



WHEY PROTEINS: HEALTH BENEFITS AND FOOD APPLICATIONS

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between all authors. Authors HJ, FA and EH designed the study and wrote the protocol. Authors FA and EH anchored the field study. Authors SAH and JM managed the literature searches and produced the initial draft. All authors read and approved the final manuscript.

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ABSTRACT

The aim of the present study was to review the effects of whey protein consumption on health and its application in food industry. By surfing through some authentic websites such as PubMed, Science Direct and Google Scholar, the related articles about the effect of whey protein on different diseases were found which all were human and animal based, although the human studies are greatly highlighted. Whey protein is one of the ingredients of milk which is considered as a useful food sources. Milk contains valuable protein sources including whey protein and casein. According to daily increase in prevalence of chronic diseases in the world, finding a suitable nutrient for lessening effects of such disease can be a great help for the community health. Moreover, milk is a valuable nutrient which is available everywhere and people can have it in their daily diet. Therefore, whey protein can be used in daily diet as a healthy and valuable food supplement by individuals. Today, excessive struggles are being made to find out new whey protein applications. This paper offers a holistic view that would guide a reader to the beneficial effects of whey protein consumption on health and its numerous utilization in food products.

Keywords: Milk; whey protein; casein; health; chronic diseases.

1. INTRODUCTION

Whey protein is one of the ingredients of milk which is considered as a useful nutrient [1]. This protein was identified about 3000 years ago. At the beginning of the 20th century, although some rules and limitations were set for reaching to this nutrient, at the same time many investigations were carried out to identify this protein. At the beginning of the 21st century,

investigations on whey protein biologic value showed the high biological and nutritional value for this protein [2-4]. Milk has two valuable protein sources: whey protein and casein [5]. The percentage of these proteins is different between human milk and cow milk. Cow milk contains about 80% casein and 20% whey protein whereas human milk has 60% whey protein and 40% casein [6,7]. Whey protein has some

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exclusive characteristics which separates it from other protein sources (Table 1). This can be referred to the high speed of digestion [8-11], the existence of alpha-lactalbumin, beta-lactalbumin, a huge amount of branched amino acids and glutamine in it in comparison with other protein sources [12-14]. Also, whey protein is soluble component of milk and rich in amino acids, minerals, vitamins, lactose [15] and glycomacropeptides (GMP) [16,17]. whey protein due to having adequate amounts of lysine can be used as a supplement for herbal proteins especially in cereals [18] Whey protein contains lactoferrin and lactoperoxidase [19]. The most important functional characteristics of whey protein is that it can solve in a wide range of pH [20,21]. Since whey protein has unique characteristics, it is used widely in the food industry to preparation vary types of cheeses and industrial breads [22,23]. Studies have shown that whey protein plays an important role in improving public health and body strength [24-26]. Also, there have been so many studies about the beneficial effects of whey protein on human's health and prevention of metabolic disease which shows positive results [27-29] (Table 2). Some studies suggest that whey protein may play a role in decreasing the risk of asthma, allergies and its symptoms in the patients by increasing production of Tcell [30,31]. Kishta and his colleagues [32] also stated that whey protein has a role in the prevention and recovery of bacterial respiratory infections. According to some studies, whey protein has a positive impact on fatty liver [33] and colitis [34] and Prevents DNA against damage [35,36]. Moreover, consuming whey protein has a direct effect on increasing the antioxidant activity of body [37,38], the muscular physical ability [39-41], decreasing blood sugar after meal [27,42-48], preventing from some cancers [37] and respiratory diseases [30,32]. Therefore, according to the previously mentioned advantages from different sources for whey protein, the goal of the present study is to investigate the effects of consuming this protein on health.

2. METHODS

By using key words such as whey protein, milk and whey and surfing through some authentic websites such as pub med, Science direct and Google scholar, the related articles were found which all were human and animal based, although the human studies are greatly highlighted.

