Narrative Review

Achieving High Protein Quality Is a Challenge in Vegan Diets: A Narrative Review

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The transition toward plant-based (PB) diets has gained attention as a plausible step toward achieving sustainable and healthy dietary goals. However, the complete elimination of all animal-sourced foods from the diet (ie, a vegan diet) may have nutritional ramifications that warrant close examination. Two such concerns are the adequacy and bioavailability of amino acids (AAs) from plant-sourced foods and the consequences for older vegan populations who have elevated AA requirements. This narrative review describes the challenges of achieving high protein quality from vegan diets. Data were synthesized from peer-reviewed research articles and reviews. Plant-sourced proteins provide poorer distribution of indispensable AAs (IAAs) and have poorer digestibility, partly due to their inherent structural components within the food matrix. The review addresses complexities of combinations of varied plant protein sources and why the inclusion of novel PB alternatives adds uncertainty to the achievement of adequate protein adequacy. Meal distribution patterns of protein and the ensuing physiological impacts deserve further research and are outlined in this review. Particular attention is given to describing the challenges of achieving sufficient protein and IAA intakes by aging populations who choose to follow a vegan diet. This review contributes to the emerging discussions of nutritional risks associated with vegan diets and adds perspective to the current dietary shifts toward PB diets.

Key words: *vegan diets, protein intake, protein quality, plant-based alternatives, elderly.*

INTRODUCTION

Nutritional deficiencies are a concern in unbalanced vegan diets.[1] Intake of micronutrients such as vitamin B_{12}, bioavailable iron, calcium, zinc, and iodine may be generally lower in vegan populations than in vegetarians and meat-eating counterparts.[2–8] For example, among young and healthy vegan men,[9] plasma values of long-chain polyunsaturated fatty acids, especially for docosahexaenoic acid,[10] were low even in contexts of sufficient α-linolenic acid intake. This reflects poor rate of enzymatic conversion from α-linolenic acid[11] via the desaturation-chain elongation system in humans.[12] Although protein intake may be lower in vegan groups compared with other diet groups, it is not necessarily below the daily requirements.[13,14] However, analysing the intake of utilisable protein deserves more attention, and the complexities of plant protein combinations and digestibility within each meal should be addressed to achieve the requirements of specific populations.[14,15] Protein deficiency is thus a relevant concern in vegan diets. This narrative review focuses on addressing the complications in achieving utilisable protein intake within the scope of a vegan diet.

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Dietary proteins provide amino acids (AAs) that perform structural, physiological, and regulatory roles in the human body.[16,17] Of importance are the 9 indispensable AAs (IAAs) that cannot be endogenously synthesized and so must be provided by food intake.[18] Diet choice is an important factor in achieving overall protein intake and adequate IAA composition for metabolic needs. Foods are unequal, however, in the distribution of fully bioavailable AAs to meet individuals' unique metabolic requirements. The provision of fully utilisable AAs denotes the protein quality of food, which varies among food sources,[16] with apparent differences between plant- and animal-derived foods.[19] Although plant-sourced foods (PSFs) provide all the IAAs, the overall profile is less favorable compared with animal-sourced foods (ASFs), due to factors such as poorer IAA composition compared with the body's requirement, the inherent structural properties of plant proteins, and the overall food matrix, which reduces their overall digestion, delivery, and bioavailability to peripheral tissues.[14,16,20]

Gross protein intake in high-income Western countries often meets and/or exceeds the daily requirement.[15] This may be attributed to predominantly omnivorous dietary patterns in these regions. A different outcome may emerge if meat and dairy were eliminated from the diet (ie, a vegan diet). A vegan diet is the most restrictive form of a plant-based (PB) diet, due to the exclusion of all ASFs,[21] which provide vital micronutrients and highly digestible AAs.[22–25] Whether protein intakes are adequate in vegan populations requires detailed research, and analysis must consider protein quality as well as total protein intake. This is an important investigation because IAA inadequacy to body tissues leads to nutritional and health concerns, especially during various stages of the life cycle (eg, pregnancy, lactation, infancy, adolescence, aging).[26,27] The strategic inclusion of varied and complementary protein sources is critical to achieve optimal intake of all utilisable AAs while maintaining a moderate food volume and caloric intake.[28] This may include pairing higher-quality legumes with cereals[29] and inclusion of novel PB alternatives that support the transition to a PB diet.

Ensuring adequate and balanced consumption of all IAAs through a diet consisting of only PSFs, although not impossible, is challenging. Adequate diet planning, knowledge, fortification, and supplementation strategies are essential. There are currently insufficient longitudinal studies to determine the nutritional and health implications of long-term vegan diets, especially in individuals with higher nutrient requirements, such as the elderly. Although research on novel PB alternatives is growing, more information on the nutritional adequacy of these foods in comparison with traditional PSFs, meat, and dairy is required.

The objective of this review was to consolidate relevant scientific findings to establish the considerations in achieving high protein quality in the contexts of a modern-day vegan diet. A secondary objective was to explore the nutritional and physiological challenges when eliminating all ASFs from the diet. This narrative review addresses the following: (1) why plant foods contribute poorer protein quality, (2) the implications of uneven protein consumption throughout the day, (3) current findings of protein quality in novel PSFs, and (4) the problems of a vegan diet in the aging population.

METHODS

Databases used to obtain relevant articles were Google Scholar, Connected Papers, and PubMed. Additional references were identified by a manual search through the reference lists of the selected articles. Duplicates were removed. Articles were selected to highlight difficulties in use of protein and AAs from PB foods and to describe the current research gaps in protein quality assessments, implications of novel PB foods, and the impact of vegan diets on the elderly population. Table 1 shows the list of search terms used to obtain relevant articles for this review.

Table 1. Search Summary Table

Concept	Search terms
General background of protein adequacy in vegan diets	"protein-quality" OR "protein intake" OR "protein consumption" AND "vegan diets" OR "plant-based diets" OR "plant-sourced foods"
Plant protein use in the body	"digestibility and utilisation of amino acids in plant foods", OR "anti-nutritional factors in plant foods" OR "absorption of plant-based proteins"
Nutritional impacts of novel plant-based alternatives	"protein in plant-based alternatives" OR "plant-based meat analogues" OR "plant-based meat alternatives", OR "plant-based-beverages", OR "plant-based milk alternatives", OR "plant-based dairy alternatives"
Protein quality (assessments and protein distribution)	"vegan diet" AND "amino acids" OR "amino acid composition" "essential amino acids" OR "indispensable amino acids", "protein distribution across a day" OR "meal protein distribution"
Vegan diets in elderly	"vegan diets in older adults", OR "elderly", OR "aging population"

Articles reporting on randomized controlled trials (RCTs), observational studies, meta-analyses, and systematic reviews were included, as were governmental and organizational reports. Open-access, full-text articles related to adoption of a vegan diet by adults and older adults (>18 years of age) from 1981 to 2024 were included. Articles not published in English and that reported on other types of PB diets (eg, vegetarian) were excluded.

