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Protein Supplementation and its Impact on the Body and Health of Athletes, Bodybuilders and Patients

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Abstract

Background. Protein supplementation and high-protein diets are widely used in sports and clinical nutrition to improve muscle mass, recovery, and body composition(1,2). However, their systemic effects on different physiological systems remain debated and appear to depend on factors such as protein source, intake level, and individual health status(3–7).

Aim. The aim of this study was to review and synthesize current scientific evidence on the effects of protein supplementation and high dietary protein intake on multiple physiological systems in athletes, bodybuilders, and selected clinical populations.

Material and methods. A narrative literature review was conducted using PubMed, Scopus, and Google Scholar databases. Peer-reviewed meta-analyses, systematic reviews, and clinical trials published between 2017 and 2026 were included. Both human and animal studies relevant to physiological mechanisms were considered, while studies involving pediatric populations and single case reports were excluded. The selected publications were qualitatively analyzed according to their reported effects on the musculoskeletal, renal, hepatic, cardiovascular, gastrointestinal, and dermatological systems.

Results. Evidence indicates that adequate protein intake supports increases in muscle strength(3), fat-free mass(3), recovery, and improvements in body composition, particularly when combined with resistance training(7,8). Higher protein intake does not appear to negatively affect bone health(5,9) and may support bone mineral density when calcium intake is sufficient(5). Current evidence does not demonstrate clear harmful effects of higher protein intake on kidney function in healthy individuals(6,10), although renal responses may depend on protein source, intake level, and underlying health conditions(6,11). Findings related to liver function(10,12), gut microbiota(6,10,12), cardiovascular outcomes(13), and dermatological effects(10,14) remain inconsistent and context-dependent.

Conclusions. Protein supplementation within recommended ranges appears safe and beneficial for most healthy and physically active individuals. However, its systemic effects depend on multiple factors, including protein source, total intake, physical activity level, and individual health status. Further long-term, well-controlled studies are needed to clarify the long-term effects of sustained high protein intake on different physiological systems.

Keywords: protein supplementation, whey protein, high-protein diet, athletes, bodybuilders, body composition, kidney function

1. Introduction

Protein supplementation and high-protein diets are widely used in both athletic populations(15) and clinical settings(16), with the aim of enhancing performance, supporting recovery, and improving body composition. In athletes and bodybuilders, increased protein intake is commonly employed to promote muscle hypertrophy and strength adaptations(1,3,5), while in clinical populations it is often used to counteract muscle wasting and support nutritional status(6). At the same time, protein intake from both dietary sources and supplements has been associated with a wide range of physiological effects that extend beyond skeletal muscle.

Despite its widespread use, the overall evidence regarding the systemic effects of high protein intake remains inconsistent and often context-dependent. Reported outcomes vary according to protein source (animal vs. plant-based), total daily intake, timing of supplementation, training status, and underlying health conditions(7). While a large body of research supports beneficial effects on muscle mass(17), recovery, and body composition, findings related to other organ systems such as the kidneys, liver, gut microbiota, cardiovascular system, and skin are less consistent and sometimes contradictory.

Therefore, a comprehensive synthesis of current evidence is needed to better understand both the benefits and potential risks associated with protein supplementation. This article aims to systematically review and organize the available literature on the effects of protein supplementation and high dietary protein intake on multiple physiological systems, including skeletal muscle, bone health, body composition, renal and liver function, cardiovascular outcomes, gut microbiota, and dermatological responses, in athletes, bodybuilders, and patient populations.

Research Objective: The objective of this study is to review and organize current scientific evidence on the effects of protein supplementation and high dietary protein intake from various sources on different physiological systems in athletes, bodybuilders, and selected patient populations.

2. Research materials and methods

2.1. Participants

Not applicable. This study is a literature-based narrative review and did not involve human participants.

2.2. Procedure

This study was conducted as a narrative literature review to summarize current evidence on the effects of protein supplementation and high dietary protein intake on health and physiological function. A literature search was performed using the PubMed, Scopus, and Google Scholar databases with keywords including “protein supplementation”, “whey protein”, “athletes”, “bodybuilders”, “kidney function”, “musculoskeletal system”, “gut microbiota”, “body composition”, “cardiovascular health”, and “liver function”.

Peer-reviewed meta-analyses, systematic reviews, and clinical trials published between 2017 and 2026 were included, many of which synthesized findings from earlier studies. Both human and animal studies were considered when relevant to physiological mechanisms. Studies involving pediatric populations and single case reports were excluded, as were conference abstracts and articles without full-text access.

The selected publications were analyzed and categorized according to their reported effects on major physiological systems, including the musculoskeletal, renal, hepatic, cardiovascular, gastrointestinal, and dermatological systems, with particular attention to athletes, bodybuilders, and clinical populations.

2.3. Data collection and analysis

Relevant studies were identified through database searches and screened based on their titles, abstracts, and full texts. Publications meeting the inclusion criteria were reviewed and their findings were extracted and organized according to the physiological systems investigated. The collected data were then qualitatively analyzed in order to identify consistent patterns, potential health benefits, and possible adverse effects associated with protein supplementation across different populations.

