed low levels of protein have a significant loss of bone density four years after the start of the study, especially in the hip and spine areas [5]. A nutritious diet including whey protein may help keep bones and muscles healthy and strong.

In Wound Healing: Protein and its amino acids are the building blocks that initiate the growth of new skin during the healing process. Inadequate amounts of protein or diets high in poor quality proteins, such as gelatin, may delay the healing process. Whey protein is a very high quality protein and is often the preferred choice for high protein products recommended by physicians following surgery or burn therapy [1].

Whey protein also contains components with protective anti-microbial properties, such as lactoferrin. In recent years companies have introduced mouthwashes and oral care products containing these protective whey protein components. The companies are taking advantage of the unique features of whey protein to create new products for diabetics and others sensitive to oral irritations [46].

CONCLUSION

Although previously whey was considered as a potent pollutant with high BOD but nowadays it is evolving into a most sought-after product because of the lactose, minerals and proteins as well as the functional properties that it imparts to food. Whey derived ingredients such as lactose, lactoferrin, lactoperoxidase, immunoglobulins, glycomacropeptide, transforming growth factors, sphingolipids and calcium can be used as concentrated bioactive whey ingredients for the promotion of intestinal health through the 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 probiotics.

To conclude, 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. Thus whey protein can serve as an attractive ecofriendly, cost effective bioceutical alternate to other nutraceuticals.

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