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Adhering to recommended dietary protein intake for optimizing human health benefits *versus* exceeding levels

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Proteins are essential nutrients that contribute to the structure of various cells and tissues in the body. Consuming adequate protein in our diet is crucial for optimal health and bodily function. This review article explores the role of dietary proteins by examining global consumption patterns and consumer perceptions of high-protein diets. It investigates recent research trends regarding the impact of proteins on human health and wellness across various countries and communities. The review analyzes key health outcomes associated with very high-protein diets, especially those exceeding recommended values. It includes the latest evidence on the influences of animal and plant proteins on health in different groups of participants. Furthermore, this manuscript delves into the scientific discussion surrounding the optimal amount of protein in the human diet.

Introduction to dietary protein consumption

Proteins, generally sourced from animals and plants, are one of the three major macronutrients in food products, alongside lipids and carbohydrates. While a balanced diet with appropriate amounts of carbohydrates, fats, and proteins is essential, recent recommendations from media, food markets, and scientific communities have strongly emphasized increasing daily protein intake. Consumers are encouraged to choose food with higher protein levels for various health benefits. Moreover, there is a growing trend promoting the selection of food items enriched with nutritious dairy and plant proteins over those primarily composed of animal proteins.

To enhance our understanding of the necessary amount of these essential nutrients in our diet, governmental organizations provide guidelines for nutritional requirements. For example, the daily Recommended Dietary Allowance (RDA) of protein by the United States Department of Agriculture (USDA) is 0.8 g of protein per kg of body weight (0.36 g lb^{-1}.) for a healthy diet.[1] The British Heart Foundation (BHF) suggests a daily protein intake of 0.75 g per kg of body weight.[2] This recommendation translates to an average daily intake of 45 grams for healthy women and 55 grams for healthy men. BHF also advises adults to consume two portions of meat, fish, nuts, or tofu daily to maintain general health. The U.S. Food and Drug Administration (FDA) provides a similar guideline and suggests a daily intake of 50 g of protein for a 2000-calorie diet.[3]

A thorough examination of these recommendations compared with the assessment of food consumption by the U.S. population as reported by The Food Surveys Research Group (FSRG) from Beltsville, MD covering the period from 2017 to March 2022 reveals that the average protein consumption in America exceeds the recommended values by a significant margin. Based on FSRG findings, men consume dietary proteins at twice the RDA while women's intake exceeds the recommendations by approximately 50%.[4] Although these data confirm that the average American diet contains ample protein, Nils–Gerrit Wunsch and the International Food Information Council report that many consumers increased their protein intake in 2022 (Fig. 1),[5,6] and 68% plan to further increase their protein consumption in 2023 (Fig. 2). It is important to mention that according to World Resource Institute (WRI) data, the overconsumption of protein is not limited to the U.S. In wealthy regions, "People are eating more proteins than they need".[7] As shown in Fig. 3, the data indicates that, excluding sub-Saharan African and Asian countries (except China and India) that have the lowest per capita protein consumption, people in all other regions consume more than the daily protein requirement of 68 grams per person per day, which is about 30% higher than RDA. The World Resource Institute estimates that the global average per capita protein consumption will increase to 80 grams per person per day by 2050.[7] Importantly, while over 50% of the U.S. population meets or exceeds the recommended total protein intake from their food, data from the Dietary Guidelines for Americans 2020–2025 (Fig. 4) shows that their diets do not meet the recommendations for the food subgroups within each food group.[1] This information suggests that consumers should

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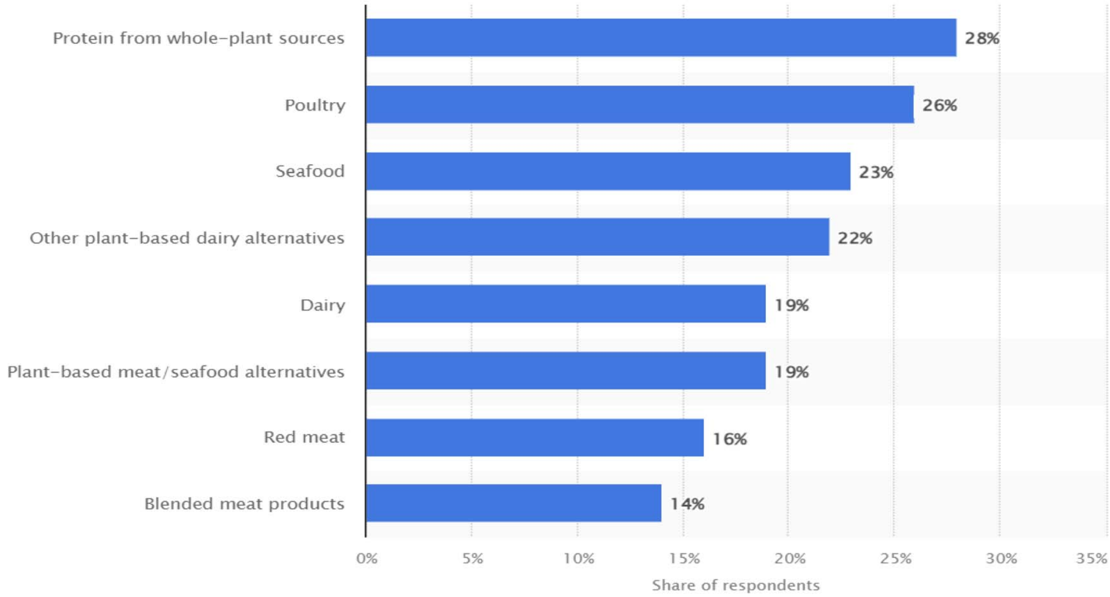

Fig. 1 Increase of protein consumption of consumers in the United States during 2022 (reported in 2023). Adapted from Wunsch[5] with permission from Statista, copyright (2025).

review their food choices if they aim to achieve a healthy dietary pattern. This article highlights key facts and findings regarding the implications of high-protein diets (HPD) and exceptionally high-protein diets (EHPD), emphasizing their significant role in promoting human health.