The study selection process involved an initial screening of titles and abstracts to remove clearly irrelevant publications. Subsequently, full-text articles were assessed for eligibility according to the predefined inclusion and exclusion criteria. Only studies meeting the methodological and thematic requirements were included in the final analysis.

2.3.1. AI

AI was utilized for two specific purposes in this research. Text analysis of clinical reasoning narratives to identify linguistic patterns associated with specific logical fallacies. Assistance in refining the academic English language of the manuscript, ensuring clarity, consistency, and adherence to scientific writing standards. **AI** were used for additional linguistic refinement of the research manuscript, ensuring proper English grammar, style, and clarity in the presentation of results. It is important to emphasize that all AI tools were used strictly as assistive instruments under human supervision. The final interpretation of results, classification of errors, and conclusions were determined by human experts in clinical medicine and formal logic. The AI tools served primarily to enhance efficiency in data processing, pattern recognition, and linguistic refinement, rather than replacing human judgment in the analytical process.

3. Research results

3.1. Muscles

Morton et al. in their meta-analysis presented in total, 49 studies from 17 countries met the inclusion criteria. Among these, 10 studies included resistance-trained participants, and 14 study groups consisted exclusively of female participants. Altogether, the analyzed studies included 1863 participants with a mean age of 35 ± 20 years.

This meta-analysis evaluated interventions involving dietary protein supplementation and their effects on muscle- and strength-related outcomes during prolonged resistance exercise training (RET; resistance exercise training). The results indicated that dietary protein supplementation enhanced training-induced adaptations compared with control conditions.

Specifically, protein supplementation augmented increases in muscle strength and fat-free mass (FFM). Improvements in FFM were more pronounced in individuals who were already resistance-trained. In contrast, the effectiveness of protein supplementation in increasing FFM decreased with increasing chronological age.

Additionally, the analysis indicated that the benefits of protein supplementation on FFM did not continue to increase when total daily protein intake exceeded approximately 1.6 g/kg/day.(1)

In the review by Antonio et al., evidence from multiple intervention studies indicates that protein supplementation can support improvements in muscle mass, strength, recovery, and body composition, particularly when combined with structured training programs.

In a controlled intervention involving 48 resistance-trained individuals, participants were assigned to a normal protein intake (~2 g/kg/day) or a high-protein intake (>3 g/kg/day) while following a periodized resistance-training program. Both groups demonstrated significant improvements in fat-free mass (FFM), strength, and performance measures. Although the normal protein group experienced greater total body weight gain, the high-protein group showed larger reductions in fat mass and body fat percentage. No adverse changes in blood parameters were observed.

Additional intervention studies also reported positive effects of protein supplementation. In endurance-trained athletes, supplementation with whey protein (30 g/day) during a two-month training period resulted in reduced body fat and increased leg muscle volume. In another randomized intervention, participants performing supervised resistance training while consuming whey protein isolate demonstrated significantly greater increases in muscle mass, strength in several muscle groups, and total work output compared with a placebo group.

Comparative studies evaluating different protein sources showed that whey protein supplementation produced greater increases in muscle size than leucine-matched collagen peptide supplementation following a resistance-training program, although no differences were observed for strength or power. In athletes from other disciplines, mixed protein supplementation containing both plant and animal proteins improved muscle function and sport-specific performance. Evidence also indicates that protein hydrolysates may facilitate recovery from exercise-induced muscle damage. (5)

3.2. Body mass

Studies summarized by Antonio et al. have examined the effects of high protein intake on body composition in physically active individuals. Under hypocaloric conditions, higher protein intake has been associated with attenuated loss of FFM and greater reductions in fat mass in both active and overweight populations.

In resistance-trained individuals, a study in which participants consumed 4.4 g/kg/day of protein reported a significant increase in total energy intake; however, no significant changes in body mass or body composition were observed compared with the control group. In another study comparing 2.3 vs. 3.4 g/kg/day of protein, both groups experienced similar increases in FFM, while the higher-protein group showed a greater reduction in fat mass.

Additionally, an 8-week crossover study in resistance-trained males reported that participants consuming 3.3 ± 0.8 g/kg/day of protein and higher caloric intake than controls (2.6 ± 1.0 g/kg/day) showed no significant change in fat mass. (7)

Studies of Patel investigating protein supplementation in patients with cancer-related cachexia have reported improvements in body mass and lean tissue. In a different study, patients with solid tumors and weight loss exceeding 5% were supplemented with a nutritional formula containing β-hydroxy-β-methylbutyrate (3 g/day), L-arginine (14 g/day), and L-glutamine (14 g/day).

After four weeks of supplementation, the treated group showed an increase in body mass of 0.95 ± 0.66 kg, whereas the control group experienced a decrease of 0.26 ± 0.78 kg.

Additionally, the supplemented group demonstrated a significant increase in fat-free mass (1.12 ± 0.68 kg).

The positive effects of supplementation were maintained over a 24-week period, with a total increase in body mass of 1.60 ± 0.98 kg ($P < 0.05$). No adverse effects or negative impacts on quality-of-life measures were reported in the supplemented group. (6)

3.3. Bone health

Evidence from consensus reports by Antonio et al. indicates that variations in protein intake within typical dietary ranges account for approximately 2–4% of bone mineral variation in adults. Higher protein intakes above 0.8 g/kg/day were associated with higher bone mineral density, a slower rate of bone loss, and a reduced risk of hip fractures in older adults, provided calcium intake was sufficient.