DISCUSSION

A Brief Overview of Protein Structure, Digestion, and Use

Although carbohydrates, fats, and protein are macronutrients that can supply sources of energy for the body's needs, protein is distinguished by its provision of nitrogen[30,31] in its building blocks: the AAs.[32,33] How AAs are assembled into the tertiary and quaternary structures of protein is elaborated in the literature.[30,34,35]

Protein digestion in the gastrointestinal tract (GIT) requires the successive cleavage of peptide bonds within the tertiary structure by hydrolytic enzymes, proteases, and peptidases to yield smaller peptides and free AAs, which can then be absorbed through the enterocytes of the small intestine.[17,30,36] Within the enterocytes, pancreatic enzymes further hydrolyze peptides to smaller molecules of 6-8 AAs (oligopeptides), which then are completely hydrolyzed at the apical brush border to yield some free AAs.[30,36,37]

The greatest amount of absorption of free AAs occurs in the distal small intestine as a result of higher activity of peptide hydrolysis by brush border enzymes in the ileal membrane.[36] Amino acids derived from exogenous protein sources are extracted from the splanchnic tissues and directed toward metabolic functions in peripheral tissues such as muscles, organs, bone, and skin.[16] Amino acids that are absorbed in the large intestine and represented in fecal measurements do not convey significant nutritional implications.[36,37] Hence, the region of the GIT where digestibility scores are obtained is relevant when assessing protein quality.

Amino acid turnover is represented by the continuous provision and use of AAs, which creates variations in the body's nitrogen pool.[17,38–40] Contribution to the AA pool is achieved when degraded proteins are replaced through dietary input and endogenous synthesis, whereas reduction of the pool is attributed to AA catabolism and protein synthesis.[17,40,41] Removal of the amino group allows reuse of AAs for protein synthesis or conversion to other nitrogenous compounds (eg, purine and pyrimidine).[17,30,39] Lysine and threonine have side chains that contain an amino and hydroxyl group, respectively, which prevent enzymatic transamination.[42] Other AAs, however, could be diverted to transamination pathways to synthesize dispensable AAs (DAAs).[39] Nitrogen is converted to urea via the urea synthesis in the liver and subsequently excreted in the urine, feces, sweat, and integument.[38,43] This process is important for removing toxic ammonia from the catabolism of AAs.[17,40]

Challenges in Digestion and Use of Plant-Sourced Proteins

Poorer digestion of plant proteins compared with animal proteins may be related to the inherent microstructural arrangement of the protein, such as protein cross-linking and protein-chain rigidity.[44] Secondary configurations such as β-conformations are hydrophobic and promote protein aggregation.[45] This reduces the accessibility of proteases, thus inhibiting digestibility.[46] Compared with meat and milk proteins,[45,46] plant protein sources such as soy,[46,47] peas,[46,48] rice,[46,49] wheat,[46,50] and oat have high levels (>40%) of β-pleated sheet.[46,51] The intercalation of plant proteins with fiber also creates steric hindrance, which reduces the access points for enzyme catalysis.[52]

Antinutritional factors (ANFs) in PSFs also reduce the proteolytic activity of enzymes and hinder plant protein digestion.[20,30,53] For instance, legumes, cereals, potatoes, and tomatoes contain inhibitors of trypsin, chymotrypsin, carboxypeptidases, elastase, and α-amylase.[53,54] Some processing techniques can reduce the concentration of these compounds, but in others, trypsin inhibitors stored in the cotyledons of food such as soybeans may fractionate with the storage proteins and reach elevated concentrations within processed foods, such as raw soybean flour.[53,55] Heat treatment may inactivate trypsin inhibitors in foods such as soy protein isolates, soy milk, and miso,[53,56] but extensive heating may reduce protein digestibility of soy products.[53] Animal models revealed a redirection of sulfur-containing AAs from the synthesis of body tissue to the synthesis of trypsin and chymotrypsin as a mechanism to compensate for the inhibition of enzyme function.[53,54]

Phytate is another ANF that is typically found in pulses, corn, wheat, and rice.[53] Its negatively charged phosphate group either chelates directly with carboxypeptidases and aminopeptidases, the mineral cofactor, or the protein substrate to inhibit enzyme activity,[53] but chelation processes could depend on pH variation in the GIT.[57] Varied processing treatments could either reduce or concentrate the quantity of phytates in plant foods. For example, extraction and purification processes convert some plant-sourced proteins (PSPs) to isolates or concentrates with digestibility that is comparable to animal-sourced proteins (ASPs).[20,58,59]

Contrastingly, phytates are relatively resistant to heat processing, which, instead, destroys heat-labile phytase enzyme.[53]

After complete protein hydrolysis, 90% of free AA is transported into the portal circulation.[36] However, attributing to the poorer digestibility of PSPs, splanchnic retention of AAs from these foods is higher,[16,60] leading to reduced availability and perfusion of AAs into the peripheral tissues for muscle protein synthesis (MPS). This may have greater implications for susceptible populations (eg, elderly individuals) who are more challenged in maintaining lean muscle mass.[28]

Urea nitrogen salvage at the loop of Henle permits the retention of approximately two-thirds of the nitrogen pool in the body that can be incorporated into AAs.[40] For example, the conditionally essential AA arginine may be synthesized from the incomplete urea cycle in the kidneys.[39] Another one-third of urea is hydrolyzed by colonic microbes, which can contribute to nitrogen cycling and urea salvage during periods of high growth or low dietary protein intake.[40] These systems may still fail in prolonged periods of protein or energy restriction when the net loss of nitrogen is not balanced by sufficient AA intake.[40]

The increased likelihood of urea conversion for some PSPs could reduce the available AAs for metabolic function in body tissues. Soy has superior digestibility compared with other PSPs.[59] However, a higher proportion of AAs from soy proteins are degraded to urea than are AAs from casein or whey, resulting in lower amounts incorporated into the protein structure of humans.[60–63] This is attributed to differences in gastric emptying and the absorption rate of these protein sources, with higher splanchnic catabolism for soy.[62] Wheat protein, which is of poorer quality, is even less incorporated into peripheral protein than soy, as evidenced by examination of postprandial 8-hour metabolic use of dietary nitrogen from wheat.[62,64] Table S1 provides a summary of the discussed challenges.

The human body can store carbohydrates and lipids but is incapable of storing reserves for protein, which must be consumed through the diet to provide an exogenous supply of IAAs, which are essential nutrients for physiological functions.[34] Protein synthesis is halted if there is even 1 limiting IAA,[65] with the excess oxidized or stored as other macromolecules (namely, glycogen and triglyceride).[66] As lysine has a slower turnover within the body, lysine may be conserved from meal to meal, but these conclusions were derived from animal studies.[67] Moreover, post-translational modifications of lysine (eg, methylation) irreversibly modify it, rendering it not usable for protein synthesis.[17,40] Protein synthesis and use can also be reduced in circumstances of limiting DAAs.[34,68] However, inadequate IAAs may surface as a bigger problem in vegan diets, because DAAs can be contributed in substantial quantities by PSPs.[69] Contrastingly, provision of IAAs from vegetal proteins is poorer.[70]

