

Whey Protein Supplement: An Exclusive Food or Need of the Hour: Review

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Background: Protein is an essential portion of food that exerts beneficial effects on body composition and metabolism. However, protein-rich foods are costly and scarcely available in developing countries, and protein deficiency is a significant public health concern. In this situation, searching for additional dietary protein sources is of utmost importance due to decreasing resources because of the growing global population. The current literature review is about whey protein as it is the cheapest, readily available protein source.

Methods: Milk is formed of two proteins, casein and whey. Whey is different from the casein in milk and is formed as a by-product of the cheese-making process. Whey (the liquid left after milk curdling) was deemed a waste by the dairy industry for decades. However, it is the cheapest protein source for the poor growing populations in developing countries. Whey protein is a complete protein as it contains all nine essential amino acids. It is low in lactose content.

Conclusion: Human body cannot make essential amino acids, so it is necessary to get enough of them from the diet. Due to the availability of carbohydrates, fat, immunoglobulins, lactose, and minerals, including essential amino acids in whey protein, it is necessary for human energy. There are many benefits related to whey protein consumption, such as muscle building and loss of fat. New possible therapeutic properties of whey protein have to be investigated further for the full utility to humans.

Keywords: *Whey protein; milk; casein; cheapest protein.*

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1. INTRODUCTION

Milk is a significant source of nutrition that is widely consumed for human health. This can be obtained from several domesticated animals like sheep, goat, buffalo, and cow. Fresh cow milk contains 3.5% total protein, 80 % casein, 20% whey protein, vitamins, and lipids. These ingredients are essential for growth [1,2]. In other words, milk is a source of energy (carbohydrate), lactose (sugar), nitrogen (protein; subcomponents of micro fractions), and calcium (for bones)[3,4]. The dairy industry was treating whey (the liquid left after milk curdling) waste for decades. As whey liquid is highly organic with high biological oxygen demand, its disposal is complicated.

On the other hand, whey is full of biologically active components, e.g., lactoferrin, lactoperoxidase, lysozyme, and immunoglobulins, etc. and is having antimicrobial properties [3,4]. Milk is formed of two proteins, casein and whey. Whey protein is often separated from the casein in milk or created as a by-product of cheese making. It is beneficial in wound healing due to high protein contents, weight loss as no fat, in infant health as full of amino acids. It is an excellent protein for all age groups, especially for marasmus children, and maintains their health [5,6]. The human body cannot make essential amino acids, so it is vital to get enough of them from the diet. Due to the availability of carbohydrates, fat, immunoglobulins, lactose, and minerals, including essential amino acids in whey protein, it is a vital source of domesticated animals' energy [7].

Whey protein may be a popular fitness and dietary supplement. It is prepared from whey, which is the liquid that separates from milk during the cheese-making process. Whey protein powder can be prepared by drying filtered whey liquid. Whey protein may be a popular choice among athletes, fitness enthusiasts, and other people eager to build muscle or reduce fat. Studies show it can help recovery from exercise, muscle building and even help lose weight by reducing appetite and boosting metabolism [2,3,4]. The whey protein can be taken by mixing it with water or with another liquid of choice. Despite its health benefits, some people are concerned about their safety. Whey protein concentration is different in different animals as sheep and goats have similar concentration but higher than bovine (cow) whey.

These days, industries present whey protein as a health supplement in place of various health food and beverages. These proteins are used for medicinal purposes and improve the health status of all age groups of humans. This protein is usually involved in controlling or maintaining blood glucose levels and provides additional benefits, including weight management [8]. Whey liquid is obtained from the milk of different domesticated animals, and then whey liquid is purified by removing several constituents (Saito T. [9]. There are three types of whey, i.e., whey protein concentrate (WPC; the low but still substantial level of fat and cholesterol; higher bioactive components), whey protein isolate (WPI; remove fat and lactose content but lower in bioactivated combinations), and whey protein hydrolysate (WPH; pre-digested and hydrolyzed; hydrolyzed whey could also be less allergenic) (Fig. 1). Besides, there are many immunological components in whey protein [5,6,7,8,9].