Protein's structure and sources

Studies have shown that both animal and plant proteins are made of 20 amino acids (AAs) and have various structures and shapes that affect their functions and characteristics in the body. Among these 20 amino acids, nine are essential, meaning they cannot be synthesized by mammalian digestive systems and must be obtained through diet. Essential and nonessential amino acids, with different chemical compositions and structural properties, link together to form peptide and polypeptide chains. The combination of these polypeptides can produce protein subunits, which then form more bonds to create the final tertiary and quaternary structures. These protein structures are important for their physiochemical properties, which impact their biological roles, including how they are broken down and utilized by the body for growth, repair, and other vital functions. For example, protein conformation influences digestibility, with tightly folded globular proteins and those containing a hydrophobic core being more resistant to enzymatic hydrolysis.[8] Therefore, understanding the relationship between protein structure and health is essential for

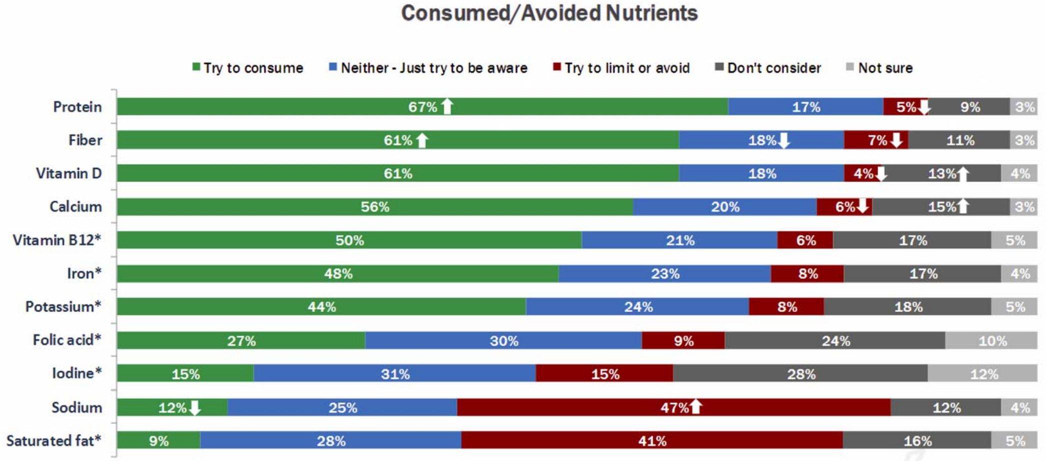

Fig. 2 Consumers reported their desire for consumption of different nutrients in 2023. Adapted from World Resources Institute,[7] with permission, copyright (2025).

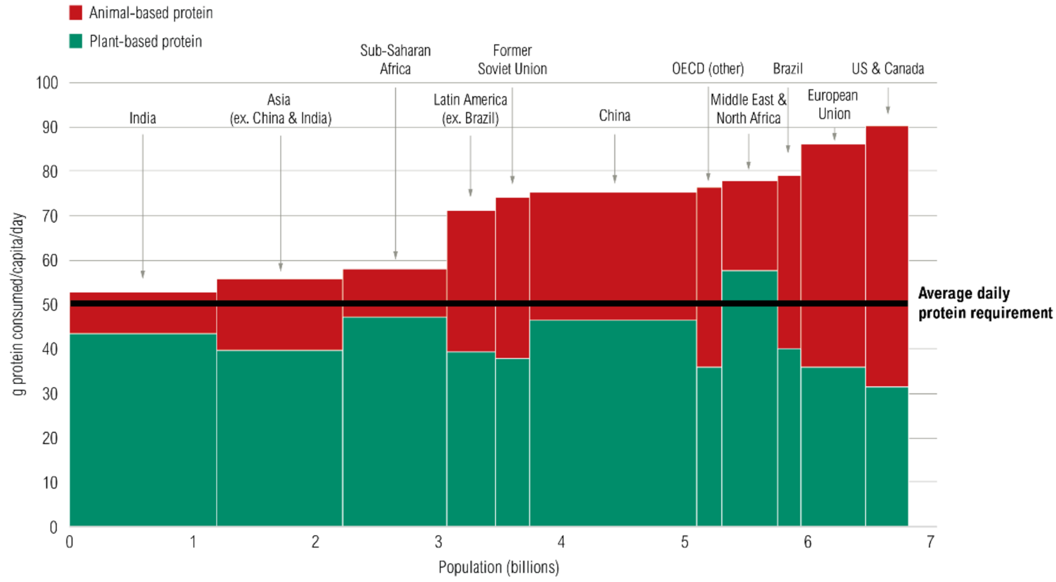

Fig. 3 The consumption of animal and plant proteins in different parts of the world and their comparison to the average daily protein requirements. Adapted from World Resources Institute,[7] with permission, copyright (2025).

determining how different types of proteins contribute to human health after consumption.

These quality properties of proteins, such as their structure and nutrient content, are largely defined by their source. Dietary proteins are divided into two groups: animal-based proteins and plant-based proteins. Animal proteins, such as meat, eggs, and milk, are known as "complete proteins" that provide all the essential amino acids that the human body needs. Plant proteins are found in pulses, soy, nuts, seeds, and grains. Plant proteins, with exceptions such as soy, quinoa, chia seeds, hemp seeds, and buckwheat, are considered "incomplete proteins" because they are missing, or do not have enough of, one or more of the essential amino acids which makes the protein imbalanced.[9] Moreover, their variable amino acid composition, and their structural complexity, can limit their digestion. For example, the presence of anti-nutrients such as phytic acid, tannins, lectins, oxalates, saponins, protease inhibitors, and glucosinolates further complicates the digestibility and nutrient

Fig. 4 Comparison of recommendation and dietary intakes of food in U.S. population ages 1 and older. Adapted from Dietary Guidelines for Americans,[1] with permission from the U.S. Department of Agriculture and U.S. Department of Health and Human Services, copyright 2020.

absorption of plant-based proteins. Phytic acid found in legumes and grains binds to essential minerals like iron, zinc, and calcium and reduces their absorption.[10] Tannins and lectins, observed in legumes and beans, can interfere with protein breakdown, form indigestible complexes, and cause digestive discomfort.[11,12] Protease inhibitors in beans and legumes can block protein digestion by inhibiting enzyme activity.[13] These anti-nutrients (less common in animal proteins), make plant-based proteins more difficult to digest and make their nutrients less bioavailable. To overcome these challenges and ensure a complete intake of essential amino acids, it is recommended to incorporate a variety of plant protein sources into the diet, which helps optimize their nutritional value and support better digestion.