Three of the 9 IAAs—leucine, isoleucine, and valine—are classified as branched-chain AAs (BCAAs) because of their aromatic branched functional groups.[66] Leucine is potentially most important for cell signaling because of its role in activating the signal transduction pathway that stimulates the mammalian target of rapamycin complex 1 (mTORC1) signal cascade.[71–74] This activation is necessary to increase in vitro MPS in skeletal muscle.[66] Muscle protein synthesis begins at the gene transcription phase and ends with mRNA translation.[74] As reviewed in the literature, the activated mTORC1 and mTORC1-associated protein phosphatase activity upregulate several phosphorylation pathways of ribosomal S6 kinases, eukaryotic initiation factor 4E binding protein-1, and p70^{s6k}, which all positively influence the initiation phase of protein synthesis.[32,75,76] Assemblage of the eukaryotic initiation factor 4F congregates ribosomes on available mRNAs, whereas activation of ribosomal protein S6 targets mRNAs and accelerates protein synthesis.[74]

Insufficient leucine results in the binding and inhibition of GATOR2, which positively regulates mTORC1 activity.[77] Leucine alone exerts the same potent effect as a mixture of BCAAs, but this is not observed with the sole provision of isoleucine or valine.[78] Reduced intake of BCAAs was observed in vegan diets[79,80] or PB diets when protein from meat, eggs, and dairy was replaced with protein from fish.[81] A comparison between vegans and omnivores, however, only found significantly lower concentrations of lysine ($P < .0001$), not leucine, among vegans.[82] Leucine and lysine could be important IAAs that contribute to normal bone health, due to their effects on insulin secretion and associated growth of osteoblasts,[82–84] but further verification is necessary.

Methionine, a sulfur AA, has an elevated role in protein synthesis due to its hydrophobic nature, which promotes the binding of initiator tRNA to eIF-2 and the 40S ribosomal unit to initiate the process of translation.[85,86] Methionine is the major donor of the methyl group, which influences cellular DNA and protein methylation.[87] Its levels are directly controlled by 1-carbon metabolism.[88] Through trans-sulfuration mechanisms, methionine facilitates production of cysteine, another sulfur AA, which, in turn, regulates the concentration of methionine.[89] The achievement of total sulfur AA can be challenging from plant proteins. Soy and pea provide lower quantities, whereas cereals provide variable ratios.[89] In an additional analysis of AA intake by vegans in Germany, significantly lower intakes of methionine (51.9%), threonine (32.6%), tyrosine (37.2%), and histidine (37.5%) were observed in vegans compared with omnivores.[90] However when compared with the Estimated Average Requirement (EAR) of the World Health Organization, the median dietary intake of all IAAs was sufficient in the surveyed vegans.[90]

As reviewed by Fernstrom et al,[91] the brain concentrations of tryptophan, phenylalanine, and tyrosine are important precursors of the neurotransmitters serotonin (from tryptophan) and catecholamines (from tyrosine and phenylalanine as co-substrates). The consequence of poor provision could reduce the conversion rate of these precursors to neurotransmitters and result in poorer physiological or health outcomes.[91]

Concentrations of these AAs, such as tyrosine, not only are influenced by protein intake from a single meal but also through prolonged diet. Although foods from animal (meat, seafood, and dairy) and vegetal (potatoes, chickpeas, soybeans, and nuts) sources provide similarly high quantities of tryptophan, lower amounts are present in cereals and maize.[91,92] According to Palego et al,[92] although tryptophan requirements are higher in infants and children than adults, the lower affinity of the AA for the apical carrier may mean the importance of a protein-rich meal to increase its gut absorption into plasma. However, this does not necessitate its transport through the blood-brain barrier, because of competition by higher quantities of other large neutral AAs, and this phenomenon is interestingly mitigated in a low-protein diet. Hence, the role of the diet in the metabolic fate of tryptophan is more complicated and requires further exploration.[92]

Protein Quality

Protein adequacy from the diet must involve the following 3 considerations: the choice of protein (plant- and/or animal-sourced), the quantity that can be consumed in 1 meal, and the quality of the food source in its composition and supply of digestible AAs. Dietary protein is more than just the sum of its AAs.[93] The overall food matrix,[93] as well as an individual's physiological state, are factors that establish the ability of food or a meal[34,94,95] to provide sufficient and biologically available AAs that are used for metabolic demands.[17,34] This defines protein quality.

Assessment of IAA Intake in Vegan Populations

Analysis of protein intake has been conducted in observational studies involving vegan populations.[96,97] Amino acid analysis is often overlooked, potentially due to paucity in the AA composition of various foods in food composition databases. However, given the important metabolic roles of each AA, understanding the contribution of AAs from PB foods provides improved clarity about their impact on nutrient adequacy and overall health outcomes.

Several studies have investigated AA intake and plasma concentrations of individuals eating vegan diets, and findings from 15 articles are summarized in Table 2. Generally, dietary intake and plasma circulation were lowest for lysine and other BCAAs. Lysine was the most limiting IAA, and lysine concentrations differed more between vegan and other diet groups than did other IAAs.[99,101,104,107–109] This is not unexpected, because many PB foods are known to contribute low quantities of lysine. Apart from 1 study,[107] none had accounted for the digestibility values of the AAs in PSPs. This can be attributed to insufficient true ileal digestibility (TID) data for many fruits and vegetables, which often have the same digestibility value.[107] Most of the studies were limited by duration and small sample size. Because low intake and concentrations of IAAs may have dire effects on vulnerable populations, such as the elderly, this analysis is a research need.

Challenges in Assessing Protein Quality of PB Foods

An earlier review highlighted that the Protein Digestibility Corrected Amino Acid Score (PDCAAS), which was intended to measure utilisable protein, was based on age-specific requirement patterns[38] and did not consider additional roles of IAAs beyond meeting nitrogen balance (NB) needs.[95] Application of the PDCAAS score is especially limited in the measurements of protein quality from a diet predominantly high in plant foods. Fecal digestibility, which is the measurement used in PDCAAS, is usually an overestimation of AA digestibility. Nitrogenous compounds synthesized by colonic bacteria and AAs that are absorbed past the terminal ileum[110,111] are both considered in the calculation, but neither is nutritionally important to human physiological requirements.[31] Higher amounts of fiber present in plant protein sources[112] not only lead to elevated fecal nitrogen loss,[40] they also increase the fermentation and release of nitrogen by colonic bacteria, which will alter the supply of AAs.[110] Additionally, the truncation of scores above 100% implies that the benefits of complementing protein sources deficient in some IAAs within a mixed meal cannot be applied. [34]

The current protein quality measure considered superior to PDCAAS is the Digestible Indispensable Amino Acid Score (DIAAS).[112] In the context of a PB diet, the DIAAS may confer advantages such as incorporating the more accurate TID values of AAs from PSPs, because tannins, phytates, trypsin inhibitors, and

