Role of Whey Protein in Nutrition, Health and Diseases: A Non Conventional Foodstuff with Amazing Nutraceutical Potential

Kriti Sharma[1] & Ekta Singh Chauhan[2*]
[1]Research Scholar, Department of Food Science and Nutrition, Banasthali Vidyapith, Rajasthan.
2Associate Professor, Department of Food Science and Nutrition, Banasthali Vidyapith, Rajasthan.

Received: May 27, 2018 Accepted: July 18, 2018

ABSTRACT *The food industry continually strives to offer new and innovative products to satisfy consumer needs. Consumer awareness and interest in nutritious, healthy foods has driven the research into healthful effects of whey and whey fractions. Evidence continues to accumulate that whey contains a variety of factors and compounds capable of improving health and preventing disease. In particular, recently discovered information in the areas of probiotics, prebiotics and viral virulence indicates that there is a good potential to produce healthy functional foods and cosmetics to reduce both infectious and chronic diseases. This brief review highlights some of the health-enhancing properties of whey and whey fractions, points to exciting areas of development for whey products and their role in clinical implications, preventing and attenuating diseases or augment conventional therapies, when delivered in amounts that exceeds dietary intakes.*

Keywords: *Whey, functional foods, nutrition, probiotics*

Introduction

Protein is the most satiating macronutrient and protein-rich diets are known to exert beneficial effects on body composition and metabolism [1, 2]. Whey (the liquid left after milk curdling) was deemed a waste by the dairy industry for decades. The effluent caused major disposal issues due to its high organic matter and resultant high biological oxygen demand [3]. Fortunately, the potential of whey as a resource is being recognized now. Whey has been quantified to contain 15–20 % of total milk proteins and that is too big an amount to let go [4]. With discovery of the high protein content, whey has consolidated its position in food sector. Now, whey protein is valued more than egg, casein and soy protein, for its high nutritional quality and fast absorption [5]. Whey protein is globular with main components as β-lactoglobulins (35–65 %) and α-lactalbulins (12– 25 %). The minor ingredients include immunoglobulins (8 %), serum albumins (5 %) and lactoferrin (1 %) [6]. Whey protein is a rich source of branched-chain amino acids (leucine, isoleucine, and valine), essential amino acids (cysteine) and peptides as well [7]. Leucine is abundant (50–75 % higher than other protein sources) and it plays key role in the regulation of skeletal muscle protein synthesis [8].
Whey protein is rich in sulfhydryl amino acid cysteine, a precursor of glutathione, the non-enzymatic thiol antioxidant obtained from diet [9]. Glutathione plays key role in reducing oxidative stress, regulating cellular processes [10]. Lactoperoxidase enzymes, glycomacropeptides (12%) and lactose are other important components of whey [11]. Glycomacropeptide is a casein-derived whey peptide, released by rennet during the manufacture of cheese [12]. This peptide has many proven benefits such as satiating effect and phenylketonuria management potential. Based on their concentration and attributes, whey proteins are marketed in various forms such as whey protein concentrate (has fat and lactose along with proteins (29–89%), whey protein isolate (90% protein) and whey protein hydrolysate (partially digested for ease of metabolism and hypoallergenicity) [13]. A broad range of functionality has been assigned to whey protein and its derivatives such as reduction of oxidative stress, promotion of muscle growth and lean body mass, appetite suppression, hypoglycemia, cardiovascular risk mitigation, phenylketonuria management and protection from ultraviolet (UV) radiation [14]. Further, its role in food processing such as emulsifier, texturizer, encapsulating agent, delivery vehicle, antimicrobial film and fat-replacer are being recognized [15].

Nutritional Characteristics of Whey Proteins

Whey proteins are known as complete proteins because of the availability of all essential amino acids. Whey is dilute liquid containing lactose, proteins, minerals and traces of fat and contains approximately 6% total solids in which 70% is lactose and about 0.7% is whey proteins [16].

Table 1 Protein and other Bioactive Components of Whey Proteins [17]

	Whey proteins
Main fractions	β-lactoglobulin α- lactalbumin Bovine serum Albumin Immunoglobulins Glycomacropeptide
Minor fractions	Lactoferrin Lactoperoxidase Lysosime

Amino Acid Content

Whey proteins have all the essential amino acids and in higher concentrations as compared to other various proteins sources. Whey proteins have high concentration of branched-chain amino acids (BCAAs) leucine, isoleucine and **v**aline **[**18].