Other studies presented in the same review indicate that protein intake above the recommended dietary allowance did not demonstrate detrimental effects on bone health. Studies examining higher protein consumption, including intakes exceeding 2.2 g/kg/day over periods of six to twelve months in physically active females, reported no negative changes in whole-body or lumbar bone mineral density compared with control groups consuming approximately 1.5 g/kg/day. Meta-analyses evaluating milk-derived protein products also indicated that protein of dairy or animal origin does not adversely affect bone health.(5)

Systematic review of Lamina included studies investigating bone-related outcomes in adult populations from multiple countries. The duration of the included studies ranged from six months to 1.5 years. The primary outcomes assessed included indicators of bone health, particularly bone mineral density. Participants were generally categorized based on their level of protein intake, with comparisons made between groups with higher protein intake and those with lower protein intake.

Across the analyzed studies, no significant differences were observed between the high-protein and low-protein intake groups in relation to the measured bone health outcomes. Overall, the available evidence in adults was insufficient to draw definitive conclusions regarding the relationship between protein intake and the risk of bone disease. (9)

3.4. Kidneys

The overview of Tidmas included findings from 13 studies describing case reports of bodybuilders with kidney-related diseases. Across these studies, several renal conditions were reported. The most frequently observed were 25 cases of acute kidney injury (AKI) or acute tubular necrosis (ATN), 20 cases of focal segmental glomerulosclerosis (FSGS), and 10 cases of nephrocalcinosis. Other reported conditions included acute interstitial nephritis (AIN) (5 cases), nephrosclerosis (5 cases), chronic interstitial nephritis (3 cases), and various other forms of glomerulonephritis (7 cases).

Protein intake levels were reported inconsistently across the included studies. Only three studies documented bodybuilders with protein intake exceeding the commonly recommended range for athletes (1.4–2.0 g/kg/day). In one study, the reported intake was approximately 2.0 g/kg/day, while in the remaining studies protein intake was not specified.

Importantly, in all three studies in which bodybuilders consumed more than 2.0 g/kg/day of protein, participants were also using anabolic steroids. In two of these studies, creatine supplementation was additionally reported. All individuals described in the case reports were male bodybuilders aged between 18 and 49 years. (18)

In an experimental animal study presented in Vasconcelos review, short-term whey protein supplementation was associated with increased plasma urea concentrations, higher urinary volume, and elevated urinary calcium excretion. Additionally, decreases in urinary pH and citrate levels were observed.

In contrast, other experimental evidence reported no significant adverse effects of whey protein supplementation on renal biomarkers. A systematic review of experimental studies found that whey protein supplementation did not significantly alter markers of kidney function, including serum creatinine and urea levels, and did not produce structural changes in renal glomeruli or tubules. (10)

Evidence from several studies suggests that whey protein supplementation does not adversely affect renal function in healthy individuals. However, higher protein intake has been associated with physiological changes such as renal hyperfiltration and increased urinary calcium excretion compared with lower protein consumption. These changes have been linked in some reports to an increased risk of proteinuria and chronic kidney disease (CKD).

Research also indicates that the type of dietary protein may influence renal outcomes. Observational data have shown that higher consumption of red meat is associated with an increased risk of end-stage renal disease. In contrast, dietary interventions involving plant-based diets have demonstrated beneficial effects. In patients with nondiabetic nephrosis, transitioning from a mixed animal–plant diet containing 1.0–1.3 g/kg/day of protein to a vegan diet containing 0.7 g/kg/day resulted in a significant reduction in proteinuria.

Large population-based analyses have also reported associations between vegetarian dietary patterns and kidney health. In a cohort of 55,113 participants—including vegans, ovo-lacto vegetarians, and omnivores—vegetarian diets were associated with a lower prevalence of chronic kidney disease and reduced prevalence of proteinuria compared with omnivorous diets. (6)

Presented by Cava et al. human studies investigating the renal effects of protein supplementation have reported mixed findings. A study conducted in 2020 observed an improvement in estimated glomerular filtration rate (eGFR) among sarcopenic older adults who consumed whey protein (WP)–micronutrient beverages.

Findings from a study conducted in 2017 involving both men and women consuming whey protein reported increases in urinary calcium excretion and a decrease in urinary pH. In another study conducted in 2021 among gym users, only slight alterations in blood urea levels were observed during protein supplement use.

A survey-based study conducted in 2023 among high-risk individuals with human immunodeficiency virus (HIV) who were consuming anabolic and performance-enhancing supplements (APES) while undergoing pre-exposure prophylaxis (PrEP) reported elevated serum creatinine concentrations in approximately 12% of users. (12)

3.5. Liver function

Studies presented by Vasconcelos investigating the relationship between whey protein (WP) supplementation and liver function have reported both adverse and beneficial outcomes. A case study described hepatic cholestasis accompanied by jaundice in a healthy young male following prolonged use of protein supplements, including whey protein and creatine, in the absence of biliary obstruction or hemolysis.

