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Original Research Article

"Whey Protein Supplements between Bodybuilders" Health, Risk of Diseases and Myth: A Narrative Review 2010-2024

Abbas Fadhul Khudhur [1*]

[1]Republic of Iraq, Ministry of Education, Kirkuk, Iraq

***Corresponding Author:** Abbas Fadhul Khudhur
Republic of Iraq, Ministry of Education, Kirkuk, Iraq

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Abstract: This narrative review evaluates the most recent studies on the health effects of whey protein (WP) supplements, with a focus on potential risks and negative consequences. WP, which is frequently taken by bodybuilders to gain muscle and lose weight, has been linked to a number of health problems. Twenty-four preclinical and human studies that provide a complete overview of the health effects of WP were included in our comprehensive review after a comprehensive search of various databases. The review provides important findings, including a possible link between WP and kidney and liver damage, changes in bowel activity, acne, effects on bone metabolism, and pancreatic beta cell activity. The above findings highlight the complex nature of the impact of weightlifting on human health, revealing both positive and negative consequences in relation to different situations in diverse contexts. Research suggests that individuals with impaired liver and kidney function, as well as those prone to acne, should be cautious when consuming protein, and polycystic ovary syndrome. However, there may be positive effects on gut activity, bone and muscle metabolism, and pancreatic activity in humans and experimental animals, emphasizing the importance of consuming WP in a balanced manner and calling for more comprehensive research to understand its long-term health consequences.

Keywords: Protein supplements, Bodybuilders, whey protein (WP), liver function, kidney function, acne, bone metabolism, The risk of physiological diseases, heart strength, polycystic ovary syndrome, testosterone.

1. INTRODUCTION

Protein supplements are widely accepted and used in today's fitness culture, thanks in large part to the influence of celebrities and media coverage. This is especially true for young adult males who want to have the perfect body. Though their use has grown, not much study has been done to examine how these supplements affect exercise capacity and cardiovascular health. By employing heart rate variability (HRV) to clinically examine the cardiovascular system and comparing the outcomes between those using protein supplements and a control group, this study seeks to close this gap [1]. Athletes, young adults, and teenagers who work out frequently utilize protein supplements, which are a great way to improve your protein intake, gain muscle mass, and speed up your recuperation. They come in powder, gummy, protein bar, and ready-to-drink smoothie forms and have been demonstrated to impact almost all bodily systems [2]. In order to sustain physical function, promote overall health, and aid in the healing process, the recommended daily intake of protein for healthy older persons is between 1.00 and 1.20 grams per kilogram of real body weight (g/kg/day). Those with severe, multiple chronic disorders, as well as those suffering from severe illness, injury, or malnourishment, may require additional increases [3]. Individuals who frequently take soy protein supplements have been shown to exhibit a significant drop in both systolic and diastolic blood pressure, whereas those who consistently take whey protein supplements show a large reduction in systolic blood pressure. It has been demonstrated to result in hyperfiltration and elevated calcium excretion in the urine, which may eventually induce chronic kidney disease. The effects of protein supplements on the human body are the main topic of this article, with special attention to the renal, endocrine, and cardiovascular systems [4]. Performance enhancing substances (PES) are commonly used by athletes to improve athletic performance or physical appearance [5]. For the past fifty years, bodybuilders and those who aspire to masculine physiques have been using these supplements to

bulk up their muscles and enhance their training regimens [6]. Whey protein (WP), a major component of milk proteins, has been found in it [7].