Amino acid content is an essential factor in bovine milk proteins, especially caseins and whey protein. In contrast, milk protein is a potential source of immunobiologically active peptides full of nutritional value. Whey protein provides all those essential amino acids which a human cannot produce itself within the body. These amino acids are nine in number with a different function. These amino acids fulfill all body requirements and keep the body fit with lean muscle mass [10,11]. Branched-chain amino acids, e.g., leucine, isoleucine, and valine, are also present in whey. These branched-chain amino acids help in protein synthesis and thus cover up to one-third of muscle protein. These amino acids are not broken in the liver, whereas other amino acids are broken by the gut and the liver. Consuming these branched-chain amino acids before physical workup can upsurge uptake into the muscle tissue and provides many profits, e.g., enhanced growth hormone circulation, lower lactate levels and better muscular oxidation. Branched-chain amino acids consumption also decrease serum concentrations of intramuscular enzymes creatine kinase and lactate dehydrogenase, etc.[12,13]. The branched amino acids are released from the liver and other internal organs to skeletal muscle. Branched-aminoacids can control blood sugar levels. Thus about 40-50 % of blood sugar during exercise is produced with branched amino acids [12,13].

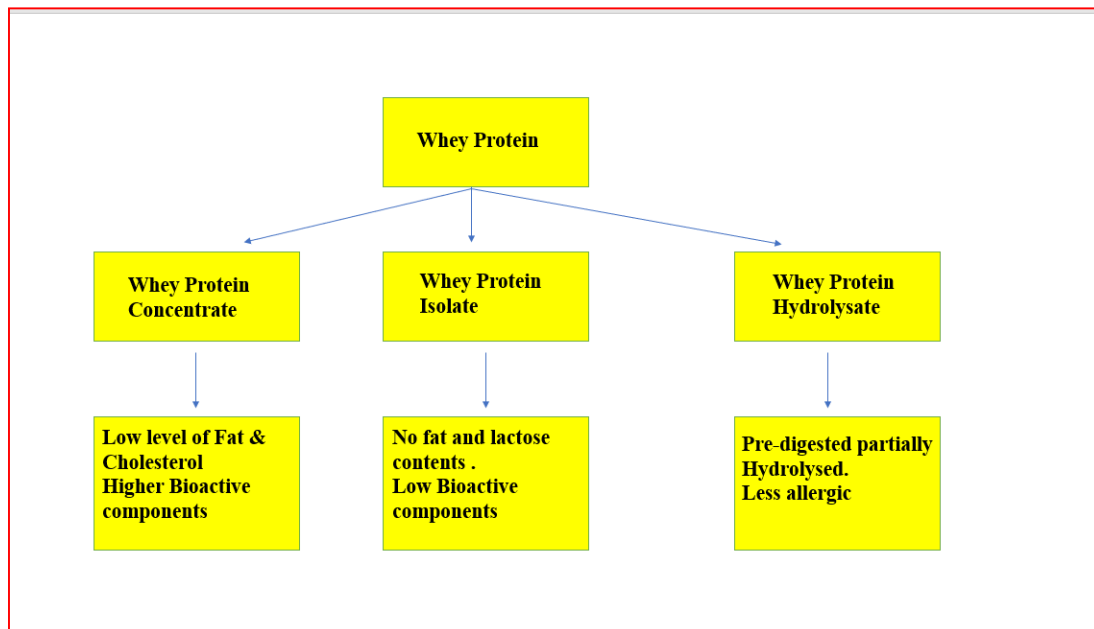


Fig. 1. Benefits of whey protein

Cysteine and methionine, which help to grow immune function through intracellular conversion to glutathione, are present in high whey protein concentrations [14]. Lactoferrin (iron-binding glycoprotein) comprises 689 amino acid residues and its strength in human milk is 2mg/ml, and colostrums are 7mg/ml. Whereas in bovine milk (0.2mg/ml) and colostrums (1.5mg/ml), respectively [15]. The lactoferrin acts as an antimicrobial and anti-inflammatory agent and can induce natural killer cells and colony-stimulating factors, including macrophages' activation[16]. In small children less than two years of age, lactoferrin is delivered through breast milk. Nowadays, bovine lactoferrin, including recombinant human lactoferrin, is obtainable commercially and is usually added to various food products, including milk, useful for the immune system. The lactoferrin possesses antibacterial and antiviral activities in the intestine against multiple pathogens. Besides, it may regulate infants and pregnant women's iron content via a receptor-mediated pathway [16].