Table 2 Concentration of Essential Amino Acid in reference Proteins, whole egg, milk protein, whey proteins, β-Lactoglobulin (β-lg) and α-Lactalbumin (α-la) [19]

Amino acid	Reference proteins	Egg protein	Milk protein	Whey proteins	β-LG	α-LA
Tryptophan	1.0	1.5	1.4	2.1	2.2	6.6
Phenylalanine + Tyrosine	6.0	10.5	10.5	7.3	7.3	9.6
Leucine	7.0	9.1	10.4	11.1	15.3	11.6
Isoleucine	4.0	6.7	6.4	6.8	6.7	6.8
Threonine	4.0	5.1	5.1	8.0	5.4	5.5
Methionine +Cystine	3.5	5.9	3.6	4.8	5.6	6.9
Lysine	5.5	6.9	8.3	9.9	11.7	11.4
Valine	5.0	7.5	6.8	6.8	5.9	4.8
Total	36.0	53.2	52.5	56.8	60.1	63.2

Content in g/100g of protein

Carbohydrates

In the form of CHO, lactose is present in whey protein concentrates. Lactose is a disaccharide that is hydrolysed by enzyme β-galactosidase into glucose and galactose molecules. As the concentration of protein in whey, protein concentrates increase the lactose concentrates range from 0.1% to 46%. The slow hydrolysis of lactose by the body during digestion generates a prolonged energy supply. Lactose stimulates the growth of acid forming lactobacilli in the intestinal tract. *Lactobacilli* help fight intestinal disorder and that lactose could be used in diet therapy for ailing infants. Lactose also promotes absorption of magnesium and zinc ions, which even in trace amount helps in better diarrhoeal management [20]**.** It may also improve the absorption of magnesium and zinc Lactose has low glycemic index and promotes healthy intestinal flora [21].

Vitamins and Minerals

The water soluble vitamins in milk remains in the serum and are collected with the whey. The following vitamins and minerals are present in WPCs.

Table 3 Vitamins and Minerals in WPCs [22, 23]

Vitamins	Amount (mg/100g)	Minerals	Amount(g/100g)
Thiamine	0.4	Calcium	0.26
Riboflavin	3.1		
Vitamin B_6	0.33	Phosphorus	0.33
Vitamin B_{12}	0.02		
Nicotinic acid	1.2	Potassium	1.0
Panthothenic acid	4.6		
Folic acid	0.6	Sodium	0.29
Biotin	0.04		

Bioactive Components of Whey Proteins

β-Lactoglobulin

β-Lactoglobulin is approximately 50% of the total whey proteins content. This protein has numerous binding sites for minerals, fat soluble vitamins and lipids and acts as transport protein for desirable lipophilic compounds such as tocopherol and vitamin A [24]. [25] found that modification of β-Lactoglobulin results in products that have strong antiviral activity against human immunodeficiency virus types 1 and 2.

α-Lactalbumin

α-Lactalbumin is one of the main protein in whey that can enhance immunity in animals. This protein possesses an excellent amino acid profile, which is rich in lysine, leucine, theronine, tryptophan and cystein. Lactalbumin is proved to be 2-4 times better than egg protein and five times better than casein with regards to immunoenhancement [26]. It plays an important role in cognition α-Lactalbumin increase the ratio of plasma tryptophan to the sum of other large neutral amino acid and it may increase brain serotonergic activity level and improves cognitive performance in stress vulnerable subjects [27].

Lactoferrin

Lactoferrin is a glycoprotein fraction that plays an important role in iron binding that occurs in cow milk; at level of 0.2 mg/ml. Lactoferrin is involved in the transport of iron in the body. Lactoferrin is first detected in bovine milk and subsequently in human milk. Lactoferrin is present in large quantities in mammalians secretions such as milk, tears, saliva and seminal fluids [28]. Lactoferrin does not affect the taste, smell and appearance of meat and foods. The 1% (w/v) solution of the lactoferrin was found to be effective for increasing the shelf life and reducing the microbial contamination of the raw milk, meat product and vegetables. The iron binding property of lactoferrin presents the oxidation of the unsaturated fatty acids, thereby reducing the changes in the rancidity of the foods [29]. Lactoferrin potentiates effect of antibiotics and antifungal agents [30].