2.1 The Effect of Whey Protein Consumption on Diabetes Type 2

It has been shown that milk protein stimulates insulin secretion much more than any other protein sources [49]. It has been also found that the consumption of

whey protein can reduce blood sugar after a meal, which could have a protective effect against type 2 diabetes [50]. These effects in whey protein are attributed to its content [42,43,51]. In several other studies, it has been confirmed that consumption of whey protein can increase the insulin secretion after a meal [27,48]. Mortensen and his colleagues studies [28] (Table 2) on 12 patients with type 2 diabetes have showed that whey protein isolate and whey protein Hydrolysate can strengthen insulin response after a meal. As mentioned, the whey protein contains significant amounts of amino acids and polypeptides with high biological activity. Upon consumption of whey protein, these peptides after entering to the digestive system could stimulate the secretion of hormones of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) especially from the colon wall. These two hormones also by stimulating pancreas beta cells could increase insulin secretion and reduces blood sugar in diabetic patient [52,53] (Table 2). Whey protein not only can cause stimulating insulin secretion [54] but also, according to Morato, et al's. Study, due to having a high levels of branched amino acids especially Isoleucine which interferes in producing GLUT-4 (which is the transmitter of glucose from plasma membrane of muscles) can play an important role in decreasing the insulin resistance in type 2 diabetic patients [55]. Frid, et al. [27] also conducted a survey on the consuming of whey protein by type 2 diabetic patients and suggested that consuming whey protein before each meal with high amount of carbohydrate intensify the insulin response and decrease their level of blood sugar (Table 2). One other mechanism to increase the secretion of insulin after consuming whey protein is decreasing the liver filtration of insulin [48]. Findings showed that consuming 20 gr of whey protein in each meal decreased the level of blood sugar and increased the level of insulin which could help diabetic patients to control their disease [44]. Decrease in the blood sugar and increase in the level of insulin after consuming whey protein have been observed in both healthy people and people with type 2 diabetes [27,56]. Shertzer, et al. [52] also mentioned that the supplement of whey protein isolate can decrease the possibility of affliction to fatty liver and type 2 diabetes. The literature review suggests that components of whey protein could reduce blood sugar after a meal and therefore be effective in controlling and preventing diabetes, by affecting hormones involved in insulin secretion [27,48,50].

2.2 The Effect of Whey Protein Consumption on Lipid Profile and Preventing Obesity

Consumption of whey protein reduces blood fat level in those who suffer from overweight and obesity [29].

New clinical intervention studies indicated that whey protein increases fat disposal during weight loss diets through unknown mechanisms [57,58]. Some studies suggest that this protein reduces triglyceride [59] and cholesterol [60,61] levels due to having bioactive components such as Lactalbumine, angiotensin conversion enzyme inhibitor and branched amino acids. Royle et al. [62] in their study indicated that consumption of GMP & WPI (whey protein isolate) may lead to weight loss and changes body composition in male mice. Salter et al stated that consumption of whey protein by Human Immunodeficiency Virus (HIV) patients does not lead to their weight gaining [53]. The known mechanism in this regard refers to calcium intake. Studies have shown that high levels of calcium intake causes limiting the levels of parathyroid hormone, 1.25 dihydroxy vitamin D and can prevent the obesity by discouraging the body from fat storing [63-65]. In another study it was demonstrated that whey protein supplements may lead to triglyceride levels in diabetes mellitus patients [66], also Pal et al. [67] (Table 2) confirmed similar results for postmenopausal women suffering from overweight

and obesity. According to some researches the role of whey protein supplement in controlling glycemia is attributed to stimulation of Incretin hormone, which itself causes insulin release [27,28,68,69]. Coker et al. [70] studied on 12 elderly persons and indicated that whey supplement together with essential amino acids reduce fat accumulation in tissues and prevent adverse effects resulting from obesity [71]. It is believed that whey protein compared to other protein sources such as gluten and casein has more contribution in reducing blood fat after meal [66,67]. Jensen et al. [72] on their study on 11 non- diabetic obese persons demonstrated that whey protein hydrolysate (WPH) may reduce non-esterified free fatty acids after meal. Also whey protein may stimulate skeletal muscles for consuming the fat as main fuel in long term [73]. However, we cannot accept definitely the impact of this protein in weight loss and reduction of body fats [68]. In a clinical trial study which was conducted by Bortolotti et al. [74] (Table 2), 11 obese women who treated with 60 gr/d whey protein supplement for duration of 4 weeks were examined. These researchers found that whey protein supplement resulted in a 20% reduction in liver fat reserves as