Conversely, several studies have reported beneficial effects of whey protein on liver-related biomarkers, particularly in individuals with existing liver conditions. In individuals with nonalcoholic steatohepatitis (NASH), 12-week supplementation with 20 g/day of whey protein isolate was associated with increased glutathione levels and improved antioxidant capacity. Additionally, in healthy subjects, consumption of 45 g/day of whey protein in bar form for 14 days resulted in increased lymphocyte glutathione concentrations. (10)

Another study presented by Cava reported effects of whey protein (WP) supplementation on liver function varied across the analyzed studies. One clinical study conducted in patients with nonalcoholic steatohepatitis (NASH) demonstrated beneficial outcomes, including reductions in hepatic steatosis and oxidative stress following WP supplementation. In contrast, another study involving recreational gym users reported slight alterations in liver function markers, including increased aspartate aminotransferase (AST) and urea levels.

Additionally, one investigation examining the use of appearance- and performance-enhancing supplements (APES), in which WP was a major component, found that approximately 8% of users developed significant elevations in liver enzymes (grade 3–4 ALT/AST).

Preclinical evidence also reported variable findings. One animal study demonstrated increased hepatic oxidative stress markers in rats supplemented with WP. Another experimental study observed liver toxicity and elevated inflammatory markers in untrained mice following WP supplementation. (12)

3.6. Cardiovascular

A randomized trial of Fakete investigating the effects of different macronutrient sources consumed with an isoenergetic high-fat breakfast and lunch evaluated postprandial blood pressure. The study included 30 healthy, non-smoking men and women with mildly elevated blood pressure (120/80–159/99 mmHg), aged 30–77 years, who were not taking antihypertensive or cholesterol-lowering medications.

The results showed that whey protein significantly reduced systolic blood pressure (SBP) 5 hours after ingestion compared with both Ca-caseinate (−15.2 ± 13.6 mmHg) and maltodextrin (−23.4 ± 10.5 mmHg).

No significant differences between treatments were observed in serum ACE activity, although the direction of the observed effects followed the order whey protein > casein > maltodextrin. High inter-individual variability in ACE activity responses was reported.(13)

3.7. Gut function and microbiota

Studies presented by Vasconcelos examining whey protein (WP) supplementation in athletes have reported changes in gut microbiota composition, including a reduction in certain beneficial bacterial populations and an increase in bacteria belonging to the *Bacteroides* phylum. Conversely, other research has observed positive microbiota modulation following WP consumption, including increased abundance of beneficial genera such as *Bifidobacterium* and *Lactobacillus*. (10)

In Patel’s study investigating the effect of protein supplementation on athletes’ gut microbiota, no significant changes in overall microbiota diversity were observed. However, an increase in the abundance of the *Bacteroidetes* phylum, associated with proteolytic activity, was reported, while health-associated taxa such as *Roseburia*, *Blautia*, and *Bifidobacterium longum* were decreased. These findings suggest that prolonged protein supplementation may negatively influence gut microbiota composition.

In contrast, an observational study of rugby players whose protein intake represented 22% of total energy intake showed a decrease in the *Bacteroidetes* phylum compared with healthy controls consuming 15% of energy from protein. These results indicate that both the quantity and source of protein may play important roles in shaping intestinal microbiota.(6)

In studies presented by Cava examining the impact of protein supplementation on athletes' gut microbiota, no significant changes in overall microbiota diversity were observed. However, an increase in the abundance of the *Bacteroidetes* phylum, associated with proteolytic activity, was reported, while beneficial taxa such as *Roseburia*, *Blautia*, and *Bifidobacterium longum* showed decreased presence.

Conversely, in athletes consuming a high-protein diet (protein contributing 22% of total energy intake), a decrease in the *Bacteroidetes* phylum was observed compared with controls consuming 15% of energy from protein. These findings suggest that both the amount and source of protein may influence gut microbiota composition. (12)

3.8. Skin

Chronic protein supplementation has been associated with increased expression of acne in individuals engaging in physical activity. Reports indicate that the nutritional composition of whey protein (WP) may contribute to these effects. The study reported by Vasconcelos observed a progression of acne lesions after two months of WP supplementation; however, no control group was included, making it unclear whether similar changes would occur in the absence of supplementation. (10)

On the other hand Muhaidat presents study where approximately half of the participants used protein supplements, with a higher proportion among acne patients (59%) than controls (42.5%), a statistically significant difference. Whey protein was the most commonly used supplement, consumed by 47% of acne patients and 27.7% of controls, also showing a significant difference. Use of other protein supplement types (casein, whey blends, creatine) did not differ between groups. Duration and frequency of supplement use were similar across cases and controls, with most participants using supplements for more than three months and over half taking them daily. Acne primarily affected the face (80%), followed by the back (43%), shoulders (28%), and chest (11%). Severity was mostly mild (66%), with moderate (19%) and severe (15%) cases. No correlation was observed between acne severity and age, BMI, smoking status, vitamin B12, corticosteroid use, or overall protein supplementation.