Whey proteins or whey are soluble milk proteins that account for about 20% of total milk proteins. Bovine whey protein consists of beta-lactoglobulin, alpha-lactalbumin, proteopeptide peptone, serum albumin, and immunoglobulins in order of abundance. They are available as an ingredient in the form of whey powder, whey protein concentrates, and whey protein isolates, which are primarily manufactured from whey—a by-product of cheesemaking. The unique properties of whey proteins such as solubility over a wide pH range, favorable nutritional profile with respect to essential amino acids, diverse functions, and relatively low cost make them an ideal ingredient in the formulation of a wide range of food products. This chapter discusses the use of whey proteins as ingredients in foods [8]. The protein content of isolate and concentrate protein supplements representing the European market was determined, the protein was 70.9% (18-92.3%) and statistically significant differences between the relative and actual protein content were observed. Among the minerals, it (4689.10 mg/kg) and calcium (3811.27 mg/kg) were shown to be the highest level, while cobalt (0.07 mg/kg) and phosphorus (0.04 mg/kg) were shown to be below the level. The study concluded that there is no quality control and regulation of these products. A high degree of harmlessness of the labelling students was also revealed. Therefore, the contributors to the access and acceptance among ordinary consumers should be evaluated [9]. It has already been shown that the use of WPI, combined with exercise (especially resistance training), leads to increased muscle protein synthesis and skeletal muscle mass [10]. As well as improved recovery from exercise [11].

Recently, Haas *et al*., [12]. Showed, in a pilot study, that vibration and resistance exercises in addition to a high-protein diet based on WPI supplementation (with or without omega-3 fatty acids) increase muscle strength in older adults, leading to improvements in leg strength and chair lift time. Cancer is the leading cause of death worldwide. Whey has attracted much attention in recent years as a natural source due to its important applications in health benefits. Whey components have become increasingly popular among consumers for their nutritional properties, making them an attractive subject for cancer research, which is a global public health issue. Researchers are using whey protein in cancer prevention and treatment [13]. In addition, it was found that whey protein improves glucose levels and insulin response, enhances a decrease in blood pressure, atherosclerosis, and improves fat image. The collective view of the current scientific literature indicates that the consumption of whey protein may have beneficial effects on some symptoms of metabolic syndrome as well as a decrease in cardiovascular risk factors [14]. Although WPI is insulating it is immune, its ability to adjust the production of a wide range of inflammatory signs has not been investigated by healthy adults. , The serum is analyzed using a multi-transmission test to measure IFN-γ, IL-1β, IL-1RA, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12P70, IL-13, IL-17A and TNF-α. , This study showed a decrease in the IL-12P70 serum in the laundry stage compared to the foundation line, as well as the laundry phase of the bridal lecoferene in relation to the intervention stage. IL-13 serum was also dramatically reduced during the intervention and washing stages. The data indicates that the whey supplementation has not greatly changed most of the measured inflammatory signs, but the concentrations of some inflammatory signs can change in the indigenous adults [15].

Generally well-liked for its alleged advantages in weight loss and muscle growth, but growing use has sparked worries about possible health repercussions, which this review seeks to explore. A number of variables, including heat treatment, storage conditions, and casein precipitation technique, can affect the characteristics of whey protein [16]. Whey protein is usually processed using a variety of techniques, such as ion exchange, microfiltration, and/or ultrafiltration. This produces three different products: whey protein hydrolysate, which facilitates absorption and reduces antigenic interactions; whey protein isolate, which contains 90–95% protein and varying amounts of fat, lactose, and minerals; and whey protein concentrate, which has a protein content of 20% to 85% and varying amounts of fat, lactose, and minerals [17]. Whey protein concentrations range from 25–99% in WP Concentrated and from 90–95% in WP Isolate, a type of whey supplement [18]. There is a lack of information addressing the possible adverse effects and long-term harm associated with WP supplements. Specifically, concerns have been expressed about the effects of large doses taken over an extended period of time by inactive individuals on liver and renal function [16]. Other concerns have been raised about whether WP may trigger allergic responses [19].