Although studies highlight health benefits from all sources of protein, data from the Food and Agriculture Organization of the United Nations shows that the consumption of animal protein is still dominant over plant protein consumption in some countries (Fig. 5A).[8] This trend is changing in the U.S. as Americans shift their protein sources in 2023 (Fig. 5B). International Food Information Council (IFIC) 2023 reports a 25% increase in Americans' consumption of poultry and whole plant proteins in 2023 compared to 2022.[6] While various justifications are reported for this shift, 60% of the participants claimed following a vegan, vegetarian, or plant-based diet would be healthier, and 36% connected their protein source change to the environment or animal welfare improvement. The study's findings on proteins and diverse health impacts regardless of protein source, highlight the importance of informing individuals about protein functions in human metabolism.

Proteins' functions and protein intake amounts

Dietary proteins, structured in various forms, serve multiple health functions that can be classified into several categories. Upon digestion, proteins are broken down into amino acids, which are essential for various metabolic reactions. These amino acids are involved in other reactions, such as their degradation, that contribute to the production of adenosine triphosphate (ATP), the primary energy source of the cell, as well as glucose and fatty acids. Amino acids are also involved in structuring and repairing other macromolecules such as body proteins, tissues, muscles, organs, and DNA. This structural role is crucial for maintaining the integrity and function of the body. Many proteins also serve as enzymes that catalyse essential biochemical reactions for metabolism and overall physiological processes. This enzymatic activity is critical for chemical reactions that sustain life. Furthermore, certain proteins act as hormones. They regulate physiological processes and play significant roles in managing body fluid levels and acid–base balance and promote wound healing and tissue regeneration.[14–16] Proteins are integral to the transport of nutrients throughout the body, ensuring that essential substances are effectively delivered to cells and tissues, which supports various biological functions. Moreover, adequate protein intake is vital for maintaining robust immune functions. Studies have shown that dietary protein deficiency impairs immune functions and antibody levels, which results in an increasing susceptibility to infectious diseases.[17,18] Lack of protein can result in slow metabolism and loss of muscle mass, strength, and balance. A diet low in protein inhibits the growth and development of children and teenagers.[19,20] Studies have documented that an adequate level of protein in the diet can boost metabolism, replace proteins that were previously broken down and utilized by the body, and may help in burning more calories than one would burn in a low-protein diet.[21,22]

Researchers have also shown that extra protein in the diet does not get stored as protein and instead is converted to carbohydrates or fats. This phenomenon can be observed in some recent studies that investigated the relationship between an EHPD and coronary heart disease.[23,24] Data from 124 prospective cohort studies, including 101 studies contributing to a meta-analysis, were followed for a period ranging from 2.2 to 30 years. The findings indicate that high total protein intake is associated with a lower incidence of cardiovascular disease (CVD).[23] This study also reported high total carbohydrate intake was associated with high CVD morbidity and high intake of total fat was associated with a decreased all-cause mortality. However, this effect varies depending on the type of the consumed fat and the fats' chemical composition.

The effectiveness of HPD in reducing obesity and cardiovascular benefits is also reported by reviewing the results of a 15 year research study on Swedish women. Authors from seven institutions in Sweden worked with 43 396 randomly selected women (ages 30–49) and found a higher risk of CVD in cohorts with high-protein consumption (62.9 ± 19 g per day).[25] The association between protein consumption and cardiovascular morbidity and mortality was investigated further by other studies and meta-analyses. It became more controversial when favourable and unfavourable outcomes were reported. Zhang *et al.* (2016) conducted an analysis of 12 prospective studies with 528 982 participants, finding no significant link between total protein intake and stroke incidence. However, the study revealed that plant protein was associated with a lower risk of stroke.[26] Qi and Shen, in a meta-analysis of 12 prospective cohort studies of 483 615 participants, showed that higher intake of total protein had no significant association with all-cause cardiovascular and cancer mortality. However, when Qi and Shen compared the outcomes of protein sources, they suggested that a higher plant protein consumption may reduce all-cause and cardiovascular mortality. While the authors did not report the percentage reduction, they concluded that animal protein consumption is associated with higher incidences of cardiovascular mortality.[27] In 2020, Naghshi *et al.* analysed 715 128 participants from 32 prospective cohort studies.[28] They reported that while intake of total protein and animal protein is not associated with the risk of cancer and CVD, an additional 3% daily energy from plant protein was associated with a 5% lower risk of death from all causes.

Despite the variations among the studies mentioned earlier, it is notable that they converge on the cardiovascular benefits associated with plant-based proteins. However, a challenge lies