Multivariate logistic regression identified whey protein intake as the only significant predictor of acne, with an odds ratio of 2.94, indicating that participants consuming whey protein were nearly three times more likely to have acne compared to non-users. (14)

4. Discussion

4.1. Muscles

The findings of meta-analysis by Morton et al.(3) indicate that dietary protein supplementation enhances adaptations to prolonged resistance exercise training (RET), particularly in relation to muscle strength and fat-free mass (FFM). These results support the role of adequate protein intake in optimizing training-induced improvements in muscle mass and strength.

The observed increases in FFM were more pronounced in individuals who were already resistance-trained, suggesting that training status may influence the magnitude of the response to protein supplementation. Conversely, the effectiveness of protein supplementation appeared to decrease with increasing chronological age, indicating that age-related physiological changes may affect the anabolic response to dietary protein.

Another important finding was that increases in FFM did not continue beyond a total daily protein intake of approximately 1.6 g/kg/day. This suggests the presence of a threshold above which additional protein intake may not further enhance muscle mass adaptations during resistance exercise training.

The findings of Antonio et al.(7) across the reviewed studies support the role of protein supplementation in enhancing adaptations to training and improving recovery in athletes. Protein provides essential amino acids required for muscle protein synthesis, which is fundamental for increases in muscle mass and strength, particularly during resistance training. Rapidly digested proteins such as whey may further support recovery by quickly delivering amino acids to muscle tissue after exercise.

Different protein sources appear to produce broadly comparable adaptations, although whey protein often demonstrates slightly greater effects on muscle hypertrophy due to its amino acid profile and rapid digestion. Plant-based proteins such as soy can still provide comparable benefits for muscle adaptation and antioxidant status when total protein intake is adequate.

Overall, the available evidence indicates that adequate dietary protein intake and protein supplementation can be effective and safe strategies for supporting muscle growth, strength adaptations, recovery, and improvements in body composition in athletes, particularly when combined with resistance training. However, the magnitude of these benefits appears to be influenced by factors such as training status, age, total dietary protein intake, and the type of physical activity performed, suggesting that optimal protein requirements may vary across populations. For example, endurance athletes may experience improvements in body composition and recovery markers, although protein supplementation does not consistently enhance endurance performance outcomes. Furthermore, current evidence suggests that the benefits of protein intake tend to plateau within recommended intake ranges, and additional supplementation is unlikely to provide further performance advantages when dietary protein consumption is already sufficient.

4.2. Body mass

In Antonio's review(7) the available evidence suggests that higher protein intake may support favorable changes in body composition, particularly in physically active individuals. Studies summarized by Antonio et al. indicate that increased protein consumption may help preserve FFM during periods of caloric restriction while simultaneously promoting greater reductions in fat mass. This effect is especially relevant for individuals undergoing weight loss interventions, where the preservation of muscle mass is an important determinant of metabolic health and physical performance.

Research conducted in resistance-trained individuals further suggests that very high protein intakes do not necessarily lead to increases in fat mass, even when total caloric intake is elevated. In several studies, participants consuming large amounts of protein experienced either stable body composition or reductions in fat mass despite higher energy intake. These findings challenge the assumption that excess energy derived from protein alone promotes fat accumulation. Instead, dietary composition and macronutrient distribution may play an important role in determining body composition outcomes.

In Patel's review(6) protein supplementation may play an important role in the management of cancer-related cachexia, a condition characterized by progressive loss of skeletal muscle and adipose tissue. The findings reported by Patel et al. suggest that supplementation with a combination of β-hydroxy-β-methylbutyrate, L-arginine, and L-glutamine may help counteract weight loss and muscle wasting in patients with solid tumors. In this study, patients receiving the supplemented formulation demonstrated increases in both body mass and fat-free mass, while the control group continued to lose weight. These results indicate that targeted amino acid supplementation may support the preservation of lean tissue during cancer-associated catabolic states.

The sustained improvement in body mass observed during the 24-week follow-up period suggests that such supplementation strategies may provide longer-term benefits in maintaining nutritional status. Importantly, the absence of reported adverse effects and the lack of negative impact on quality-of-life measures indicate that this type of nutritional intervention may be well tolerated in clinical populations. Nevertheless, further research is required to determine the optimal composition, dosage, and duration of protein supplementation in patients with cancer-related cachexia.

Overall, current evidence indicates that high-protein diets may be beneficial for maintaining lean tissue and supporting favorable body composition changes, particularly among physically active individuals engaged in resistance training. However, further long-term studies are required to clarify the effects of sustained high protein intake across different populations and training conditions.

4.3. Bone health

Results contained in the work of Antonio et al.(5) challenge the longstanding assumption that high-protein diets negatively affect bone health. The misconception largely stems from the acid-ash hypothesis, which proposes that high intake of protein and grain products increases dietary acid load, leading to greater net acid excretion, elevated urinary calcium, and mobilization of calcium from bone tissue. However, this mechanism has several limitations. Evidence suggests that increased urinary calcium during high-protein intake may partly result from enhanced intestinal calcium absorption rather than bone resorption. Furthermore, dietary patterns must be considered holistically, as reduced consumption of fruits and vegetables—important sources of potassium and alkalizing compounds—may contribute to dietary acidity rather than protein intake alone.