Lactoperoxidase

Lactoperoxidase is a natural enzyme of peroxidase family, present in the milk. Bovine milk contains about 0.03g/l of lactoperoxidase. The level of lactoperoxidase activity in human milk is about 20 times lower than the bovine milk [31]**.** Lactoperoxidase inactivates or kills a broad spectrum of microorganism through an enzymatic reaction. Enzymatic reaction involves two cofactors, hydrogen peroxide and thiocyanate ions which together with lactoperoxidase constitute the Lactoperoxidase system (LP-S). The activation of enzymes results in the formulation of hypothiocyanite, which is responsible for antimicrobial action [32].

Glycomacropeptide

Glycomacropeptide (GMP), the glycosylated portion of caseinomacropeptide (CMP) is present in sweet whey formed following the cleavage and casein precipitation by rennin; it is absent in acid whey. GMP or peptides have many biological and physiological properties like reduction in gastric secretion, dental plaque and dental caries inhibitior, product for control of phenylketunoria, inhibitors of platelets aggregation and others **[**33].

Nutraceutical Applications of Whey Proteins

Whey protein in its various derivative forms (concentrates, isolates and hydrolysates) has been verified to encompass diverse physiological properties. The sections below embody the recent key studies and their profound results. Figure 1 illustrates the whey protein components and the validated health benefits.

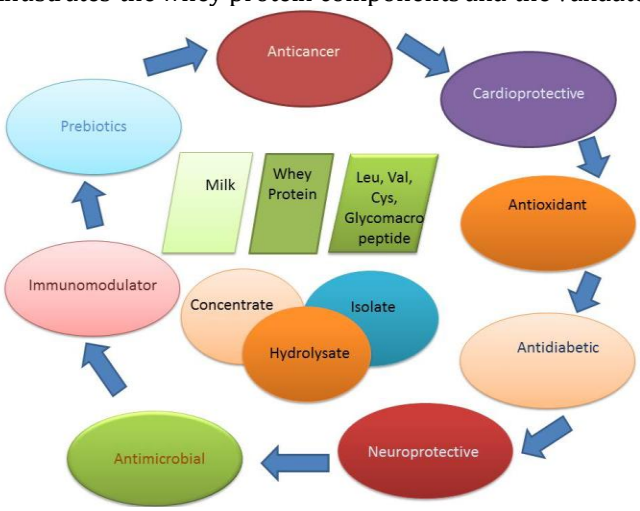

Figure 1 Constituent and Applications of Whey Proteins

Antioxidant, anti-inflammation and hepatoprotection

Inflammatory or oxidative stress begets cystic fibrosis, pneumonia, diabetes, cancer, atherosclerosis, myocardial infarction, aging and a host of other degenerative diseases [34]. As precursor of the antioxidant glutathione, whey protein holds eminese in nullifying the adverse effects of the stressors. Hyperbaric treatment of whey protein accelerated the release of bioactive peptides, raised intracellular glutathione level and abated the *in vitro* generation of interleukin IL-8 (this cytokine is believed to mediate pathogenesis of respiratory tract diseases) [35]. It was observed that one month dietary supplementation with pressurized whey (20 g/day) in cystic fibrosis patients significantly reduced serum C-reactive protein (CRP level is the metric of inflammation in body) level [36]. Alcalase hydrolysed whey protein was screened for anti-oxidative peptides. Two fragments, P4 and P4c (a pentapeptide Val-HisLeu-Lys-Pro) demonstrated significant protection of human lung fibroblast MRC-5 cells from H2O2 abuse [37]. The anti-inflammatory effect of a new enteral diet (tube feeding) MHN-02, rich in antioxidants and whey peptide was evaluated in rats [38].

It was suggested that supplementation of enteral diets enriched with whey peptide and antioxidants might protect against hepatitis. The evidence supporting the role of whey protein in augmenting glutathione synthesis in neurons and alleviating neurodegenerative maladies was reviewed [39]. The feasibility of using pressurized whey protein for lowering the risk of pulmonary infection by this pathogen was investigated [40]. Decreased level of inflammatory response, oxidative stress, and lung damage in the pressurized whey-fed mice was observed. The *in vitro* free radical scavenging activity of sheep whey protein was determined. Results showed that the protein efficiently scavenged 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid (ABTS) and hydroxyl radicals, increasing glutathione level [41].