Table 2. Summary of Studies on IAA Intake in Vegan Populations

Reference	Study design	Study objective	AA intake/status
Abdulla et al (1981)[98]	Cross-sectional study of 3 adult men and 3 adult women	Compare chemical analyses of vegan diets and Swedish mixed diets to determine nutrient intake and health status.	Lower intake (mg kg^{-1} BW) of isoleucine, leucine, lysine, threonine, and valine by vegans compared with nonvegans.
Anderson and Blendis (1981)[99]	Cross-sectional analysis of 32 Canadian adults	Determine the relationship between habitual food intake with plasma NAA ratios.	Plasma tyrosine, phenylalanine, valine, and leucine were lowest in the vegan group.
Rana and Sanders (1986)[100]	Cross-sectional study of 48 adults in the United Kingdom	Investigate effects of vegan diet and omnivore diet on plasma AAs.	Mean values of plasma threonine, valine, leucine, and lysine were lower in vegans than omnivores.
Schmidt et al (2015)[101]	Cross-sectional study; Oxford arm of EPIC; $n = 379$ adult men	Compare differences in plasma metabolites in relation to metabolism among self-declared omnivores, vegetarians, and vegans.	Lowest plasma concentrations of leucine, valine, lysine, methionine, tryptophan, and tyrosine in vegans
López et al (2015)[80]	Crossover design; consume single meal of each diet; $n = 15$ adult women	Compare the plasma AA profile of rural (PB protein sources) and urban Mexican diets.	Lower plasma concentrations of leucine, isoleucine, valine, phenylalanine, tyrosine, and proline in rural diet than urban diet
Schmidt et al (2016)[79]	Cross-sectional study; Oxford arm of EPIC; $n = 392$ adult men	Compare differences in intakes and plasma concentrations of AAs between self-declared omnivores, vegetarians and vegans.	Lower plasma concentrations of BCAAs, lysine, and tryptophan in vegans. 50% lower lysine and methionine intake between vegans and meat eaters. Significant correlations of lysine and tyrosine with non-soya plant intakes, inverse correlations of valine, lysine, methionine, and tyrosine with soya products
Draper et al (2018)[102]	Randomized, crossover, controlled trial with 21 adults in Switzerland	Compare 48-h vegan diet with omnivorous diet in macronutrient composition and metabolic measurements.	Reduced intake of mean cysteine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, tyrosine, and valine in vegan diets compared with animal diets, for both sexes. Decreased plasma BCAAs and other EAAs in vegan diet
Kahleova et al (2018)[103]	Randomized trial with 75 overweight participants	Investigate role of plant protein on body composition and insulin resistance.	Reduction in leucine and histidine intake in vegan diet compared with control diet
Lindqvist et al (2019)[104]	Cross-sectional study of 120 adults of varied diet groups in Sweden	Assess if the analysis of serum samples with magnetic resonance can objectively distinguish diet patterns	BCAAs and lysine were among the most important metabolites to distinguish between vegan/nonmeat eaters and meat eaters/vegans.
Wang et al (2019)[105]	Cross-sectional study of 36 adults of varied diet groups	Explore links between gut microbiota and circulating metabolites.	Lower circulating BCAAs in vegetarian and vegan diets compared with omnivorous diet
MacArthur et al (2021)[106]	Simulation models of diet patterns using the NHANES database consisting of 2 24-h dietary recalls	Analyze total protein and AA composition of food items and dietary patterns (omnivorous vs PB).	AA intake ratios indicated higher intake of histidine, BCAAs, lysine, methionine, threonine, and valine by omnivorous than by vegans. Small magnitude of difference (<0.5%) for AAs, apart from lysine
Dietrich et al (2022)[90]	Cross-sectional study of 36 vegans and 36 omnivores in Germany	Compare dietary intake and plasma concentrations of AAs between vegans and omnivores using 3-d food diaries.	For the same energy intake, vegans had lower median intake of the 9 IAAs than omnivores, but intake was higher than the EAR (mg kg^{-1} day^{-1}). Of the 9 IAAs, only plasma lysine intake was significantly different between vegans and omnivores.
Conzuelo et al (2022)[107]	Scenario-based analysis of 2-d vegan menu days of the EAT-diet, using Swiss Food Composition data	Evaluate changes to protein quality when combining different protein sources in a vegan diet	Fulfillment of lysine, valine, threonine, leucine, isoleucine and histidine occurs with combination of legumes, cereals, vegetables and fruits. Lysine was most limiting in all scenarios when DIAAS method was incorporated.

(continued)

Table 2. Continued

Reference	Study design	Study objective	AA intake/status
Tallman et al (2023)[108]	Food-modelling analysis of 3 different diets with varied protein intake (g kg^{-1} day^{-1})	Analyze nutrient and EAA content of different dietary patterns for patients with chronic kidney disease.	Lysine intake was below reference value in the vegan diet, at 0.6 and 0.8 g of protein kg^{-1} day^{-1}.
Aaslyng et al (2023)[109]	Cross-sectional study of 40 Danish vegans	Analyze protein requirements and EAA composition of the vegan diet.	Lysine was the most limiting AA, followed by sulfur-containing AAs, leucine, and valine.

Abbreviations: AA, amino acid; BCAA, branched-chain amino acid; BW, body weight; DIAAS, Digestible Indispensable Amino Acid Score; EAA, essential amino acid; EAR, estimated average requirement; EPIC, European Prospective Investigation into Cancer and Nutrition; IAA, indispensable amino acid; NAA, neutral amino acid; NHANES, National Health and Nutrition Examination Survey; PB, plant-based.

reactive lysine in processed foods are accounted for.[15,53,112] An exception would be foods that have undergone industrial or home-based heat treatments in which the true TID values for some AAs like methionine and tryptophan are not well reflected.[28,113] One limitation persists in DIAAS use: the reference pattern used in PDCAAS is still applied in the mathematical derivation of the DIAAS. Recent evidence from indicator AA oxidation (IAAO) and NB assessments has suggested an increase of 16% and 55%, respectively, in requirements from the current Recommended Dietary Allowance (RDA) of 0.8 g kg^{-1} day^{-1}.[114] These conclusions were related to the recognition of functional roles provided by both IAAs and DAAs.[114] Because this reference value assumes that high-quality protein is consumed,[73,115,116] requirements may be elevated in diets comprising protein sources of more inferior quality. Additionally, the representation of many PB foods, including novel PB alternatives (PBAs) in DIAAS databases is lacking.[116]

Furthermore, the challenge of determining the effect of food-component interaction on bioavailability is not overcome, because many attained DIAAS values were based on single or isolated food proteins[28] and do not adequately represent the mixed diets of humans.[14,60] The generalized nitrogen-to-protein conversion factor of 6.25 is still used to calculate the DIAAS, but this assumes that all AAs have the factor.[116] Greater discrepancies between conversion factors emerge with less accurate scores for plant foods than animal foods.[116] To overcome these limitations, a crucial step is to build an extensive database comprising experimentally verified TID scores of traditional and novel plant foods.

The protein quality of a vegan meal could be improved by complementing a low-quality protein source with a high-quality source (eg, soy), based on their untruncated DIAAS,[117] or by adding the TID scores of PSPs with different limiting IAAs.[118] Possibly, for PSPs with low DIAAS values (<75%), intakes higher than the RDA may be necessary to meet the higher metabolic demands of certain populations.[118] Appropriate quantities of varied plant foods must be selected from different permutations to ensure all IAAs are met, but this can be difficult due to commonly limiting IAAs among plant foods.[118] Blends with cereals (eg, maize) that are not complemented by other protein sources lead to the presence of at least 1 limiting IAA and higher quantities of oxidized and nonabsorbed AAs, compared with blends containing soy, pea, and animal-derived proteins.[42] As demonstrated, blending protein sources with different limiting IAAs (eg, rice and pea) in the correct ratios increases the overall DIAAS score and amounts of utilisable AAs.[42] It is important to note that although a vegetarian can include some sources of ASPs (eg, milk, eggs) that provide higher concentrations of IAAs such as leucine,[94,119] vegans have more limited choices that can be added in a complementary manner to achieve meals of high protein quality. Attaining a balanced intake of all IAAs, therefore, is a key challenge in vegan diets.