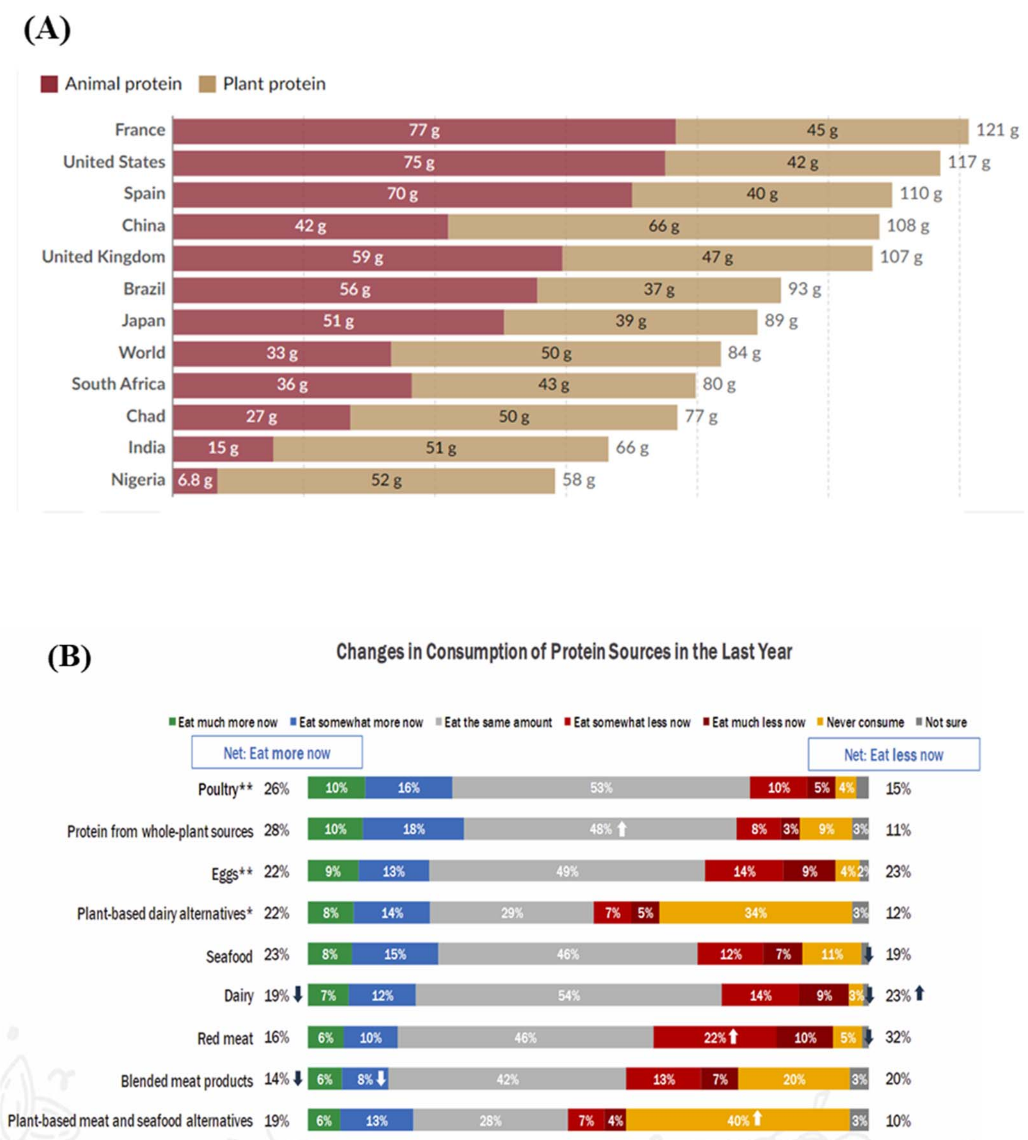

Fig. 5 (A) Daily protein supply (gram per person per day) from animal- and plant-based food in different countries in 2020. (B) Americans changes in consumption of proteins sources in 2022–2023. Adapted from International Food Information Council,[6] with permission from the International Food Information Council, copyright 2023.

in the assessment of protein quantity in participants' diets. These studies typically compare the lowest and highest levels of protein consumption, often overlooking analysis based on moderate protein intake. Mantzouranis *et al.* attempted to fill this gap and assessed the effects of both normal and extra high-protein content diets on CVD risk in adults with no established cardiovascular disease. Their meta-analysis from three cohorts of 90 231 participants who received more than 18% of their total dietary energy intake from protein showed no association with a lower risk of stroke. Moreover, analysis of 13 studies of 525 047 participants with normal protein intake showed no statistically significant differences for non-fatal myocardial infarction, stroke, or cardiovascular death among the participants.[24] The authors concluded that extra high-protein consumption may not affect cardiovascular prognosis.

In contrast to these studies that reported neutral or slightly positive effects of protein on CVD, stroke, and risk of death, Zhang *et al.* reported different outcomes of EHPD on CVD. Zhang *et al.* performed a 2 month mice study and worked with a Standard Western diet (Std.WD) with 42% fat and 15% protein *versus* excessive protein Western Diet (HP WD) with 43% fat and 46% protein (3 times more protein).[29] Although the results showed positive effects of a high-protein diet on body weight and glucose tolerance, an increase in atherosclerotic plaque was observed in mice fed with an exceptionally high-protein diet (Fig. 6). The authors also reported a significant increase in mice plaque complexity when the HP WD was continued for 16 weeks. Studies have also investigated the effects of diets with high, low, and normal protein intakes on kidney functions and examined the effects of extremely high protein and protein

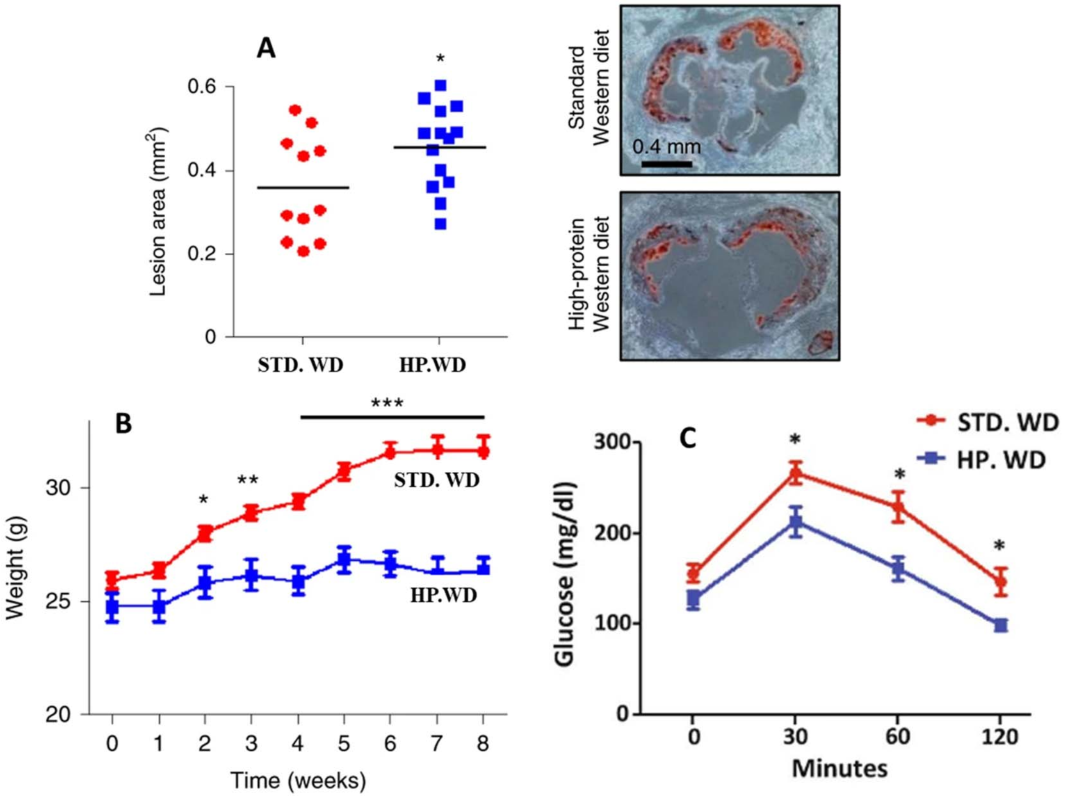

Fig. 6 Comparison between (A) atherosclerotic plaque burden, (B)total body weight, (C) glucose tolerance of ApoE-null mice fed by standard Western Diet (STD.WD) or high protein Western diets (HP WD) for 8 weeks. Adapted from Zhang *et al.*,[29] with permission from Nature Research, copyright 2020.