Anticancer

Several studies have suggested that whey protein may confer benefits on cancer patients. Further it has been demonstrated that the hydrolysis of the protein might improve the anticancer efficacy. Rat with colon cancer, when fed with whey protein hydrolysate developed significantly less macroscopic and microscopic tumours compared to the group, fed with untreated whey protein [42]. Anticancer effect of whey protein was investigated using melanoma B16F10 cells as the model. Caspase-3 expression increased significantly in the whey protein isolate-containing media [43]. A 48-year-old Caucasian female with recurrent cervical cancer was administered with whey protein (10g thrice daily) and a weekly intramuscular injection of testosterone enanthate before and during the standard-of-care (SOC) chemotherapy. As a result of the combination therapy, improvement of lean body mass, physical activity, and overall quality of life was observed [44]. The protective effect of whey protein hydrolysate against oxidative damage on rat pheochromocytoma PC12 cells was studied. At a dose of 100-400μg hydrolysate/ml, the viable cells increased by 20–30 % compared to those incubated in H_2O_2, suggesting antioxidant potential of the former [45].

Immunomodulation

Whey protein concentrates enhance innate mucosal immunity during early life and have a protective role in some immune disorders [46]. The effect of whey protein concentrate on blood parameters, plasma cytokine profiles, immune cell proliferation and migration was investigated in mice model [47]. It was observed that *in vitro* migration of B cells, T cells and dendritic cells towards the two cytokines significantly increased in whey protein-treated group compared to the control. Psoriasis is chronic autoimmune disease causing thick skin, dry scales and red patches. It was investigated whether bioactive whey protein isolate can increase glutathione levels and resultantly combat the severity of systemic inflammation due to psoriasis. The intake of 20 g/day whey protein isolate improved the conditions of the patients [48].

Cardio-protective and hypotensive

Whey protein intake reduces cardiovascular disease (ischemic stroke) risk, but precise role of their peptides in regulation of vascular endothelial function has not been adequately investigated. Whey-derived extract (NOP-47) ingestion increased impaired brachial artery flow-mediated dilation (improved endothelial function). Postprandial plasma amino acids level increased. The improvement in arterial dilation was found to be independent of the circulating vasoactive compounds such as nitric oxide, prostacyclin and endothelium-derived hyperpolarizing factor. It was inferred that cardiovascular risk might be alleviated using rapid-absorbable extracts derived from whey [49]. The effects of whey protein supplementation and resistance training on antioxidant status and cardiovascular risk factors were examined in overweight young men [50].

Gut function and prebiotic

Gut dysfunction (delayed gastric emptying, abnormal motility patterns, and weak intestinal barrier) is a serious issue in critically-ill patients. It was suggested that whey protein fortification might impart inflammation and improve tolerance towards enteral nutrition [51]. In order to exert its therapeutic property, lactic acid bacteria and yeast need to be viable. Ensuring their high survival rate in the inhospitable gastrointestinal environment poses a critical challenge. Further, storage period tends to inhibit the probiotic strains. Whey protein gels have shown efficacy in protecting the microbes against the adverse conditions [52]. The role of whey protein in conferring stability to probiotics and prebiotics was investigated. Lactobacillus acidophilus and Bifidobacterium were viable in yogurt beverages stabilized with high-methoxyl pectin and whey protein concentrates [53].

Obesity Management

Dietary adjustment has been shown to fight obesity and in this regard, whey protein is considered helpful. A 1-week trial with mice fed ad libitum with high-fat diet containing generous amount of whey protein, or supplemented with leucine was performed. It was inferred that the ameliorating effects of the protein-rich diet on metabolic disorders are precisely due to modulation of satiety mediated by liver lipogenesis attenuation [54]. A 12-week study showed that whey protein concentrate preloads conducted 30 min prior to the ad libitum main meal exerts stronger beneficial effects than that of soy protein isolate on appetite, calorie intake, anthropometry (body mass index and waist circumference) and body composition (body fat mass and lean muscle) of obese men [55].