Table 1. Biological functions and concentrations of the whey proteins in cow and human milk ([115-122])*

Whey components	Constituents whey protein		Benefits/Functions
	Cow milk	Human milk	
Total whey protein	5.5-7.0 (g/l)	6.2-8.3 (g/l)	
Casein/Whey ratio	4.7	0.4-0.5	
Beta-lactoglobulin	3.2-3.3	0	Source of essential and branched chain amino acids, Retinol and fatty acid binding; possible antioxidant.
Alpha-lactalbumin	1.2-1.3	1.9-3.4	Source of essential and branched chain amino acids, lactose production, calcium transport, immunomodulator; anticarcinogen.
Immunoglobulins	0.5-1.0	0.96-1.3	Pathogen binding inhibition (chelates iron), anti-microbial, activation of phagocytosis, anti-inflammatory, response to allergens.
Serum albumin	0.3-0.4	0.4-0.5	Antioxidant, growth inhibition effect on human breast cancer cells, opioid agonist.
Lactoferrin	0.02-0.1	1.5-2.0	Antioxidant, antibacterial, anticarcinogen, antiviral, antifungal, promotes growth of beneficial bacteria, together with beta-lactoglobulin and alpha-lactalbumin suppress tumor development.
Lysozyme	trace	0.1-0.89	Antimicrobial, synergy actions with immunoglobulins and lactoferrin.
Others (lactoperoxidase, transferrin)	0.8	1.1	Antibacterial and antioxidant.
Proteose-peptone	1.2	-	Structural protein.
Glycomacropeptide	1.2	-	Antiviral, bifidogen.

* Adapted from: Laursen, [119]; Marshall, [1]; Korhonen and Pihlanto-Leppälä, [122]; Saarela, [121]; Parodi, [118]; Bösze, 2008; Ballard and Morrow, [116]; Claeys et al. [117]

Table 2. Whey protein and chronic disease

Authors*/Year of publication	Type of survey/load of sample	General result
Mortensen, L.S 2012 [28]	RCT/ 12 type 2 diabetic subjects	The whey protein isolate and whey protein hydrolyzate caused a higher insulin response after a meal.
Pal, S 2010[29]	RCT /Seventy men and women/12 weeks	Consuming WP supplement for 12 weeks caused the level of fat and fasting insulin decreased in fat and overweight subjects
Frid, A.H 2005 [27]	RCT /Fourteen diet-treated subjects with type 2 diabetes	Consumption of WP before each meal with great amount of carbohydrate in type 2 diabetic subjects caused an increase in insulin response and decrease in blood glucose
Aldrich, N.D 2011 [76]	Random parallel 18 individuals	Whey protein consumption may reduce fat and blood pressure in adults
Bortolotti, M 2011 [74]	Random clinical trial of 11 obese women for 4 weeks	Consumption of whey protein supplement for 4 weeks may reduce the fat content of liver cells and triglyceride on fasting basis in non- diabetic obese women
Pal S 2010 [68]	Control case 70 males and females	Long term consumption of protein can reduce blood pressure and improves vascular performance. Whey protein consumption has no effect on inflammatory markers.
Sheikholeslami Vayani, D 2012 [102]	Blind one- way clinical trial 30 healthy men in three equal groups	Although exercise only may increases anti-oxidant capacity and prevent risk factors of heart diseases, combining exercises with whey protein consumption enhances these effects and yields more useful results.
Pal, S 2010 [67]	Crossover 20 postmenopausal women having overweight and obesity	Using single dose of whey protein may protect heart veins of postmenopausal women who have overweight or obesity from lipoprotein particles enriched with triglyceride compared to a diet containing glucose with casein and so a reduction in cardiovascular diseases is resulted.

well as a 15% reduction in fasting triglycerides. In another study it was demonstrated that whey protein particularly β - lactalbumine may prevent obesity and overweight [75]. In general, both in studies performed on humans and animals, protective effects of whey protein in reduction of overweight and obesity are confirmed [29,43,75,76].