types on kidney health.[30–32] Esmeijer *et al.*[33] found that high dietary protein intake (DPI) accelerates kidney function decline over time in older adults with a history of heart disease. Patients consuming ≥1.2 g per kg per day protein had a 2-fold faster eGFR decline compared to those with <0.8 g per kg per day. Jhee *et al.*[34] reported high dietary protein intake linked to a 3.5-fold higher likelihood of kidney hyperfiltration in 9226 South Koreans. The study found this effect was stronger in people with preexisting kidney hyperfiltration and was confirmed in a larger cohort of 40 113 participants. Although the definitions used for hyperfiltration and rapid kidney decline were arbitrary, the findings suggest that high DPI may worsen kidney function, especially in those with hyperfiltration. This suggests that long-term high DPI may harm kidney health. Recently Narasaki *et al.* investigated the correlation between daily protein intake (DPI) and the intake of protein of higher biological value (HBV), such as meats, to all-cause mortality among American adults with varying kidney functioning (impaired *versus* normal kidney function). The 11 year continuous study of 27 604 adults showed that higher DPI (>1.4 gkgday) and greater intake of HBV protein led to a greater risk for premature death in participants with impaired kidney function, whereas low DPI (<0.6 g per kg per day) increased mortality in those with normal kidney function. The authors suggest that additional research is necessary to clarify the specific mechanisms linking higher DPI to health outcomes in CKD.[35] These results agreed with researchers from Brigham and Women's Hospital (BWH) who studied the correlation between EHPD and glomerular filtration rate (GFR), a measure of kidney function.[36] They reported a significant decline in GFR of women with high DPI and impaired kidney function when the decline was three times the GFR in women with the lowest DPI. The BWH study, based on data collected from 1634 women aged 42 to 68 over 11 years, highlights the significance of protein sources and recommends that older women, who are more likely to have decreased kidney function, consult a physician to assess their kidney health before starting a high-protein diet.

Another concern with EHPDs that warrants more investigation is the possibility of their adverse effects on bone health. While it is believed that high protein may not affect blood pH and serum bicarbonate levels of healthy consumers,[37,38] some studies have hypothesized that higher acidic load from animal proteins could mobilize calcium carbonate of skeletal origin to act as a buffer and lead to osteoporosis.[39] Recent studies and meta-analyses have questioned the hypothesis and found no association between osteoporosis and high-protein diets in older participants when adequate dietary calcium intake is ensured. For example, Wu *et al.* concluded a meta-analysis of twelve prospective cohort studies with 407 104 adults aged 18–89 years with protein intake of low to high (the highest <98 g day^{-1}). The authors grouped the data based on total protein, animal protein, and vegetable protein, and analysed their effects on four fracture types: all fractures of whole body, hip fracture, vertebral fracture, and limb fracture.[40] It was concluded that total protein intake higher than the Recommended Dietary Allowance (RDA), from any source, may reduce the risk of hip fractures by 11%, but does not affect the risk of all fractures and limb fractures. They emphasize that the specific effects on hip fractures were not differentiated between diets high in animal or vegetable proteins. In response to high-protein diets and their impact on bone health, Massey argues that excess dietary protein from any source may not necessarily benefit bone health.[41] However, other constituents in the diet may counteract the effects of EHPD on bones. Heer *et al.* hypothesized that EHPD (1.45 g per kg per day) combined with recommended calcium and potassium plus an additional 0.72 g branched-chain amino acids per day would prevent bone loss in women who are on bed rest.[42] The comparison of the data with those who received 1g per kg per day of protein showed that high-protein intake can increase bone loss during bed rest. While the authors suggest further long-term investigations on the effects of protein on muscle mass without the risk of reducing bone mineral density, their results are aligned with other studies that related the efficacy of diets' protein content to their inclusion of essential amino acids and lifestyle behaviours such as being physically active. Other evaluations of the efficacy of HPDs in human health are done by investigating the outcomes from a combination of HPD with other parameters, such as low carbohydrate intake and high exercise. Lagiou *et al.* concluded that low carbohydrate-high protein diets (without considering the carbohydrate or protein sources) may increase CVD risks.[25] Clifton *et al.* studied similar diets and reported that adding of 5% or more of protein intake can affect body fat mass, insulin, and fasting triglyceride levels. The authors did not report differences in blood lipids and glucose levels in low carbohydrate diets combined with excessive protein.[43]

Similar analysis was done by Chen *et al.* when they combined extra high whey protein diets (1.6 g per kg per day, two times more protein than RDA suggestion) with exercise intervention to examine the effects of very high protein and exercise on cardiometabolic health in middle-aged adults with obesity.[44] After 12 weeks of intervention, the authors stated that the combination of exercise and whey protein (EP) resulted in lower total cholesterol and triglycerides compared to the control group (C) (Fig. 7). While within-group comparisons of EP diet did not affect LDL and CHOL/HDL, a significant decrease in HDL was reported in diets with high whey protein. The authors also reported that exercise effectiveness in abdominal fat mass remained consistent between standard diet and exercise (E) and EP groups where the insulin sensitivity index improved in the EP group ($p = 0.016$) and had "a trend to improve" in the E group ($p = 0.052$). Chen *et al.* reported no changes in skeletal muscle mass before and after the intervention in all groups.[44] This observation agrees with Bhasin *et al.* study who examined the effect of protein intake greater than RDA on maintaining lean body mass in older adults.[45] While the author did not specify the protein source, their randomized clinical trial (of 92 men, average 73 years) shows that increasing protein intake from 0.8 g kg^{-1} d^{-1} to 1.3 g kg^{-1} d^{-1} does not affect lean body mass, muscle power, or strength.