2. MATERIALS AND METHODS

2.1 Inclusion Criteria and Means

The review followed the parameters of the Narrative Review Article Rating Scale [20], and it was carried out utilizing a number of databases, including PubMed, Scopus, and Google Scholar. The search terms that were utilized were "whey protein" or "whey protein supplements" along with "gastrointestinal problems" or "contraindications" and "adverse effects" or "side effects." Hearts function" "kidney function "" reproductive system " polycystic ovary syndrome" testosterone " Bone Metabolism " vitamin D3" cancer " lung function " With this calculated move, a thorough corpus of research on the negative and positive impacts of whey protein supplements on bodybuilders will be produced.

2.2 Data Extraction

The method used throughout the whole literature review process, from the first database search to the last round of study selection for the review. Describing the quantity of papers found, vetted, and assessed, which eventually results in the final selection of pertinent research to be included in the review.

3. RESULTS

A review of 9 studies [21-45] revealed diverse results regarding the effect of WP on different health aspects. Details of these studies on health and side effects of WP supplements are presented in Table (1).

Table 1: Shows the side effects resulting from whey supplements for human and animal health

1-Effects on Liver function				
Authors	**Year**	**N. of Patients**	**Outcomes**	**Reference**
Yang *et al*.,	2011	38	6 weeks	[21]
Kerstetter *et al*.,	2015	75	12 weeks	[22]
Cengiz *et al*.,	2017	30 rats	4 weeks	[23]
2-Effects on kidney function				
Tracy *et al*.,	2014	100	12 weeks	[24]
Antonio *et al*.,	2016	75	8 weeks	[25]
Vatani *et al*.,	2012	40	8 weeks	[26]
3-Effects on Bone Metabolism				
Amanzadeh *et al*.,	2003	55	10 weeks	[27]
Kiremit *et al*.,	2023	60	6 weeks	[28]
Wright *et al*.,	2017	60	36 weeks	[29]
4- Effects on Heart function:				
Dos Santos *et al*.,	2023	60	12 weeks	[30]
Azhar *et al*.,	2020	30	12 weeks	[31]
Giezenaar	2021	40	36 weeks	[32]
5- Effects on lung function:				
Zhao & Zhan *et al*.,	2020	212	60 weeks	[33]
Srinivasaraghavan	2022	100	4 weeks	[34]
Xiao *et al*.,	2023	34	33 weeks	[35]
6- Effects on skeleton muscles mass:				
Kim *et al*.,	2023	40 rats	8 weeks	[36]
Qiu *et al*.,	2023	60	34 weeks	[37]
Kim *et al*.,	2023	40	8 weeks	[38]
7- Effects on reproductive system:				
Zare *et al*.,	2023	200	120 weeks	[39]
Zumbro *et al*.,	2021	15	7 days	[40]
Zumbro *et al*.,	2020	70	7 days	[41]
8- Other Effects				
Mohr	2020	60	20 weeks	[42]
Danby	2010	34	10 weeks	[43]
Des Robert	2010	40 rats	4 weeks	[44]
Rosa *et al*.,	2020	30	4 weeks	[45]

4. DISCUSSION

4.1 Effects on Liver Function:

Studies seem to differ on the impact of WP on liver function. Yang *et al*., [21] reported positive outcomes in human trials, such as a decrease in oxidative stress and fatty liver in NASH patients. Aspartate aminotransferase (AST) and urea levels, two indicators of liver function, showed slight variations in gym-goers, according to Kerstetter *et al*., [22]. As a result, grade 3–4 ALT/AST increases were observed in 8% of patients utilizing appearance and performance boosting supplements (APES), primarily represented by WP, according to Cengiz *et al*., [23].

4.2 Effects on Renal Function:

WP micronutrient drinks were found to improve the estimated glomerular filtration rate in older individuals with muscular atrophy. Tracy *et al*., [24] found that people who consumed WP had higher urine calcium and lower urine pH and Antonio *et al*., [25] discovered that 12% of APES users who were also receiving chronic interferon therapy concurrently had higher serum creatinine levels. In a study involving sedentary rats, Vatani *et al*., [26] found that high

protein intake enhanced kidney volume and calcium excretion; however, these benefits were less noticeable during endurance activity.