Antidiabetic

Diabetes remains a major public health issue of epidemic stature that begets many complications such as loss of vision, angiopathy and reduced blood flow leading to tissue hypoxia and ulcers with difficult healing [56]. Type-2 diabetes is treated both by controlled diet and hypoglycaemic drugs. Whey protein have been demonstrated to reduce serum glucose level in healthy individuals, maintain muscle mass, boost the release of satiety hormones (cholecystokinin, leptin, and glucagon like-peptide 1 (GLP-1) and lower the secretion of hunger hormone ghrelin [14]. It was shown that cysteine; a key component of whey protein could be used as an ancillary therapy in glycaemia and vascular inflammation control in the diabetics [57]. A hydrolyzed whey protein-based supplement was fed to rats for 30 days. It resulted in a higher leucine level followed by increased insulin level [58].

Conclusion

The findings above testify that whey is no more a mere by-product of dairy processing. Increasing number of nutritionists is endorsing whey protein as an excellent nutrient. An array of whey protein-enriched formula can be prepared for target group such as infants, cardiac-risk group and diabetics. Whey protein is proving to be an immune-nutrient and its dietary intervention to tackle cancer could be a promising area of research.

References

1. Bertenshaw EJ, Lluch A, Yeomans MR (2008) Satiating effects of protein but not carbohydrate consumed in a between-meal beverage context. Physiol Behav 93:427–436.
2. Chou CJ, Affolter M, Kussmann M (2012) A nutrigenomics view of protein intake: macronutrient, bioactive peptides, and protein turnover. Prog Mol Biol Transl Sci 108:51–74.
3. Ahn WS, Park SJ, Lee SY (2000) Production of Poly(3-hydroxybutyrate) by fed-batch culture of recombinant Escherichia coli with a highly concentrated whey solution. Appl Environ Microbiol 66:3624–3627
4. Yalçin AS (2006) Emerging therapeutic potential of whey proteins and peptides. Curr Pharm Des 12:1637–1643
5. Sindayikengera S, Xia W (2006) Nutritional evaluation of caseins and whey proteins and their hydrolysates from protamex. J Zhejiang Univ Sci B 7:90–98.
6. Smithers GW, Ballard FJ, Copeland AD, et al (1996) New opportunities from the isolation and utilization of whey proteins. J Dairy Sci 79: 1454–1459
7. Hulmi JJ, Lockwood CM, Stout JR (2010) Effect of protein/essential amino acids and resistance training on skeletal muscle hypertrophy: a case for whey protein. Nutr Metab (Lond) 7:51.
8. Chen W-C, Huang W-C, Chiu C-C, et al (2014) Whey protein improves exercise performance and biochemical profiles in trained mice. Med Sci Sports Exerc 46:1517–1524.
9. Bell SJ (2000) Whey protein concentrates with and without immunoglobulins: a review. J Med Food 3:1–13.
10. Trachootham D, Lu W, Ogasawara MA, et al (2008) Redox regulation of cell survival. Antioxid Redox Signal 10:1343–1374.