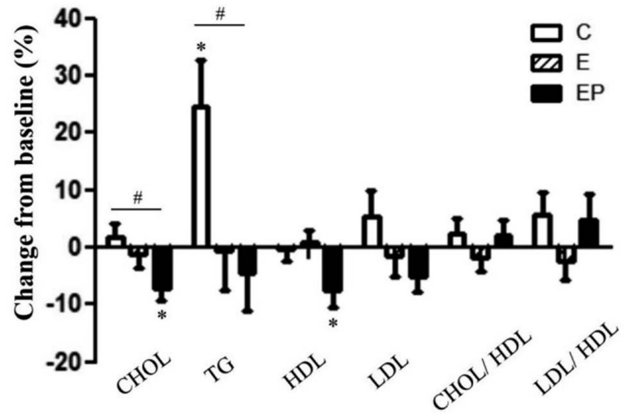

Fig. 7 Effects of high whey protein diet combined with exercise (EP), standard diet and exercise (E), and a control group (C) on triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (CHOL), CHOL/HDL, and LDL/HDL on 69 middle-aged adults with obesity. Adapted from Chen *et al.*[44] permission from Frontiers, copyright (2025), under CC BY license.

Health impacts of high-protein, low-carb, low-fat diets

A recent survey from the International Food Information Council in 2023 reports that when consumers were asked about the definition of healthy food in 2023, the top three definitions for healthy food were "fresh" (40%), "low in sugar" (37%), and "good source of protein" (33%). The survey also reports that 14% and 19% of the respondents picked "low carbohydrates" and "low calorie", respectively, as other definitions of healthy food.[6] It is a common understanding that many people decrease their calorie intake by reducing their total dietary fats. Moreover, the survey reports that 23% of the respondents reported a reduction in their carbohydrate intake. Although it is not clear what portion of this 23% pool decided to increase their protein intake, there is no information on how the compensation for low carbohydrate diets would bring other macronutrients into their diet. These all necessitate considering the impacts of a high protein, low carbohydrate, low fat diet on the individual's health.

The complexity of low-carbohydrate and high-protein diet is two-sided and may cause different health concerns with micronutrients abundance and deficiency. For example, children with low carbohydrate diets can have low calcium, iron, and magnesium. They may also have low levels of other biologically active phytochemicals of fruits, vegetables, and grains, and high blood urea nitrogen and uric acid levels.[46] The concern intensifies when protein consumption exceeds the recommended level. This excess consumption can lead to an increase in glomerular filtration rate (GFR), which may raise blood urea nitrogen levels and place a greater load of uric acid on the kidneys.

Studies also reported that high-protein, low-carbohydrate diets may pose clinical problems for patients with coronary artery disease, such as diabetes, nephropathy, higher LDL, and increased circulating free fatty acids.[46–49] It is also stated that high-protein, low-carbohydrate diets are not superior weight loss diets and there is no need to cut carbohydrates if caloric intake remains constant. In 2021, Dimosthenopoulos *et al.* performed a short-term study and compared three dietary patterns including high-protein/low-carbohydrate (HPLC), Mediterranean/low glycaemic index (MED), and a reference diet (REF) in 15 patients with type 1 diabetes over three-week periods with washouts.[50] As shown in Table 1, HPLC (20% carbs) showed better glycaemic outcomes than MED (40% carbs) and REF (50% carbs), with less time spent in hypoglycaemia and lower variability. Although HPLC performed significantly better in some metrics like time in range (TIR_{70-180}), which tracks the percentage of time a person's blood glucose levels stay within a healthy range (70–180 mg dL^{-1}), there was no significant difference in overall TIR when the target range was narrowed to 70–140 mg dL^{-1} across the groups. The authors suggested more research is needed to validate these results and assess long-term implications for diabetes management.

Results from a long-term meta-study analysis from 24, 32, and 33 individuals compared the effects of high-protein, low-fat diets to normal-protein, low-fat diets and showed no significant difference in obesity, cardiovascular disease, or glycaemic control.[51] The study concludes that "it seems premature to recommend high-protein diets in the management of overweight and obesity". While a limited number of studies examined the effects of high-protein, low-fat diets on weight loss, there are uncertainties about high protein and low-fat consumption particularly. However, it is important to note that proteins induce greater satiety compared to carbohydrates and fats and elevate energy expenditure and thermic effect of food (TEF), refers to the energy expended by the body in digesting, absorbing, and metabolizing nutrients from food.

Studies have also reported benefits from diets with high protein and low fat (HPLF) compared to those with moderate protein and fat, or high protein and high fat (HPHF) consumption.[52,53] They also compared two types of diets: high-protein, low-fat (HPLF) and standard-protein, low-fat (SPLF), both with the same calorie restrictions. The authors concluded that an isocaloric HPLF diet compared to a SPLF diet provides modest improvements in weight loss, fat reduction, and triglyceride levels. The comparison of HPHF and HPLF showed no diet-induced differences in overweight and underweight subjects, but a significant increase in basal metabolic rate (BMR) of normal weight subjects with HPHF diets. BMR is the number of calories burned by the body during basic lifestyle. Some studies reattributed their findings to the higher protein content of HPHF diets by considering equal thermogenic response for fats and carbohydrates.[53,54] The authors did not provide the fatty acid compositions (FACs) of the fats in the diets, nor specify the similarity or differences of FACs between the low- and high-fat diets. Additionally, they did not mention the protein sources used in the study. This information seems critical for accurately calculating the thermic effects of food and understanding their impacts on body metabolism.