4.3 Effects on Bone Metabolism:

Amanzadeh *et al*., [27] observed in a preclinical study that high protein intake in mouse models led to changes in urine pH and calcium concentration as well as decreased bone density. Kiremit *et al.*, [28] observed in human research that people who consumed WP had decreased urine pH and increased urinary calcium excretion. Wright *et al*., [29] looked into the effects of WP consumption in older subjects and found that there were changes in serum levels of calcium and calcidiol as well as decreased parathyroid hormone levels.

4.4 Effects on Heart:

In patients with chronic HF with a lower LVEF, WPI supplements are encouraged for 12 weeks to improve body composition, it is clear from an increase in structural muscle mass and low body fat. Isolated WPI supplements (without accompanying physical exercise) may be beneficial to these patients, who cannot exercise or limit themselves to reaching exercise programs under supervision. Current results may help change the need for the need to exercise during WPI supplements, which is especially useful in the specific population of HF patients [30]. Another study by Azhar and others [31] showed that on an effect on a variety of physical performance parameters as well as cardiovascular function for a low -density exercise program, most individuals who suffer from HFPEF can do that are long -term participation. We have found that individuals with HFPEF who consume about 1.2 grams of protein/kilogram/day may benefit in terms of physical and blood vessels from an exercise program that is likely to be considered sufficient to enhance large physiological adaptations. Following ingestion of 70 g whey protein, healthy older men exhibited a sustained fall in BP, despite an increase in HR, whereas in younger men there was no change in BP. BP may need to be monitored after high protein meals in older people at risk of postprandial hypotension [32].

4.5 Effects on Lung Function

The nutrients directly enter the patient's intestine, correspond to the form of the movement of the digestive system, and will not increase the intestinal disorder pregnancy. The digestive system of the patient is small and the adaptation is good, which leads to slow and uniform absorption of various nutrients and reduces the stimulation of the digestive system. In addition, due to the need for rapid water before surgery, early intestinal feeding support can stimulate the secretion of the digestive system, enhance the absorption of the digestive system, restore the functions of the digestive system, and help improve immunity function [33]. Whey protein contains many biochemical properties that make it an ideal nutritional supplement in cancer. This metabolic analysis aims to assess the effects of whey on the results surrounding surgery in cancer. Secondary results included a 6 -minute walking test, LOS length (LOS), and re -admission for thirty days. Among the ten experiments, six serum whey to fulfill the requirements of protein is about 1.2 mg/kg/day, and four whey complementing differently [34]. Intensive research has indicated from large future dust studies and analytical investigations continuously over recent decades that dairy foods have preventive effects, which reduces the risk of colon and rectal cancer. Most literature explored the potential role of milk and vitamins in the management of colon and rectum. Their strong binding rapprochement enables them to be effective carriers for small molecules or medications aimed at treating colon cancer. Moreover, many studies have emphasized anti -inflammatory and antioxidants from whey proteins in the prevention of cancer. In addition, it turns out that serum proteins lead to the death of programmed cells, hinder the proliferation of tumor cells, and hinder a malignant tumor. Consequently, this comprehensive review does not prove the importance of merging the ingredients of whey protein into a balanced daily diet, but it also emphasizes its potential to protect against the beginning and development of colon and rectal cancer [35].