Mechanistic evidence also supports a beneficial role of protein in bone metabolism. Bone tissue itself contains a substantial protein component, accounting for roughly half of its weight and one-third of its mass, indicating that adequate protein intake is essential for maintaining bone structure. Protein consumption also stimulates the production of insulin-like growth factor-1, a hormone that promotes bone formation. In addition, higher protein intake supports increases in muscle mass and strength, which can increase mechanical loading on bone tissue and stimulate bone adaptation over time.

The findings of Lamina's review(9) indicate that dietary protein intake does not appear to negatively influence bone health in adults. Across the analyzed studies, which included populations from multiple countries and study durations ranging from six months to 1.5 years, no significant differences were observed between groups with higher and lower protein intake in relation to bone health outcomes, including bone mineral density.

Overall, current evidence indicates that higher protein intake does not harm bone health and may contribute positively to bone mineral density and fracture prevention when consumed as part of a balanced diet with adequate calcium intake. Consistent with this, studies have reported no significant effects of dietary protein intake on bone turnover markers, including markers of bone formation and bone resorption.

4.4. Kidneys

According to Tidmas et al.(18) current dietary guidelines recommend protein intakes of approximately 0.75–0.8 g/kg/day for the general population, with higher recommendations of 1.4–2.0 g/kg/day for athletes to support training adaptations, muscle growth, and the maintenance of FFM. Protein plays a fundamental role in muscle anabolism, and higher intakes may be particularly beneficial for strength and power athletes, including bodybuilders.

Evidence from the reviewed literature suggests that high protein intake alone is rarely identified as the primary contributor to kidney dysfunction. In many reported cases, additional factors such as the use of anabolic substances or other lifestyle behaviors were also present. Studies examining isolated high-protein diets in healthy individuals have generally not demonstrated detrimental renal effects, although most interventions have been relatively short in duration. For example, research involving resistance-trained men consuming between approximately 2.5 and 3.5 g/kg/day of protein for extended periods (up to one or two years) did not report significant changes in kidney function markers such as serum creatinine, blood urea nitrogen, or estimated glomerular filtration rate.

Nevertheless, protein intake is an important physiological regulator of kidney function. High-protein diets can induce glomerular hyperfiltration and increase intraglomerular pressure, which may potentially contribute to structural renal damage over time. Acute hemodynamic responses to high protein intake have been observed even in healthy individuals, and some long-term epidemiological studies have reported associations between higher protein consumption and faster declines in kidney function. For individuals with pre-existing chronic kidney disease, lower protein intake is commonly recommended to reduce the risk of disease progression.

In the context of bodybuilding, dietary strategies often vary depending on the phase of training. Athletes typically follow periods of caloric surplus to promote muscle growth and phases of caloric restriction before competitions to reduce body fat. While carbohydrate intake is often the primary macronutrient manipulated during these phases, protein intake generally remains high throughout. Importantly, many studies describing kidney dysfunction in bodybuilders do not report the specific training phase or detailed dietary patterns of the individuals involved.

This lack of information limits the ability to accurately determine protein intake levels and their potential role in renal outcomes.

In Vasconcelos review(10) alterations in urinary parameters such as decreased urinary pH, hypocitraturia, and hypercalciuria are recognized risk factors for nephrolithiasis. These changes may occur in the context of high-protein diets and have therefore raised concerns about the potential renal consequences of prolonged high protein intake.

Some studies included in Vasconcelos review(10) have associated hyperproteic diets with kidney-related outcomes in both animal and human models. Experimental evidence has shown that short-term supplementation with whey protein can increase plasma urea concentrations, urinary volume, and urinary calcium excretion while simultaneously decreasing urinary pH and urinary citrate levels. Such changes may create a urinary environment that favors the formation of kidney stones.

One of the primary theoretical concerns regarding high-protein diets is the potential for increased renal workload. Protein metabolism produces urea, which must be excreted by the kidneys. As a result, high protein intake may increase glomerular filtration rate and intraglomerular pressure, potentially leading to renal hyperfiltration. This mechanism has been suggested as a possible contributor to long-term kidney stress.

However, evidence from systematic reviews suggests that renal hyperfiltration in response to higher protein intake may represent a physiological adaptive mechanism rather than a pathological process in healthy individuals. Supporting this interpretation, experimental studies examining whey protein supplementation have reported no significant changes in kidney function biomarkers such as serum creatinine or urea. Furthermore, these studies did not observe histological alterations in renal glomeruli or tubules.

In Patel's review(6) the relationship between dietary protein intake and kidney health remains complex and dependent on several factors, including the amount and type of protein consumed, as well as the health status of the individual. While evidence suggests that protein supplementation does not impair kidney function in healthy individuals, excessive protein intake may increase renal workload through mechanisms such as hyperfiltration and increased calcium excretion.

The type of protein consumed may also play an important role in renal outcomes. Animal-based proteins, particularly red meat, have been associated with a higher risk of advanced kidney disease in some populations. In contrast, plant-based dietary patterns appear to be associated with lower prevalence of chronic kidney disease and proteinuria, suggesting potential protective effects.