Metabolic Characteristics of PSPs and ASPs

Nutritional values of protein sources differ greatly based on the IAA content and digestibility.[120] The AA profile, rather than the consumed quantity of the protein, is the most important attribute of the food's functional properties.[121]

A highly digestible protein provides a larger quantity of absorbable AAs[119] in a smaller consumed amount, compared with poorly digestible protein sources.[122] The ratio of protein mass to energy is generally higher in ASPs than PSPs,[118] and even soybeans, which have higher protein quality scores, contribute more calories for an equivalent quantity of protein than do ASPs.[44] Cereal grains, the dominant source of plant protein globally,[44,123] have a relatively low protein to energy ratio[118] and are limited in lysine concentration.[14] Increased consumption of plant foods is required to meet the daily requirements for IAAs, but this strategy inevitably increases intake of carbohydrate, caloric density, and fiber, potentially resulting in impractical and unrealistic intakes, as well as some unfavorable health outcomes.[44,118] Higher proportions of high-fiber foods contribute to satiety, placing limits on consumption quantity.[44,46]

The most practical approach to achieve IAA requirements in a vegan diet is to consume a variety of complementary plant foods.[93,124] However, dietary practices such as complementing rice (limited in lysine) with beans (limited in sulphur AAs) may not always be culturally appropriate in certain regions of the world or acceptable to individuals who are new to a vegan dietary pattern.[14,125] Sufficient knowledge and having keen dedication to meal preparations[126] are vital to achieve adequate nutrient intake in a vegan diet.

Overall protein accretion in the body may depend on differing mechanisms attributed to "fast" and "slow" proteins, which then affect the acute response of MPS.[127] One study found that isolated whey and soy, which were classified as fast protein sources, significantly increased the mixed muscle protein fractional synthetic rate in 3 small sample groups of healthy young men ($n = 6$ in each group), as compared with casein, a slow protein with a slower rate of gastric emptying.[127] However, a significant difference between whey and soy was observed only after resistance exercise,[128] which may provide a synergistic effect in anabolic signaling.[93] This may be related to small differences in digestion rates between the 2 protein sources, leading to lower blood concentrations of leucine and higher oxidation rates of AAs in postexercise conditions.[129] In a similar comparison of ASPs and PSPs in healthy older men ($n = 60$; >71 years old), the consumption of casein and whey protein resulted in greater postprandial increase in plasma AA concentrations, particularly leucine, and a greater rate of myofibrillar protein synthesis, compared with an equivalent ingestion of wheat protein.[130] Yet another study of 13 older men (60-75 years old) found prolonged phosphorylation of p70S6K, an indication of the MPS response, 4 hours after exercise only in whey protein ingestion; this was unobserved with an equivalent quantity of soy.[131]

Trials assessing associations between PSP intake and outcomes on skeletal muscle mass found poorer outcomes for muscle mass retention in adults consuming higher proportions of PSPs compared to those with a higher intake of ASPs.[132–134] A recent RCT ($n = 19$ healthy older adults) found contrasting evidence that a strict vegan diet, based on a 57% daily intake of mycoprotein-based protein source (Quorn; Monde Nissin, Laguna, Philippines) provided an equivalent daily myofibrillar protein synthesis rate when compared with an isonitrogenous omnivorous diet.[135] However, apart from 3 individuals who were vegetarians and thus assigned to the vegan group, none of the participants habitually consumed a vegan diet, so results from a 3-day trial may not represent significant outcomes of MPS in long-term vegans.

These trials provide evidence that isolated ASP stimulates greater MPS than does PSP and suggest a vegan diet is disadvantageous for this outcome. In terms of selecting the PSP with the highest protein quality, isolated soy protein is most likely to provide a source of complete and digestible AA[136] that is of near comparison to whey protein. However, most meals throughout the day consist of mixed ingredients. More research is required to understand how mixed vegan diets can compare with animal-inclusive diets in stimulating postprandial MPS. This is more essential for older adults who face greater anabolic resistance of MPS and require higher doses of bioavailable AAs.[137]

Although AAs primarily modulate muscle synthesis and turnover, the skeletal muscle is a dynamic tissue that is affected by stimuli from hormones, physical activity, and a perfusion effect of insulin.[137,138] Resistance exercise appears to modulate the impact of food on MPS and enhance muscle sensitivity to dietary influx of AAs.[93] However, the exercise magnitude, timing of protein dose from exercise, effect of energy contribution from protein, and individual variability in the size of skeletal muscle are other important factors.[139] One study highlighted that MPS does not translate to muscle hypertrophy after repeated bouts of exercise over 2 weeks.[140] This phenomenon could be attributed to higher muscle protein turnover rate due to perpetual activation of the mTOR1 signal pathway, and periods of low activation are necessary to improve insulin and AA use for long-term muscle mass maintenance.[140]

Although exercise may increase sensitivity to MPS, provision of sufficient IAAs through dietary protein remains crucial for muscle protein accretion. Accumulation of IAA deficiencies over a prolonged period not only halts MPS but promotes Muscle Protein Breakdown (MPB) as compensation to supply IAAs endogenously for physiological functions in body tissues.[16,141] Vegans choosing foods of lower protein quality may be at a greater disadvantage.

Protein Intake and Distribution Throughout the Day: Key Considerations

Although 2 individuals may consume the same quantity of protein in a day, meal distribution patterns may be different, and the frequency of consumption could influence the sensitivity of signaling pathways to postprandial AA concentration, MPS, and net protein balance.[93] An even distribution of protein in temporal patterns of 3-5 hours throughout the day could increase MPS and support muscle protein accretion.[59,73,142,143] The meal threshold for protein intake is proposed to be a 2- to 3-fold increase of plasma leucine level to achieve maximum activation of mTORC1.[73,144] Approximately 20-30 g of protein per meal to supply 10 g of IAA (of which 5 g is BCAAs) may be essential to maximize MPS for 2-5 hours for healthy young adults.[16]

In contrast, time-restricted feeding, or intermittent fasting, is proposed to coincide with the body's circadian rhythm by regulating the balance between mRNA and proteins and hence control aspects of protein metabolism.[145,146] In such infrequent meal patterns, perhaps ensuring at least 1 meal of sufficient protein intake with adequate leucine is crucial, with greater importance imposed for the first meal of the day (breakfast) to overcome the catabolic state of an individual after an overnight fast.[16,147] However, energy restriction and low insulin states in intermittent fasting compromise MPS and net muscle balance with higher protein oxidation in longer periods of starvation over 24 hours.[148,149] Because IAAs are not produced or stored in the body, periods of such prolonged meal abstinence are disadvantageous for lean muscle mass promotion, especially within the context of vegan diets characterized by low protein quality. A combination of plant protein sources is crucial to achieve sufficient AAs in vegan diets. This is easier to achieve with frequent meal intake than smaller eating windows when fasting intermittently.