2.3 The Effect of Whey Protein Consumption on Antioxidant Activity and Enhancing the Power of Immune System of Body against Infection

Jamal Badr et al. [77] in their studies on mice demonstrated that whey protein supplement could cause the immune system to strengthen and the wounds resulting from diabetes could improve. Wong & Watson also confirmed the effect of whey protein on immune system [78]. However, some studies rejected such an effect [79]. It has been suggested that different compounds of whey protein such as α -lactalbumin, β - lactalbumin and lactoferrin probably prevent the formation of interleukin 6 (IL-6) and other inflammatory factors [80]. Moreover, it has been shown that whey protein supplement can cause an increase in Plasma glutathione in HIV patients noticeably [81]. It has been mentioned that whey protein can prevent the tumor growth and the formation of colon cancer [82-86] this an effect is

greater and more powerful in hydrolysate whey protein [87]. Nascimento, et al. [88] declared that enteral formula containing whey protein, compared with casein, reduces inflammation and increase antioxidant defense in elderly patients with a history of myocardial infarction. Whey protein Supplement may use as a treatment for diseases associated with stress oxidative [89]. It is believed that one of the reasons for anti-inflammatory activity of whey protein is associated with its performance in reducing adipose tissue stores. Fat tissues in the human body can release various cytokines and therefore increase inflammatory activity. Thus, as discussed earlier in the effect of whey protein on lipid profile, whey protein consumption could reduce the release of inflammatory factors by preventing the accumulation and storage of fat in the tissues [90,91].

The survey of Sattler, et al. [53] which was conducted on HIV patients demonstrated that although whey protein supplement could have not caused weight gain in these patients, it was able to increase the number of CD₄ cells and resulted in strengthening their immune system. Therefore, this survey confirms the previous results, especially those that supported the effect of consuming whey protein on the immune system [92]. Recent studies indicated that supplementation with whey protein in diabetic mice can cause increasing longevity; recovery of diabetes wounds and

strengthen their immune system [93]. Whey protein influences immune cells, secretion of cytokines, antibodies, phagocyte activity, granulocytes and the activity of natural killer cells [94]. Badr, et al. [77], have suggested that consuming whey protein supplement can cause recovery of wounds in diabetes patients by increasing the lifespan of macrophages. Some decreases in stress oxidative by consumption of whey protein have been reported in human based studies [88,95,96] and moreover, supplementation with 20gr whey protein isolate each day for 12 weeks can increase glutathione and the whole antioxidant capacity in non- alcoholic fatty liver [96]. In healthy people consuming 45 gr of whey protein increased glutathione level in lymphocytes [95]. So many other studies also show the antioxidant activity of whey protein [97-102]. It has been mentioned that whey protein may increase antioxidants of glutathione peroxidase, catalase, and superoxide dismutase.

On the other hand whey protein may decrease pre-inflammatory and inflammatory factors like: IL-1 β , IL-6 and TNF- α in obese people, diabetics and patients with myocardial infarction [103]. Also, some studies support the recovery of multiple sclerosis (MS) symptoms by using whey protein [104-106]. This protein can strengthen the immune system [107] because of its anti- cancer effects [108]. Badr, Et al. [109] suggested that whey protein can strengthen the production of T cell and B cell which also has been confirmed in some surveys. Vilela, et al. [110] demonstrated that whey protein has anti-inflammation effects such those HIV patients suffered from deficiency in glutathione and inflammation. Moreover, the study of Micke, et al. [81] showed that by daily consuming 45 gr of whey protein for 2 weeks, the level of glutathione had increased. In another survey, such an increase in glutathione by using whey protein in 6 month was confirmed [111]. It is said that the lactoferrin in whey protein causes protection of patients after surgery by adjusting immune system and causes a decrease in the infection rate after operation [112]. Gad, et al. also demonstrated that whey protein concentrate has antioxidant activity and causes the elimination of free radicals [97]. However, Pal, et al. [113] claimed that more studies are necessary to prove such an activity. At last Badr, et al. [109] suggested that whey protein supplement can be used as a medicine for strengthening the immune system in diabetic patient.