11. Abdel-Salam AM, Effat LK (2010) Preparation and evaluation of a novel therapeutic dairy-based drink for phenylketonuria. N Am J Med Sci 2:66–70.
12. Neelima SR, Rajput YS, Mann B (2013) Chemical and functional properties of glycomacropeptide (GMP) and its role in the detection of cheese whey adulteration in milk: a review. Dairy Sci Technol 93: 21–43.
13. Barth CA, Behnke U (1997) Nutritional physiology of whey and whey components. Nahrung 41:2–12
14. Sousa GTD, Lira FS, Rosa JC, et al (2012) Dietary whey protein lessens several risk factors for metabolic diseases: a review. Lipids Health Dis 11:67
15. Fernández-Pan I, Royo M, Ignacio Maté J (2012) Antimicrobial activity of whey protein isolate edible films with essential oils against food spoilers and foodborne pathogens. J Food Sci 77:M383–M390.
16. Zall RR. Sources and composition of whey and permeates. In J.G Zadow (Ed) whey and lactose processing. Barking: Elsevier Science Publisher 1992; 1-72.
17. Singh S, Ladkani BG, Kumar A, Mathur MN. Whey utilization for the manufacture of ready to serve soups. Indian J Dairy science 1994; 47(6): 501-504.
18. Devraj HC, Vankateshaiah BV, Sharanagouda B. Whey Proteins-A potent Nutraceutical. Indian Dairyman 2006; 58(6):35-39.
19. Renner E. Milk and dairy products in human nutrition. Volkswirtschaftticer Verlag, munich 1983.
20. Ziegler EE, Fomon SJ. Lactose enhances mineral absorption in infancy. J Pediar Gastroenterol 1983; 2:288-294.
21. Lifran EV, Hourigan JA, Sleigh RW, Johnson RL. New whey for lactose. Food Australia, 2000; 52(4): 120-125.
22. Delaney RAM. Composite on, properties and use of whey proteins concentrate. J Soc Dairy Tech 1976; 29: 91-101.
23. Renner E, Salam ABD. Application of ultra filtration of dairy industry. El in: whey and lactose processing Zadow JG (Ed). London New York, Elsevier Applied Science, 1991: 439.
24. Perez MD, Calvo M. Interaction of beta lactoglobulin with retinol and fatty acids and its role as a possible biological function for this protein- a review. J Dairy Sci 1995; 78 (5): 978-988.
25. Swart PJ, Kuipers ME, Smit C, Pauwels RDe, Bethune MPDe, CleroqE, Meijer DK, HuismanJG.Antiviral effects of milk proteins; acylation results in polyanionic compounds with portent activity against human immunodeficiency virus types1 and 2 in vitro. Aids Res. Human Retroviruses 1996; 12:769-775.
26. Bounous G, Kongshaven P, Gold P. The immune enhancing property of dietary whey protein concentrates. Clin Invest Med 1988; 11: 271-278.
27. Markus R, Berend O, Edward HF, De H. Whey protein rich in α-Lactalbumin increase the ratio of plasma tryptophan to the sum of the other large neutral amino acids and improves cognitive performance in stress-vulnerable subjects. Am J Clin Nut 2002; 75:1051-1056.
28. Sanchez L, Calvo M, Brock JH. Biological role of lactoferrin. Archives of disease in childhood 1992; 67:657-661.
29. Devtkal S, Mandiratta SK, Kaur S. Therapeutic and commercial application of lactoferrin. Livestock International 2003; 7:7-9.
30. Wakabayashi RP. Cooperative anti-candida effects of lactoferrin or its peptides in combinations with azole antifungal agents. Microbiology and Immunology 1996; 40(11):821-825.
31. Losendahl KJ, Wang H, Aslam HZS, Hurley WC. Antimicrobial factors in milk-a review. Bo Ekstrand Food Biotechnology1989; 3(2): 105-126.
32. Wit D, Van JN, Hooijdonk ACM. Structure functions and application of lactperoxidase in natural antimicrobial systems. Netherlands Milk and Dairy J 1996; 50: 227-244.
33. Salam EL, Shibiny ELS, Buchheim W. Characteristics and potential uses of the casein macro peptide. Int Dairy J 1996; 6(4):327-341.
34. Essick EE, Sam F (2010) Oxidative stress and autophagy in cardiac disease, neurological disorders, aging and cancer. Oxidative Med Cell Longev 3:168–177.
35. Piccolomini AF, Iskandar MM, Lands LC, Kubow S (2012) High hydrostatic pressure pre-treatment of whey proteins enhances whey protein hydrolysate inhibition of oxidative stress and IL-8 secretion in intestinal epithelial cells. Food Nutr Res.
36. Lands LC, Iskandar M, Beaudoin N, et al (2010) Dietary supplementation with pressurized whey in patients with cystic fibrosis. J Med Food 13:77–82.
37. Kong B, Peng X, Xiong YL, Zhao X (2012) Protection of lung fibroblast MRC-5 cells against hydrogen peroxide-induced oxidative damage by 0.1–2.8 kDa antioxidative peptides isolated from whey protein hydrolysate. Food Chem 135:540–547.
38. Takayanagi T, Sasaki H, Kawashima A, et al (2011) A new enteral diet, MHN-02, which contains abundant antioxidants and whey peptide, protects against carbon tetrachloride-induced hepatitis. JPEN J Parenter Enteral Nutr 35:516–522.
39. Ross EK, Gray JJ, Winter AN, Linseman DA (2012) Immunocal® and preservation of glutathione as a novel neuroprotective strategy for degenerative disorders of the nervous system. Recent Pat CNS Drug Discov 7:230–235.
40. Kishta OA, Iskandar M, Dauletbaev N, et al (2013) Pressurized whey protein can limit bacterial burden and protein oxidation in Pseudomonas aeruginosa lung infection. Nutrition 29:918–924.