Clinical guidelines for individuals with chronic kidney disease often recommend dietary protein restriction to slow disease progression and reduce the risk of end-stage kidney disease. However, the effectiveness of protein restriction remains debated. Lower protein intake may help reduce renal stress, but excessive restriction can contribute to protein–energy wasting, particularly in patients with advanced disease.

One approach used in clinical practice is the supplementation of very low-protein diets with ketoanalogues. These compounds can be converted into amino acids through transamination and may help maintain nutritional status while limiting nitrogen intake. Evidence from pooled analyses suggests that very low-protein diets supplemented with ketoanalogues are associated with a lower relative risk of adverse outcomes compared with low-protein diets alone. Nevertheless, the benefits observed in these studies may also be influenced by differences in overall protein intake levels or protein quality.

The available human studies presented by Cava et al.(12) suggest that the renal effects of protein supplementation may vary depending on the population studied, the type of supplementation, and underlying health conditions. In older adults with sarcopenia, whey protein supplementation combined with micronutrients was associated with improvements in estimated glomerular filtration rate, suggesting potential benefits for maintaining kidney function in this population.

Conversely, other studies have reported physiological changes associated with protein supplementation, including increased urinary calcium excretion and reduced urinary pH. While these changes may reflect alterations in renal handling of minerals and acid–base balance, their long-term clinical significance remains unclear.

Evidence from recreational gym users indicates that protein supplementation may lead to minor changes in markers such as blood urea levels, although these changes appear to be relatively small. In contrast, individuals with additional medical factors, such as those receiving antiviral therapy or undergoing pre-exposure prophylaxis for HIV, may experience greater alterations in renal biomarkers such as serum creatinine during supplementation with anabolic and performance-enhancing supplements.

Overall, current evidence suggests that high-protein diets do not independently increase the risk of kidney dysfunction in healthy bodybuilders, as reported cases of renal disorders are often associated with additional risk factors and underlying health conditions, making individuals with pre-existing kidney impairment more vulnerable. While high protein intake and supplementation may induce short-term physiological changes in renal function and urinary composition, there is limited evidence that whey protein supplementation causes structural kidney damage in healthy individuals. The renal effects of protein intake appear to depend on multiple factors, including protein quantity, protein source, individual health status, and concurrent treatments, indicating that dietary protein management—particularly in individuals with chronic kidney disease—should be individualized rather than based on uniform restriction. However, the current evidence base remains limited, and further long-term, well-controlled studies are needed to clarify the clinical significance of these renal responses across different populations.

4.5. Liver function

According to Vasconcelos review(10) the potential impact of high-protein diets on liver function remains a topic of ongoing debate. Excessive protein intake may increase metabolic workload in the liver due to the need to process amino acids through deamination and the urea cycle, which converts ammonia into urea for excretion. This process may theoretically increase hepatic stress when protein intake is chronically elevated. However, the metabolic fate of amino acids may differ depending on physiological conditions such as physical activity. During exercise, circulating amino acids derived from whey protein are more likely to be utilized by skeletal muscle for protein synthesis, primarily through activation of anabolic signaling pathways such as the mammalian target of rapamycin (mTOR). Increased amino acid uptake by muscle tissue may therefore reduce hepatic amino acid metabolism and urea production.

Despite these physiological considerations, evidence linking whey protein supplementation to liver injury in healthy individuals remains limited. A case report described the development of hepatic cholestasis and jaundice in a young individual following prolonged use of protein supplements, including whey protein and creatine. However, isolated case reports cannot establish a causal relationship and should be interpreted with caution.

Conversely, several studies suggest that whey protein may exert beneficial effects on liver health, particularly in individuals with pre-existing liver conditions. Whey protein supplementation has been associated with increased glutathione levels and improved antioxidant capacity, which may help reduce oxidative stress and inflammation in liver diseases such as nonalcoholic steatohepatitis (NASH) and chronic hepatitis.

According to Cava(12) although some studies suggest that increased protein intake may negatively affect liver function in the long term, evidence from human studies remains limited. Elevated liver enzyme activity and increased creatinine levels have been reported in individuals undergoing chronic pharmacological treatment, suggesting potential hepatic and renal stress associated with high protein availability. Similarly, protein supplementation has been associated with alterations in hepatic and renal markers, including increased ALT and AST levels. Notably, these alterations appear to be more pronounced under sedentary conditions, whereas resistance training may exert a mitigating effect on these outcomes.

The protective role of physical activity is further supported by preclinical evidence. Experimental studies in animal models have demonstrated that prolonged protein supplementation in untrained subjects can lead to increased markers of liver toxicity, enhanced apoptotic signaling, and elevated inflammatory mediators, including IL-6, IL-7, and TNF-α. Additionally, higher levels of hepatic oxidative stress have been observed in supplemented animals compared with non-supplemented controls. One proposed mechanism is that, during physical exercise, a greater proportion of amino acids is directed toward skeletal muscle for protein synthesis, thereby reducing the metabolic burden on the liver.

These findings highlight the complexity of the relationship between whey protein supplementation and liver health. While it may have potential therapeutic benefits in certain clinical populations, further research is needed to clarify its long-term effects on liver function. At the same time, its unsupervised or indiscriminate use, particularly among sedentary individuals, may pose potential risks to hepatic health.