Simply measuring overall protein intake per day without considering protein distribution over the meals of the day potentially gives false impressions of protein adequacy. Furthermore, the recommendation of 0.8 g kg^{-1} day^{-1} is based on assumptions of high-quality protein intake spread across 3 meals.[150] Even if daily protein intake can be met by a skewed pattern, as commonly observed in evening meals,[151,152] the meal threshold is only achieved once a day and no additional signal for MPS is stimulated in saturation (the refractory period), leading to oxidation rather than use of surplus IAAs.[73,152] Redistributing protein to meals throughout the day is contrastingly more efficient with improved stimulation of MPS, as observed by a 25% increase in 24-h fractional mixed-muscle MPS.[143] Especially for older adults who are less tolerant to large food volumes in 1 meal (eg, pulse feeding), even protein distribution is beneficial to overcome a higher per-meal protein threshold and promote anabolism.[153] Uneven patterns are associated with increased frailty and possibly reduced MPS activation.[154] Clearly, more empirical data are necessary to confirm the impact of meal distribution patterns on physiological impacts, especially for the vegan population and older adults for whom frequent food intake could attenuate challenges in obtaining diets of high protein quality.

Consideration of IAA Intake to Establish Protein Requirements

Nitrogen equilibrium, or NB, reflects the balance of protein intake, synthesis, and losses.[120,155] Indispensable AA quantity is key to promote net NB.[156] Nitrogen balance thus provides an estimated measure of daily nitrogen use in the body throughout the day (Figure 1) to derive the minimum quantity of protein intake for the prevention of nutritional inadequacies in 97.5% of healthy adults.[74,153] Nitrogen balance may be imprecise in determining overall optimal protein intake and distribution across meals.[73,120,132] Questionable reliability of NB studies to ascertain protein requirements can be related to variability among individuals and difficulty in determining if nitrogen sources were from endogenous synthesis or only through food.[157] Other studies have found IAA intake past the point of equilibrium for EAR and RDA is beneficial, especially for more vulnerable populations.[158,159] Additionally, the validation of the NB technique remains uncertain in contexts where a biological accommodation due to low protein intake (eg, in a vegan diet) occurs. A zero balance may simply be a reflection of lower nitrogen excretion rather than poorer intake.[16,160]

Nevertheless, a negative NB of 1.38 g day^{-1}, indicating a catabolic state of the body, was observed among 18 minimally active male adults aged 20-45 years who consumed a vegan diet.[155] To reestablish NB among vegans, the recommendation of 0.8 g kg^{-1} day^{-1} protein based on NB was insufficient, and the authors of that study recommended an additional 12 g of protein, leading to a 20% increase in daily protein requirement (0.96 g kg^{-1} day^{-1}).[155] This may not always be realistic for older adults who cannot tolerate larger volumes of food, or individuals concerned with higher caloric intake.[107,161] However, there is still insufficient evidence for whether an intake above this recommendation is justified and safe for all individuals.[73] Since the measurements only consider overall protein intake rather than those related to the unique metabolic roles of each AA,[73] even if protein intake is increased, inefficient use of IAAs as a result of at least 1 limiting IAA from either a poor-quality or single-sourced plant protein leads to nitrogen losses due to increased AA oxidation and deamination.[60,120] Achieving nitrogen accretion requires adequate protein but also a balanced profile of AAs, which is often the more challenging aspect in a diet consisting only of PSPs.

In circumstances of adequate caloric intake, PB diets can usually meet and even exceed protein recommendations with the provision of all AAs, including the 9 IAAs.[116] A calorie-restrictive vegan diet may increase the likelihood of low glucose intake, which drives the catabolism of protein for gluconeogenesis rather than MPS.[141,162,163] Vegans in high-income countries who have greater opportunities to consume diverse foods in a mixed diet are likely to achieve these requirements, but those whose main protein source is from cereals

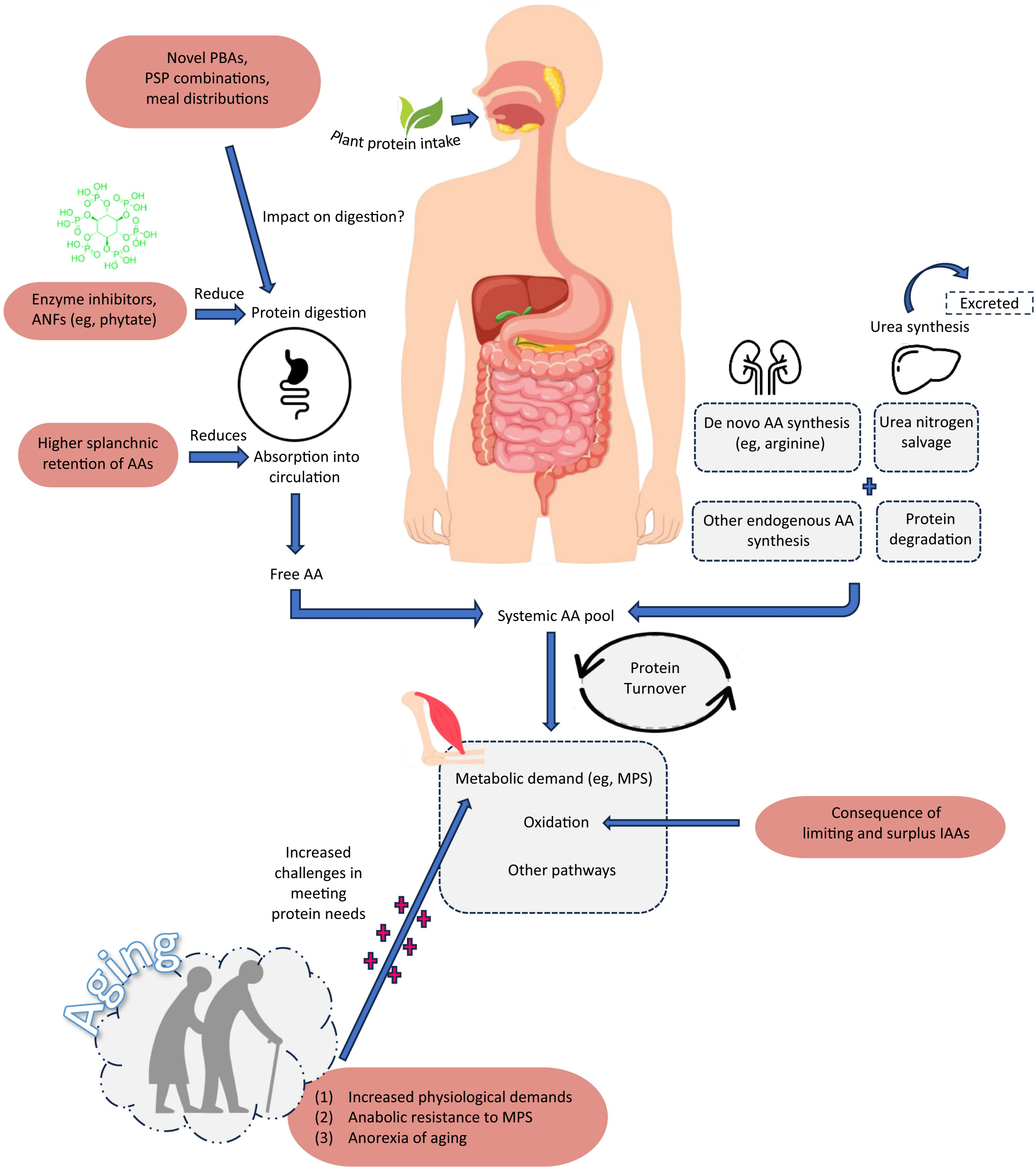

Figure 1. Plant Protein Use in the Human Body and the Associated Challenges. Ovals with outgoing arrows indicate potential challenges and considerations associated with achieving nitrogen balance and protein adequacy. These involve the contexts of plant protein intake and impact of aging. Abbreviations: AA, amino acid; ANF, antinutritional factor; IAA, indispensable amino acid; MPS, muscle protein synthesis; PBA, plant-based alternative; PSP, plant-sourced protein. This figure was created with information adapted from Wolfe et al[41] and Weiler et al.[114] (Design created with images from a Paid Canva Pro account and PowerPoint.)