Whey protein also contains immunoglobulins (blood group proteins) that are useful for enhancing immunity. The highest concentration of these immunoglobulins is present in colostrum (first milk after birth). The immunoglobulins help control various bacterial infections and present in the form of various antibodies, i.e., IgG, IgM, IgA, secretory IgA and Ig [17]. These immunoglobulins deliver passive maternal immunity to infants

through breast milk and help to maintain our immune system. These immunoglobulins are about 10-15% of total whey proteins from bovine milk [17]. The colostrum of cow, sheep, and bovine is full of lactoferrin [16]. Bovine milk contains the enzyme lactoperoxidase, which has antibacterial properties against many pathogens. This enzyme, in combination with hydrogen peroxide (H_2O_2) and thiocyanate (SCN^-), works as an antimicrobial agent in raw milk samples [18,19,20]. Whey contains lactalbumin, one of the significant milk serum proteins, i.e., alpha-lactalbumin, which has antiproliferative effects in human cell lines adenocarcinoma as Caco-2 and HT29. The content of alpha-lactalbumin is much higher in cow's milk and may cause an allergic reaction in some cases [21,22]. Goat milk free of allergic reaction is thus useful in young children. The concentration of alpha-lactalbumin is different in different animals, e.g., cow (52.9-53.6%), sheep (8.97-17%), and goat (13.31-34.7%) [21,22,23]

2. VARIOUS HEALTH BENEFITS OF WHEY PROTEINS

Whey protein is a cheap and readily available protein source in developing countries like India. It is full of many benefits to human beings in its various derivative forms (concentrate, isolate, and hydrolysate).



Fig. 2. Showing the health benefits of whey proteins in various forms

2.1 Gut and Prebiotic Action

In seriously ill patients, the gut does not function appropriately and becomes unable to absorb even a bland diet. This affects the health of patients. It is not possible to give parenteral nutrition to all such patients due to high cost. In these patients, whey protein protection might impart inflammation and enhance enteral nutrition [23]. To exert their therapeutic property, lactic acid bacteria and yeast need to be viable. The prebiotic action of whey on the gut may be not that effective due to the hostile gastrointestinal environment and whey storage. Whey protein gels can encapsulate the protecting the microbes, and its efficacy is more against the adverse conditions. The encapsulating *Lactobacillus rhamnosus* CRL 1505 in whey protein and pectin survive better at low pH. Similarly, pectin beads with a whey protein layer could be used as a probiotic carrier in acidic functional foods [24].

Lactobacillus acidophilus and *Bifidobacterium* in yoghurt beverages are stabilized with high-methoxyl pectin and whey protein concentrate [25]. This proves the role of whey as a probiotic and prebiotic stabilizer. Whey protein isolate and alginate microparticles have shown suitability as oral delivery systems for probiotic yeast *Saccharomyces boulardii* [26].

2.2 Muscle Strengthening

All eccentric and concentric skeletal muscle exercises result in muscle damage and produce inflammatory markers (muscle proteins in the blood) [27]. The anabolic protein hydrolysates and amino acid supplements accelerate the repair. Leucine-derived metabolite β -hydroxy- β -methyl butyrate ingestion results in the healing of muscle injury. Resistance exercise, such as weight-lifting, raises oxidation products in plasma disturbs leukocyte redistribution and leukocyte functionality [28]. The whey protein diet is better than the casein diet to heal injuries sustained due to isometric and concentric exercises. [29]. The low-protein (6.25 g) beverage can be as effective as a high-protein dose (25 g) at stimulating myofibrillar protein synthesis rates when supplemented with a high (5 g) leucine content [30]. Leucine, an amino acid (10 % of the total whey amino acid), is essential for muscle hypertrophy. Health parameters, performance, and body composition effects produced by a 12-week intake of hydrolyzed whey protein were compared in players. Ingestion of the hydrolyzed whey protein helped drop in the muscle damage markers (creatine kinase and lactate dehydrogenase) [31]. Lean body mass gains are significantly high in whey protein consumers than soy protein, and the good response was correlated with the elevated levels of leucine and faster absorption. [32].