Health benefits comparison of animal and plant protein

Researchers also performed studies to compare the health benefits of animal protein with plant protein in diets. Li *et al.* performed a meta-analysis of 5774 individuals with and without hyperlipidaemia (with a median age of 54 years, 5 : 3 women to

Table 1 The effect of three different diets on glycaemic control, glycaemic variability, and insulin needs. Adapted from ref. 51] with permission, copyright (2025)[a]

Diet	REF				HPD				MED				
Variable	Mean	SD	Median	IQR	Mean	SD	Median	IQR	Mean	SD	Median	IQR	*p*-Value
TIR_{70-140} (%)	48.33	13.72			54.87	14.11			50.53	12.81			0.105
TBR_{70} (%)			14.00	20.00			12.00	16.00			9.00	17.00	0.008*
TAR_{140} (%)	37.40	16.05			36.20	15.61			38.33	17.11			0.745
TAL_{140} (n)	13.53	3.56			13.07	3.99			14.40	2.97			0.459
TBL_{70} (n)	8.47	6.78			5.53	4.50			7.20	5.21			0.143
TIR_{70-180} (%)	67.53	12.73			74.33	12.85			70.20	12.86			0.055
TBR_{54} (%)			4.00	12.00			3.00	5.00			3.00	8.00	0.408
TAR_{250} (%)			2.00	4.00			1.00	4.00			1.00	4.00	0.068
TAR_{180} (%)			15.00	11.00			13.00	10.00			14.00	13.00	0.793
AvgGlu (mg dL^{-1})	128.87	22.01			131.53	21.04			132.60	24.65			0.620
CV (%)	41.48	8.69			36.18	9.30			38.15	9.10			0.032*
Total insulin dose (U)	32.16	9.43			29.00	12.99			36.00	15.17			0.025*
Prandial insulin (U)	12.00	10.17			10.50	9.50			13.00	10.83			0.825
Insulin correction (U)	3.10	2.58			3.33	2.45			2.80	1.55			0.584

[a] Abbreviations: AvgGlu, average glucose level; CV, coefficient of variation; HPD, high-protein/low-carbohydrate diet; IQR, interquartile range (Q3–Q1); MED, Mediterranean diet; REF, reference diet; SD, standard deviation; $TAL_{>140}$, times above limit 140 mg dL^{-1}; $TAR_{>140}$, times above range 140 mg dL^{-1}; $TBL_{<70}$, times below limit 70 mg dL^{-1}; $TBR_{<70}$, times below range 70 mg dL^{-1}; TIR_{70-140}, time in range 70–140 mg dL^{-1} *Statistical significance at the 0.05 level ($p < 0.05$) using repeated measures ANOVA (for parametric) and the Friedman test (for non-parametric).

men) and substituted their dairy and animal protein intake with plant protein.[55] As a result of this replacement, the study showed a reduction of 4% in each element of their cholesterol analysis including low-density lipoprotein cholesterol (LDL-C), non-high lipoprotein cholesterol (non-HDL), and apolipoprotein B. The authors reported a substantial heterogeneity for LDL-C and non-HDL results and concluded that "more high--quality randomized trials are needed to improve our estimates".[55] In agreement with Li *et al.*, Glenn *et al.* evaluated the association of vegetarian dietary patterns with major cardiovascular outcomes in 197 737 participants (with and without diabetes). They stated that "very low-quality evidence indicates that vegetarian dietary patterns are associated with reductions in coronary heart disease (CHD) mortality and incidence, but not with CVD and stroke mortality". Like the Li group's recommendation, Glenn *et al.* emphasized the need for additional research in various populations to increase the accuracy of their estimates.[56]

Investigation of the effects of EHPD on health is continued by other studies that examined the effects of protein amount and type on the risk of type 2 diabetes (T2D). *Via* a meta-study of 3 cohort studies of 4 146 216 individuals (with mean ages of 36, 51, 53), Malik *et al.* reported 7% and 13% higher risk of T2D in participants with the highest quantities of total protein and animal protein, respectively. The authors also report that the replacement of one serving of animal-protein foods (dairy foods, poultry, eggs, red meat, and processed meat) with one serving of vegetable-protein foods (variable comprising of whole grains, legumes, peanuts, peanut butter, and other nuts) decreased T2D risk by 23%.[57] Although the authors attributed the lower risk of T2D to the plant-protein content, a closer examination of the diet ingredients may reveal the impact of other micronutrients on the study's outcomes. Nuts for example, have a low glycaemic index (GI) and contain diverse fatty acid profiles, fibres, vitamins, and magnesium, all of which may positively affect blood sugar levels and diabetes. The comparison of the effect of consumption of total protein, animal protein, and plant protein on diabetes was also done by Shang *et al.* in 2016 (21 523 healthy participants, 61.7% women).[58] Like Malik *et al.*, the authors reported a 19% increased risk of T2D for higher animal protein intake across their studied geographic regions. A positive association of T2D risk (9%) with total protein intake was recorded for European or U.S. populations, and T2D risk was 5% lower in women and the U.S. population with higher plant protein intakes. It is important to note that the inverse association between plant protein intake and the incidence of T2D in some participants may be linked to the fibre, magnesium, vitamins, and fatty acids present in plant-protein diets. While the exact long- and short-term effects of EHPD on insulin sensitivity and type 2 diabetes (T2D) remain undetermined, Bawadi *et al.* reported the effects of very high-protein intake (of any type) on glycaemic control in diabetic patients (990 participants over 40 years old). Patients with 131.6 g daily protein intake (2.5 times higher than RDA but providing 19% of their average energy) showed 261% increased risk of poor glycaemic control (PGC) than those who took 35.5 g protein (lower than RDA). The authors also reported a positive relationship between protein intake and poor glycaemic control, with odds ratios (ORs) of 1.00, 1.68, and 1.62 (95% confidence interval) for diets containing 35.5 g, 58.7 g, and 79.9 g of protein, respectively.[59] An OR measures the strength of association between two events and compares the possibility of an event occurring in one group to another. An OR of 1 indicates no association, with equal odds in both groups. These analyses disagree with Gutierrez-Mariscal *et al.*, who worked with 1002 patients with CHD and suggest increasing plant protein intake as a therapy for type 2 diabetes; however, the study is not clear on the type of protein and whether the effects of other micronutrients (not just proteins) in the plant protein diets were taken to the account or not.[60] In another study, González-Ortiz *et al.* analysed the 7 day dietary records of 1221 participants 70–71 years of age and associated a higher insulin sensitivity and lower inflammation with a plant-based diet in elderly men with non-dialysis chronic kidney disease (CKD) stages 3–5. The authors also highlighted the higher amounts of vegetables, fruits, carbohydrates, potassium, and fibre, and the lower intake of fat and animal foods in the high plant-based diet that may affect the study outcomes.[61]