41. Kerasioti E, Stagos D, Priftis A, et al (2014) Antioxidant effects of whey protein on muscle C2C12 cells. Food Chem 155:271–278.
42. Attaallah W, Yilmaz AM, Erdoğan N, et al (2012) Whey protein versus whey protein hydrolyzate for the protection of azoxymethane and dextran sodium sulfate induced colonic tumors in rats. Pathol Oncol Res 18:817–822.
43. Castro GA, Maria DA, Bouhallab S, Sgarbieri VC (2009) In vitro impact of a whey protein isolate (WPI) and collagen hydrolysates (CHs) on B16F10 melanoma cells proliferation. J Dermatol Sci 56:51–57.
44. Dillon EL, Basra G, Horstman AM, et al (2012) Cancer cachexia and anabolic interventions: a case report. J Cachex Sarcopenia Muscle 3: 253–263.
45. Zhang Q-X, Ling Y-F, Sun Z, et al (2012) Protective effect of whey protein hydrolysates against hydrogen peroxide-induced oxidative stress on PC12 cells. Biotechnol Lett 34:2001–2006.
46. Perez-Cano FJ, Marín-Gallén S, Castell M, et al (2007) Bovine whey protein concentrate supplementation modulates maturation of immune system in suckling rats. Br J Nutr 98(Suppl 1):S80–S84.
47. Badr G, Ebaid H, Mohany M, Abuelsaad AS (2012b) Modulation of immune cell proliferation and chemotaxis towards CC chemokine ligand (CCL)-21 and CXC chemokine ligand (CXCL)-12 in undenatured whey protein-treated mice. J Nutr Biochem 23:1640– 1646.
48. Prussick R, Prussick L, Gutman J (2013) Psoriasis improvement in patients using glutathione-enhancing, nondenatured whey protein isolate: a pilot study. J Clin Aesthet Dermatol 6:23–26.
49. Ballard KD, Kupchak BR, Volk BM, et al (2013) Acute effects of ingestion of a novel whey-derived extract on vascular endothelial function in overweight, middle-aged men and women. Br J Nutr 109: 882–893.
50. Sheikholeslami Vatani D, Ahmadi Kani Golzar F (2012) Changes in antioxidant status and cardiovascular risk factors of overweight young men after six weeks supplementation of whey protein isolate and resistance training. Appetite 59:673–678.
51. Abrahão V (2012) Nourishing the dysfunctional gut and whey protein. Curr Opin Clin Nutr Metab Care 15:480–484.
52. Gerez CL, Font de Valdez G, Gigante ML, Grosso CRF (2012) Whey protein coating bead improves the survival of the probiotic Lactobacillus rhamnosus CRL 1505 to low pH. Lett Appl Microbiol 54:552–556.
53. Walsh H, Cheng J, Guo M (2014) Effects of carbonation on probiotic survivability, physicochemical, and sensory properties of milkbased symbiotic beverages. J Food Sci 79:M604–M613.
54. Freudenberg A, Petzke KJ, Klaus S (2013) Dietary L-leucine and Lalanine supplementation have similar acute effects in the prevention of high-fat diet-induced obesity. Amino Acids 44:519–528.
55. Tahavorgar A, Vafa M, Shidfar F, et al (2014) Whey protein preloads are more beneficial than soy protein preloads in regulating appetite, calorie intake, anthropometry, and body composition of overweight and obese men. Nutr Res.
56. Casqueiro J, Casqueiro J, Alves C (2012) Infections in patients with diabetes mellitus: a review of pathogenesis. Indian J Endocrinol Metab 16(Suppl 1):S27–S36.
57. Jain SK (2012) L-cysteine supplementation as an adjuvant therapy for type-2 diabetes. Can J Physiol Pharmacol 90:1061–1064.
58. Toedebusch RG, Childs TE, Hamilton SR, et al (2012) Postprandial leucine and insulin responses and toxicological effects of a novel whey protein hydrolysate-based supplement in rats. J Int Soc Sports Nutr 9:24.