2.3 Immunomodulator Action

Whey protein concentrates enhance essential mucosal immunity during early life and has a protective role in some immune disorders [33]. The infants may suffer from atopic dermatitis as being a major vulnerable group. A meta-analysis of the systematic review revealed that atopic dermatitis incidence was considerably lower among infants in the partially hydrolyzed whey-based formula group than the bovine milk group [34]. The finding suggested that whey-based formula might protect infants from atopic dermatitis. Psoriasis is chronic autoimmune disease-causing thick skin, dry scales, and red patches. Bioactive whey protein isolate can decrease systemic inflammation due to psoriasis by increasing glutathione levels. The intake of 20 g/day whey protein isolates improved the Psoriatic patients [35].

2.4 Antioxidant Action

Inflammatory or oxidative stress can cause cystic fibrosis, pneumonia, diabetes, cancer, atherosclerosis, myocardial infarction, ageing, and many other degenerative diseases [36]. Whey is full of the antioxidant glutathione and can eradicate the adverse effects of the stressors. Hyperbaric treatment of whey protein accelerated the release of bioactive peptides, raised intracellular glutathione levels, and decreased the in vitro generation of interleukin IL-8, a cytokine responsible for respiratory tract diseases [37]. The dietary supplementation of pressurized whey (20 g/day) in cystic fibrosis patients decreases serum C-reactive protein level significantly [38]. The antioxidant and anti-inflammatory effects of pressurized whey protein isolate and native hydrolysate in human epithelial colorectal adenocarcinoma Caco-2 cells exposed to H₂O₂ were compared [37]. The results suggested that whey protein isolate hydrolysates can lessen inflammation and oxidative stress in intestinal cells exposed to oxidative injury. The consumption of whey protein hydrolysate boosts HSP70 expression [38]. Thus the whey protein hydrolysate can enhance cell survival factors such as HSP90 and vascular endothelial growth factor (VEGF) [40]. Pressurized whey protein can decrease the level of the inflammatory response, oxidative stress, and lung damage. Thus whey protein subjected to hyperbaric treatment has superior biological quality. It protects the airway proteins from oxidation and stimulates leukocytes to kill the pathogens, thus saving them from *Pseudomonas aeruginosa* [41]. Whey protein

hydrolysate has an antioxidant effect against paracetamol-induced hepatonephrotoxicity [5].

2.5 Anticancer Action

Several studies have suggested that whey protein hydrolysate may help treat cancer patients and improve colon cancer anticancer efficacy [42,43,44]. A 48-year-old female patient with increased serum levels of leucine, isoleucine, valine, lysine, and threonine was administered with whey protein (10 g 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, improved lean body mass, physical activity, and overall quality of life were observed in recurrent cervical cancer [45].

2.6 Cardioprotective

Whey protein intake reduces cardiovascular disease (ischemic stroke) risk. Whey-derived extract (NOP-47) ingestion increased impaired brachial artery flow-mediated dilation (improved endothelial function). Postprandial plasma amino acids level increased. Arterial dilation improvement was independent of circulating vasoactive compounds such as nitric oxide, prostacyclin, and endothelium-derived hyperpolarizing factors. The cardiovascular risk might be lessened by using rapid-absorbable extracts derived from whey [46,47].

2.7 Antidiabetic Action

Diabetes affects all human organs accompanied by many complications such as loss of vision, angiopathy, reduced blood flow leading to tissue hypoxia, and nonhealing ulcers [48]. Type-2 diabetes is managed by diet control and hypoglycaemic drugs. Whey protein has been demonstrated to reduce serum glucose levels 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 the hunger hormone ghrelin [49]. For ancillary therapy in glycemia and vascular inflammation control in people with diabetes, cysteine in whey proteins is very useful [50].

The whey protein helps in diabetic wound healing by restricting inflammatory cytokines' access by maintaining standard IL-10, TNF- α , IL-1 β , and IL-

6 levels. Higher serum levels of leucine, isoleucine, valine, lysine, and threonine help in Insulin secretion in the body [51,52].