could have more deficient intakes of IAAs such as lysine, which often is the first limiting AA in PB diets.[14,164] For a vegan to achieve protein intake and quality that support health, sufficient food intake and the incorporation of diverse and complementary protein sources are necessary strategies.

Protein Quality of Novel PBAs

Alternative protein sources are increasingly ubiquitous in a modern vegan diet; this is partly a result of marketing messages related to environmental sustainability, animal welfare, and health benefits.[165] In contrast to "traditional" PB sources, which are largely unprocessed, novel meat and bovine milk alternatives undergo varied levels of processing to mimic the sensory characteristics of meat and milk, and could offer convenient and supportive foods to individuals newly transiting to a PB diet.[166] Commonly, the production of PB meat alternatives (PBMAs) isolates proteins from legumes, cereals, and oilseeds, in combination with fats from coconuts and seeds.[167] More studies are investigating the nutrient profiles of novel foods, but further research is still required to determine how the nutritional compositions of these foods compare with traditional PB alternatives and animal-derived proteins, especially in the context of nutrient bioavailability.[167] Table S2 provides a consideration of protein quality in novel PBAs.

Less-purified plant proteins such as those in wheat cereals have poorer digestibility of <80%, as measured with PDCAAS, and this value is further decreased with the inclusion of plant cell walls, ANFs, levels of processing, and heat treatment.[110] Contrastingly, the removal of cell wall constituents in purified plant proteins results in products such as wheat gluten, wheat flour, and soy protein isolates, which have comparable digestibility to ASPs.[110] Extrusion processes used in the manufacture of PBMAs similarly increase protein digestibility.[168,169] Hence, consumption of isolated plant proteins in these foods may exceed the protein requirements of an individual.[14] However, because phytic acid is stored in the protein bodies of the endosperm in legumes, phytates may attach to proteins when they are extracted to form an isolate.[169,170] Hence, bioavailability of AAs from these foods is an important question that remains unanswered.

Food formulations comprising mixed sources of PSPs can overcome limitations in single-food formulations to improve overall functional properties and close the compositional difference with animal proteins.[171] Efficiency, cost, and sustainability are important considerations in extracting plant protein biomass trapped by cellulose and hemicellulose fibers.[171] Use of high quantities of fat as a lubricant may inhibit the protein denaturation process,[172] and nutritional implications as a result of these procedures warrant attention.

Food preparation techniques affect AA digestibility. Although germination, fermentation, and soaking could reduce ANFs[34,173,174] and improve the accessibility of proteases to peptides,[53] heat processing, even at home, may chemically alter AA function.[34,173] High temperatures could affect an AA's nutritional viability, such as for threonine, which undergoes uncontrolled phosphorylation, and the resulting phosphothreonine cannot be directly used for protein synthesis.[113] Racemization of L-AAs and the development of cross-linked peptide chains through alkaline and heat processing result in the same underuse for lysine and cysteine.[175] Reactive side chains of lysine and cysteine may undergo Maillard reactions with reducing sugars or aldehyde compounds[113,175] that reduce their overall absorbability and utilization for protein synthesis.[34] Sulphur-containing AAs (ie, cysteine and methionine), tryptophan, and threonine are also susceptible to oxidation.[112, 76] Products from these reactions may not be accounted for accurately in calculations of TID,[113] although DIAAS calculations can account for the true digestibility of "reactive" lysine.[30]

Protein Content and Quality From Novel PBMAs

Supermarket audits in several regions reported varied protein content in PBMAs. Although a large percentage of products in Australia and Sweden were eligible to make the "source of protein" claim,[169,177] a survey in the United Kingdom found the protein content of PBMAs was lower than in meat-derived products in 4 of 6 categories, with burger patties having the largest difference.[178] Similar observations of this variation between products were found in Sweden and Spain.[169,179] Details of AA composition are usually absent on nutrition labels.[180] Thus, consumers need to be well-informed and discerning when selecting these PBMAs.

Analyses of AA composition and bioavailability of PBMAs are limited. One study compared metabolite classes between beef and PBMAs and found that AAs were among several metabolites for which there were the most pronounced differences.[180] Owing to the important physiological roles of various food metabolites, van Vliet et al[180] argued that the nutritional inequivalence between ASPs and novel PBMAs is of crucial importance because under- or oversupply of certain nutrients can translate to negative implications for human health. Hence, the authors asserted that these products should fulfil a more complementary role in the diet, rather than as a complete replacement of ASPs.

An analysis in the United States that compared 3 brands of PBMA burger patties (comprising pea, pea protein isolate, wheat, soy protein concentrate, and black beans) with ground pork and beef found comparable crude protein content between the PBMAs and animal-derived products.[167] Total IAA content was similar with raw PBMAs, ranging between 70 and 76 mg g^{-1}, compared with 66-68 mg g^{-1} for raw animal products, but concentrations of specific IAAs such as histidine, methionine, and lysine were highest in beef. This was also a conclusion arrived by Andreani et al,[172] who further stressed the large nutrient variability among all PBMAs analyzed. As expected, measurement of cooked bean and pea isolates had higher isoleucine and phenylalanine content,[167] but in the context of just 1 deficient IAA, the surplus of other IAAs are oxidized in catabolic pathways, because excess is never stored within the body.[27,33] As acknowledged by the authors of 1 of the articles included in the present review, ANFs and fibrous compounds in these plant products must also be considered because of their inhibiting effect on protein digestibility.[181]

Challenges in Achieving High Protein Adequacy in PB Beverages

Several analyses found that PB beverages (PBBs) had poorer nutritional composition and quality when compared with bovine milk. In reviewing the importance of setting nutrition standards of PBBs, Drewnowski et al[182] highlighted the inferior protein content observed in a wide range of PBBs, with a large number of PBBs surveyed containing <1 g 100 g^{-1} plant protein, compared with 1% bovine milk, which contains 3.3 g 100 g^{-1} protein.[182,183] Poorer protein contribution from PBBs was corroborated by other similar studies, with the only exception being soy milk,[126,184–186] which, in 1 study, had values ranging from 2.50 to 3.16 g per 100 mL[187] and was comparable to the protein content from bovine milk.[126,185,188]