4.6 Effects on Skeleton Muscles Mass:

However, in vivo research on the effect on muscle strength and protein synthesis is still lacking. Furthermore, commercial whey protein increased muscle mass and grip strength compared to commercial whey protein. Native whey protein also increased the phosphorylation of mammalian target of rapamycin and ribosomal protein S6 kinase, proteins essential for muscle protein synthesis. These results suggest that native whey protein promotes muscle strength and protein synthesis more effectively than native whey protein [36]. Skeletal muscle atrophy is a condition associated with increased morbidity and mortality, and the gut microbiota is thought to play a role in the pathogenesis of this condition, which can be reversed by whey protein intervention. Gut phenotypes predict muscle function and weight, underscoring the potential role of gut microbiota in modulating muscle atrophy and underscoring the therapeutic opportunities for interventions that alter gut microbiota through whey protein activation [37]. WP was shown to be effective in enhancing physical performance in terms of measures of dynamic balance and muscle health, as demonstrated by increased grip strength (left), upper arm circumference, and flat leg circumference from baseline. These results suggest that L. casei DK211-bioconverted whey protein was the most effective protein supplement for enhancing muscle health in adults undergoing regular resistance exercise [38].

4.7 Effects on Reproductive System:

WP may be recommended to athletes and active individuals in place of traditional protein supplements by evaluating its dosage and efficacy in relation to different types of training. WP may enhance lean mass compared to other protein sources, enhance antioxidant status, and reduce oxidative stress. WP supplementation has had inconsistent effects on testosterone and cortisol levels. WP supplementation may be beneficial, especially after muscle damage, high-intensity/high-speed exercise, or repeated bouts of strenuous exercise [39]. In study of Zumbro *et al.*, hypothesized that supplementation with 35 g of whey would improve insulin sensitivity and glucose handling while reducing biomarkers associated with NAFLD in patients with PCOS. Twenty-nine age-matched women completed oral glucose tolerance tests after baseline (day 0) and acute (day 1) and short-term (day 7) whey supplementation. Whey had an interactive effect on glucose and insulin, with glucose remaining constant and insulin increasing with whey supplementation. Improved insulin sensitivity with whey was associated with increased glucagon secretion, and after whey, reduced fat accumulation in the PCOS group after whey. Whey provided a stabilizing effect on insulin and glycemia in women with PCOS with the potential to combat the consequences of NAFLD [40]. Nutritional interventions, therefore, that can ameliorate PCOS-related issues are warranted. Whey protein has recently been shown to have improved glycemic homeostasis, reduced chronic inflammation and enhanced protein anabolism effects in people with or without insulin resistance. Women with PCOS and CON consumed 35g of whey protein for 7 days [41].

4.8 Other Effects:

Mohr *et al*., [42] noted alterations in the gut microbiota of cross-country runners in human studies, including a rise in the Bacillus phylum and a fall in Roseburia and Blautia, two beneficial bacteria. In human trials, Danby [43] regularly observed that people taking WP supplements had more severe acne and developed lesions. After stopping the WP supplementation, improvements were seen. These research' consistent results point to a clear correlation between WP supplementation and more severe acne, especially in certain populations like male bodybuilders and teenagers. Des Robert *et al*., [44] saw notable increases in food intake, weight gain, and a number of metabolic markers in rats, including blood insulin, leptin, and triglycerides, in a preclinical context. Furthermore, this investigation noted alterations in the quantity of pancreatic beta cells and the size of adipocytes, indicating extensive metabolic impacts of WP in animal models.

A study by Abbas *et al*., reported the anti-proliferation and apoptotic effects of whey drinks containing probiotics in human prostate cancer cell lines (PC-3 and DU-145). Whey drinks containing Lactobacillus acidophilus La-05, Lactobacillus acidophilus La-03, Lactobacillus casei-01, and Bifidobacterium animalis Bb-12. The whey drinks compounds induced widespread apoptosis in both cell lines [45].

5. CONCLUSIONS

The information above leads us to the conclusion that whey protein is bad for bodybuilders' health. Since this publication has discussed the possible advantages and disadvantages of whey protein, a more demonstrative investigation is warranted. The evidence appears to be in favor of retaining adequate muscle mass in the elderly, rather than definitely pointing to a faster deterioration of bone mass due to its substantial effect on liver and renal function. More thorough research is required to determine whether supplementing with WP can have any negative consequences.

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