Whey protein fractions (whey isolate and whey hydrolysate) added to a fat-rich meal lowered postprandial triglyceride responses in type 2 diabetic subjects. Both components provoked a higher insulin response [53]. A hydrolyzed whey protein-based supplement may result in a higher leucine level, followed by an increased Insulin level [54].

2.8 Obesity Management

Whey protein helps in the reduction of obesity. The ameliorating effects of the protein-rich diet on metabolic disorders are precisely due to the modulation of satiety mediated by liver lipogenesis attenuation [55]. The whey protein concentrate employs more substantial 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 and thus reduce obesity [56].

2.9 Side Effects of Whey Protein

Whey protein is a beneficial nutritional food, and there is no other natural protein equivalent to this. Still, there can be risks from nutritionally refined foods such as whey, as it is a heavy protein. Acne can develop if a person takes whey protein for a long time. Most whey protein's side effects are related to digestion and may experience bloating, gas, stomach cramps, and diarrhoea. However, most of these side effects are due to lactose intolerance. It is due to a deficiency of the enzyme lactase needed for lactose digestion.

Moreover, lactose intolerance is quite common, and about 75% of people are affected worldwide. In such cases, whey protein isolate powder can be used as a whey protein isolate is more refined. It holds a smaller amount of fat and lactose than whey protein concentrate.

People with a cow's milk allergy may be allergic to whey protein. Cow milk allergy exists up to the initial three-year age, and after that, 90% of people outgrow cow's milk allergies. A cow's milk allergy symptoms are hives, rashes, facial swelling, throat, tongue swelling, a runny or stuffy nose, and rarely anaphylaxis, a severe, life-threatening allergic reaction [57,58].

2.10 Interaction with Drugs

Levodopa-Whey protein interferes with the absorption levodopa and thus decrease the effectiveness of levodopa. So, avoid taking whey protein and levodopa together.

Albendazole -Whey protein interferes with absorption and can decrease albendazole absorption in the body and decrease albendazole's effectiveness. So avoid taking both together.

Alendronate (Fosamax)-Whey protein can decrease the absorption and effectiveness of alendronate. So, avoid taking whey protein within two hours of taking alendronate (Fosamax).

Antibiotics (Quinolone antibiotics). Whey protein and antibiotics should not be taken together due to decreased absorption. Do not take whey protein supplements and tetracycline together, and a gap of one hour is essential. Other antibiotics that might react with whey protein are Quinolone antibiotics such as ciprofloxacin, norfloxacin, sparfloxacin, etc.

Antibiotics (Tetracycline antibiotics)- As whey protein contains calcium that can attach to tetracyclines in the stomach and decrease tetracyclines' absorption. To avoid this interaction, take whey protein four hours after taking tetracyclines [57,58]

3. A FEW REASONS NOT TO TAKE WHEY PROTEIN [59]

1. Lactose — Whey protein supplements (WPC) still retain lactose, which leads to digestive distress if there is lactose intolerance.
2. Unintended weight gain- Whey protein contains sugars and fat in addition to protein. The accumulative ratio of macronutrients like sugars and fat add extra calories to a normal diet. Thus, there is extra addition of calories in the body that causes unplanned weight gain over time.
3. High Cost — whey protein products are relatively more costly than whole foods such as tuna, peanut butter and skim milk which is an economical supplement equivalent to whey protein.
4. Lack of Nutrients — Whey protein supplements contain lower levels of

essential nutrients like zinc, iron, vitamins, omega 3 and fibres that many whole food sources of protein provide.

5. Contaminants — In India, dietary supplements do not undergo the same regulation before being sold over-the-counter in the open market or online purchase, unlike conventional foods. Whey protein supplements may get exposed to certain contaminants, impurities or banned ingredients [59].

4. CONCLUSION

Whey protein is an essential and economical protein source full of nine amino acids and branched amino acids. So, it is a first-rate nutrient. Only whey protein can fulfil the increasing demand for an economical protein source for humans in developing nations. Excess of everything is bad, so is whey protein. Whey protein is full of immunoglobulins and can challenge cancer as an immune nutrient. Still, whey is an underutilized resource, and new strategies should be planned to increase its utility for human welfare.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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