2.4 Food Applications of Whey Protein

Probably the greatest story in dairy industry in the earlier decades has been the escalation of new uses for whey and whey proteins [114]. Once considered a waste product in the cheese making, whey and whey

protein products nowadays are widely used for a variety of functional and nutritional properties [22, 23]. The applications of whey protein in different food products differ depending on the aim of its utilization. However, whey protein is generally used for enhancing biological value, developing a superior physical, textural or other food functional properties, improving sensory attributes and formulating high-protein and/or low-lactose products. Whey protein is applied as ingredients in many foods such as dairy products (particularly cheeses, yogurts, dairy-based dry mixes and dairy-based beverages), medical foods, sport foods, enteral foods, beverages, soups and protein bar applications. In cheese making, whey protein particularly in the form of whey protein concentrate (WPC) and whey protein isolate (WPI) is used for producing different cheeses like feta, ricotta, processed and spread cheeses. Other uses of whey protein include baked goods, meat products, low-fat spreads, desserts and toppings. Nowadays, great efforts are being made to find out new whey protein applications, e.g. production of edible films. Edible or biodegradable films constitute a convenient means to prolong the shelf life of foods and increase their quality without contributing to environmental pollution. These films are "green" alternatives to traditional plastics. Based on its excellent oxygen-barrier properties, WP films can be competitive biodegradable materials replacing nylon or polyesters, which are typically used as oxygen barriers [114].

3. CONCLUSION

In summary, whey protein is one of the useful and important protein sources for human's health due to having bio-active components. Since this protein has unique characteristics, it is considered as a valuable protein source. By reviewing the previous studies about this protein some valuable results about its nutritional properties can also be obtained. Whey protein is effective on glucose metabolism in obese people. Studies demonstrated that, this protein can prevent type 2 diabetes and diseases associated with fat accumulation. The effect of whey protein consumption on the muscles function and on increasing the ability of the body especially in athletes had been recognized from many years ago.

Whey protein can be effective on insulin secretion and decreases insulin resistance by different mechanism. These beneficial effects of whey protein attributed the copious amounts of some amino acids such as isoleucine in its composition. Besides, this protein prevents hyperglycemia. Studies support the effect of this protein on weight loss and reduction of fat accumulation in body. Based on some studies, due to having branched amino acids whey protein is

effective in reducing triglyceride and cholesterol levels. Also, this protein causes the fat being disposed of body and prevents accumulation of fat in body.

However, no accurate suggestion is found in this regard. In one study it was found that whey protein may increase fat consumption in skeletal muscles during exercise and may lead to weight loss. One of unique characteristics of this protein is reduction of cardio-vascular diseases and blood pressure occurrence. It has been suggested that these effects of whey protein are promising concerning obtaining a kind of food stuff that could reduce the weight. Other studies also support useful effects of this protein in reduction of cardio-vascular diseases. Therefore, whey protein could be used in daily diets particularly for those who suffer from overweight and obesity.

Other unique characteristic of this protein is strengthening of the immune system, increasing the body's antioxidant activity, preventing the spread of a variety of infections such as respiratory infection, diabetic wounds and HIV disease. Eventually reducing damage to the DNA molecule through reducing oxidative stress has been reported in some studies. Also the reinforcing effects of whey protein on the immune system due to its different compounds such as α -lactalbumin, β -lactalbumin and lactoferrin have been approved. Studies demonstrated that Whey protein can decrease pre-inflammatory and inflammatory factors such as IL-1 β , IL-6, TNF- α in obese people, diabetic patients. By producing T cell and B cell, this protein can cause strengthen immune system in HIV patients. As a whole, whey protein can be used for improving physical performance, as an substitute to milk for people with lactose malabsorption/intolerance, as a food complement, for substituting milk-based infant formulas, and for retreating weight loss and accumulation of glutathione (GSH) in persons with HIV disease. Whey protein is besides applied for obesity and weight loss, preventing allergies in infants, protein allergy, high cholesterol, asthma, late-stage cancer and colon cancer. Given above mentioned facts, we can suggest that whey protein could be used as a healthy and useful food supplement for humans and we can benefit from the advantages of this protein by having milk in dairy diet. Given the substantially low amount of protein in milk and its low beneficial effects in the short term, therefore, it is recommended that whey protein supplements could be used alternatively for the prevention and treatment of metabolic diseases.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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