4.6. Cardiovascular

The findings of Fekete study(13) suggest that whey protein may exert beneficial effects on postprandial blood pressure compared with other macronutrient sources. Specifically, whey protein consumption resulted in a greater reduction in systolic blood pressure several hours after ingestion compared with both casein and carbohydrate sources. These results support previous observations indicating that dairy proteins, particularly whey protein, may contribute to improved cardiovascular outcomes.

One of the proposed mechanisms underlying the hypotensive effects of milk proteins involves the inhibition of angiotensin-converting enzyme (ACE), which plays a key role in blood pressure regulation. Although the present study did not demonstrate significant differences in serum ACE activity between treatments, the observed trend—showing greater effects for whey protein compared with casein and maltodextrin—may partially support this mechanism. However, the high inter-individual variability observed in ACE responses suggests that additional research with larger sample sizes is necessary to clarify the role of ACE inhibition in mediating the blood pressure–lowering effects of whey protein.

Overall, these findings indicate that whey protein supplementation may have potential benefits for cardiovascular health, although further studies are required to better understand the physiological mechanisms involved and to confirm these effects in larger and more diverse populations.

4.7. Gut function and microbiota

Diet and physical activity are recognized as important factors influencing the composition of the intestinal microbiota. Dietary patterns may induce both beneficial and adverse modifications in microbial populations. Physical activity has also been shown to modulate the gut microbiota, partly through alterations in intestinal transit time and the promotion of beneficial bacterial growth.

Evidence from Vasconcelos(10) suggests that whey protein supplementation may influence intestinal microbiota, although the findings are inconsistent. Some studies report potentially beneficial increases in probiotic-associated bacteria, while others describe less favorable shifts in microbial composition. These discrepancies may be explained by differences in study design, including supplementation duration, protein dose, baseline diet, training status, and inter-individual variability in gut microbiota.

Similarly, Patel(6) reports that protein supplementation can modulate gut microbiota composition, but the direction of these changes is inconsistent. Some observations indicate a reduction in beneficial taxa and an increase in proteolytic bacteria with higher protein intake, whereas other findings show opposite or neutral effects depending on total dietary protein and overall nutritional context. Variability in protein source and study protocols further contributes to these divergent outcomes.

Consistent with this, Cava(12) also highlights that protein supplementation may alter gut microbial composition, with some studies suggesting increased proteolytic bacteria and reduced beneficial taxa following prolonged or high-protein intake. However, moderate high-protein diets may produce different effects depending on baseline dietary patterns and energy contribution from protein. As with other reviews, heterogeneity in methodology, small sample sizes, and differences in participant characteristics limit the ability to draw definitive conclusions.

Overall, the available evidence indicates that protein intake can influence gut microbiota composition, but the effects appear highly context-dependent. Further large-scale, well-controlled studies are needed to clarify the relationship between protein supplementation and intestinal microbial health.

4.8. Skin

Evidence from Vasconcelos(10) indicates that the relationship between whey protein supplementation and behavioral or dermatological outcomes remains inconclusive. Some studies suggest potential associations with increased acne incidence or changes in mood, such as anger, although these findings are limited by methodological weaknesses, including lack of control groups and insufficient adjustment for confounding variables. Proposed mechanisms include the presence of insulin-like growth factor 1 (IGF-1) in some dairy-derived products, which may promote sebaceous activity, cutaneous cell proliferation, and hormonal changes involved in acne development, even though whey protein itself does not contain IGF-1.

Similarly, Muhaidat(14) reports that dietary factors, including dairy products and high-carbohydrate intake, may contribute to acne development through insulin- and IGF-1-mediated pathways. Whey protein supplementation is associated with a higher likelihood of acne, potentially due to its insulinotropic effects that stimulate sebum production, follicular hyperkeratinization, and inflammation. However, these findings are based on cross-sectional data with limited sample sizes, and therefore cannot establish causality.

Overall, both reviews suggest a possible link between whey protein intake and acne development, but the evidence remains limited and inconsistent. Further large-scale, prospective studies measuring hormonal markers such as insulin and IGF-1 are needed to clarify these associations and determine their clinical relevance.

5. Conclusions

Overall, the available evidence suggests that adequate protein intake supports improvements in muscle strength, fat-free mass, recovery, and body composition when combined with resistance training, with benefits tending to plateau above ~1.6 g/kg/day(3). Beyond muscle-related outcomes, higher protein intake may also contribute to favorable changes in body composition, bone health, and cardiovascular function. Importantly, there is no clear evidence that higher protein intake is harmful to kidney function in humans; renal effects appear to depend on factors such as protein source (plant vs. animal)(6), total intake, and individual risk profile rather than protein intake alone. Evidence regarding liver function, gut microbiota, and dermatological outcomes remains inconsistent and highly context-dependent. Overall, protein supplementation appears safe and beneficial within recommended ranges for most healthy and active populations(15), although further long-term studies are needed to clarify its effects across different physiological systems and clinical conditions.

Disclosure

The authors declare no financial or personal relationships that could have influenced the work reported in this paper.

Supplementary Materials

Not applicable.

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Conflicts of Interest

The authors declare no conflict of interest.

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