Wu highlights the importance of amino acid composition in protein diets and compares the effects of increased intake, optimal intake, and deficient intake, as well as the impacts of specific amino acid excess or deficiency in human diets.[62] Based on this literature, higher intake of AAs or protein increases AA oxidation, with excess AAs oxidized to CO_2, water, and urea. At optimal levels for protein synthesis, AA oxidation is minimized, and at below-required intake, AA oxidation is reduced to preserve AAs for protein synthesis. On the other hand, an excess of a specific AA in a protein-adequate diet increases its own oxidation without affecting others. A deficiency in an essential AAs may increase the oxidation of other AAs, as the deficiency limits their use for protein synthesis. Wu also illustrates the relationships between amino acid oxidation and dietary AAs intake in humans (Fig. 8).[62] As shown in Fig. 8, in individuals consuming a protein-adequate diet, an excess of a specific AA leads to increased oxidation of that particular AA without necessarily affecting the oxidation of other AAs. Conversely, if a diet is deficient in an AA, especially an essential amino acid, the oxidation of other AAs progressively increases with a higher dietary intake of AAs or protein. These factors all highlight the importance of selecting quality proteins in the human diet.

George *et al.* (2020) compared specific plant and animal proteins in diets by supplementing 40 g per day soy or casein to 135 individuals for three months. George's group did not report any differences in tartrate-resistant acid phosphatase (TRAP), and bone alkaline phosphatase (BALP) of the participants with different diets. However, they reported a positive effect on serum IGF-1 (insulin-like growth factor 1) in people on a soy diet (85.2% compared to 26.1% in a casein diet) and related this result to the favourable effects of the high amount of isoflavones (96 mg) in soy.[63] Insulin-like growth factor 1 is a hormone in our body that manages the effects of growth hormone (GH). This conclusion agrees with Akhlaghi *et al.*, who report the beneficial effects of soy isoflavones on body mass index and bone health.[64] The impacts of a 12 week diet with different combinations of

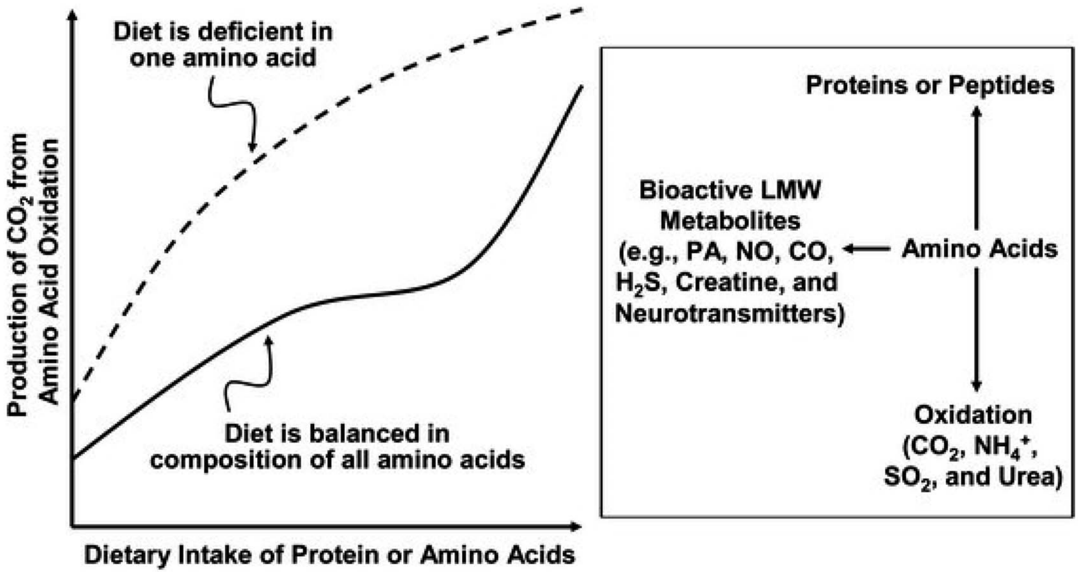

Fig. 8 Interrelationships between amino acids oxidation and dietary intake of amino acids or protein with or without a deficiency of one essential amino acid, adapted from Wu *et al.*,[62] with permission from CRC Press, copyright 2025.

plant and animal proteins (30 : 70, 50 : 50, and 70 : 30) on the bone health of 136 participants (aged 20–69) is documented by Itkonen *et al.*[65] The authors did not provide the daily intake (g) of each type of protein, but they did report an increase in bone turnover in plant-protein diets. This turnover is toward bone degradation and the breaking down of bone components because plant proteins are poor in calcium and vitamin D. While the comparison of the reviewed information shows some consistencies among the studies, the presence of significant inconsistencies and various hypotheses about the effects of protein content and type on human health remains irresolute and necessitates further investigation.

Conclusion

The information provided in this review highlights the significance of protein intake, particularly very high protein consumption, on individuals' metabolic processes. The reviewed studies show that various parameters such as age, body weight, and health conditions can affect proteins' functional properties. It highlights the potential advantages of consuming protein which can be maximized by adhering to the recommended intake and considering factors such as type (animal *vs.* plant), quality, and sources. Achieving this balance is crucial not only for individual health but also for addressing broader environmental and ethical concerns associated with dietary choices. Furthermore, the review identifies a gap in current research and emphasizes the need for further detailed investigation into the balance between adequate intake of all essential nutrients. This suggests that future studies should explore the complex interactions between dietary proteins and overall human health outcomes, particularly by considering the diverse needs and circumstances of individuals. Given the continuous development of the food industry, exploring the potential benefits of emerging protein sources, such as those derived from microorganisms, algae, and insects, could offer new opportunities to improve both health and sustainability. As the food industry continues to innovate, the development and commercialization of novel protein sources, such as those derived from microorganisms, algae, and insects, hold significant potential for improving both health outcomes and sustainability. Moreover, with ongoing advancements in nutritional science, new areas of research, such as the role of gut microbiota and the gut-brain axis, are becoming increasingly important in understanding how protein intake influences health. These areas of study offer promising directions for future investigations into how individual health conditions, age, and metabolic mechanisms interact with dietary proteins, providing a more comprehensive understanding of their effects on long-term health.

Data availability

Since this publication is a review article, all the data presented have been selected from reviewed journal articles or government agency websites. Therefore, the data can be obtained from these sources, and we do not have any additional data to provide.

Conflicts of interest

There are no conflicts to declare.

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