A few studies evaluated the protein quality of PBBs by measuring the AA content or comparing the PDCAAS or DIAAS for isolated ingredients, such as soy and pea, which may be from raw food commodities rather than within the formulation of a PBB.[183,185,186,189] Generally, the authors of these studies concluded that the contribution of adequate IAAs was lower from PBBs compared with bovine milk, which, in contrast, supplied all essential AAs.[187,189] Measurements of AA bioavailability are uncommon, but when adjusting for reactive lysine, soy beverage had the highest reactive lysine percentage of all PBBs, but absolute reactive lysine content was still lower than in bovine milk.[186] Although PBBs provide palatable and reliable alternatives for consumers who cannot tolerate dairy, the absence of bovine milk in a vegan diet could be disadvantageous from a protein quality perspective, especially for young children and the elderly, who may require efficient sources of digestible proteins. The blending of plant proteins to achieve a formulated beverage that overcomes limiting AAs could be proposed. This is limited, however, by the paucity of digestibility values for mixed protein sources, taste profiles,[182] and the difficulty in obtaining commonly limiting AAs—chiefly lysine and methionine—from varied plant foods.[34,187]

Further Considerations of PBAs in Vegan Diets

Under the NOVA definition of ultra-processed foods, novel PB foods and beverages would fall under this category due to food processing technology,[190] even if some have good nutritional value.[191] Considerable concerns exist about the elevated levels of saturated fat, sodium, sugar, and other additives in these foods.[166] However, the current understanding of how such nutritional profiles translate to overall health is still deficient and potentially hindered by heterogenous survey methods and product variations.[166,186] If novel foods must be grouped under ultra-processed foods, then a long-term vegan diet may inevitably need to include these processed foods,[190] especially if they are micronutrient fortified and developed with processing techniques that improve protein digestibility.

Indices like the Healthy Plant-Based Dietary Index and the Unhealthy Plant-Based Dietary Index attempt to separate "healthy" and "unhealthy" PB foods on the basis of the level of processing and association with health outcomes.[192,193] However, this does not accurately account for the discrepancies of specific nutrients, and foods grouped in the healthy category may not sufficiently address the gap of protein adequacy,[190] especially for bioavailable AAs. Subject to ethical considerations, RCTs investigating the nutritional impact on protein when replacing ASPs with PBMAs and PBBs would provide more conclusive evidence of the benefits or risks of these alternatives.

Increased Risks of Protein Deficiency in Special Populations

Protein and AA requirements are elevated relative to total energy requirements at certain life stages, such as during pregnancy, lactation, early life, and aging.[26,153,194] Protein deficiency and protein quality are relevant concerns in these populations and even more challenged if a vegan diet is adopted. Some studies of protein intake and metabolomic analysis of plasma AAs have been conducted with young vegan participants.[195,196] Trends show a growing number of adults eating vegan diets in Western countries.[197] This may potentially increase in the following decades.

Apart from perspectives and reviews, long-term empirical studies on older adults are scarce. This is a research priority in the context of an aging global population and the associated physiological changes in aging that complicate the efficiency of protein use.[198] Old age is characterized by reduced anabolic response to protein, increased insulin resistance, and elevated inflammatory responses from emerging age-associated diseases.[153,199,200] Aging is a risk factor for protein misfolding diseases, in which amyloids are formed and commonly observed in various neurodegenerative disorders.[198] The unfolded protein response in the endoplasmic reticulum reduces protein synthesis to mediate endoplasmic reticulum stress.[201] This is an added problem for aging muscle, which already faces increased anabolic resistance to protein synthesis due to reduced mTOR activation.[137]

Overall, higher splanchnic AA retention is observed in older, as compared with younger populations. This decreases the distribution of plasma AA levels and perfusion to the skeletal muscle, further inhibiting MPS.[202] An added burden in aging is the increase in inflammatory conditions that could be linked to increased splanchnic extraction and subsequent diversion of leucine to the immune system, liver, spleen, inflammatory areas, and other core body functions, rather than to skeletal muscle.[161,162] Increased chronic conditions among the elderly reduce nitrogen accretion and use.[203]

In people older than 65 years, low protein intake is associated with increased risk for death, whereas higher intake reduces the risks for the loss of lean mass and bone density and provides important AAs.[204] Epidemiologic studies have found associations between poorer outcomes for body and bone mass with suboptimal MPS response and net protein balance.[153] These outcomes exacerbate occurrences of sarcopenia and osteoporosis, debilitating health conditions in old age that increase the risk of falls and fractures.[153,205]

Frailty is associated with lower blood levels of BCAAs.[71] Paoletti et al[206] found increased requirement of total sulphur AAs (namely, methionine and cysteine) for older adults, with a RDA of 32.1 mg kg^{-1} day^{-1} for men and 23.7 mg kg^{-1} day^{-1} for women aged ≥60 years to handle increased synthesis of the antioxidant glutathione or meet the requirement of methyl substrates for methylation. A 75% higher requirement of total sulphur AAs may be needed for elderly men than elderly women, potentially due to the positive association of elevated oxidative stress and insulin resistance in the former group.[209] Leucine requirement in the older population is 2.2 times that of young adults,[207] as measured by IAAO method. A recent study using the IAAO method found that lysine requirements were higher than current recommendations of 30 mg kg^{-1} day^{-1} for older women but not older men. These findings from recent bioassay methods convey the importance of revisiting the current IAA reference patterns of the United Nations Food and Agriculture Organization,[112] which combine requirements of older adults with younger adults, with an added consideration of stratifying requirement patterns by sex.

The consumption of 1.2 to 1.6 g kg^{-1} body weight day^{-1} is proposed for older adults to overcome anabolic resistance, mitigate increased insulin resistance, prevent loss of muscle mass, and reduce risks of frailty.[27,153,208,209] As reviewed by Traylor et al,[210] IAAO measurements have shown higher protein requirements of 0.94 g kg^{-1} day^{-1} for older men[211] and 0.96 g kg^{-1} day^{-1} for older women[212] compared with results from NB measurements. Elango and Ball[194] addressed the limitations of IAAO methods, which chiefly are related to using a constant phenylalanine intake amidst increasing test protein consumption. The relevance of the short-term IAAO method for long-term health implications and necessity for longer adaptation periods for accurate IAA requirements were also concerns.[213,214] Nevertheless, the minimally invasive method over short test periods (8 hours) is suitable for vulnerable populations.[214] Assessing the validity of this technique for new protein and IAA requirements for different populations is crucial. Recent assessments that compared isocaloric and isonitrogenous meals in 16 older adults over 2 test days found higher postprandial muscle MPS in whole-food omnivorous meals than in whole-food vegan meals.[215] Research is increasing in this area, but most studies have been short term. Understanding the long-term impacts of vegan diets on this population is a priority.

Caloric restriction, weight loss, and anorexia in aging lead to reduced food consumption.[28] Energy requirements also decrease with age.[206,216] Thus, an effective eating strategy is to consume foods that provide higher protein density in relation to energy.[203] This is undeniably more easily achieved from ASFs (eg, dairy) than PSFs. As it is, intake data in the United States,[217] as reviewed by Traylor et al,[210] showed a trend of reduced dietary protein intake with advancing age and of less than the current protein EAR. Achieving sufficient protein intake is likely even more uncommon for elderly individuals consuming a vegan diet (Figure 2).[28]

Approximately 25-30 g of high-quality protein with approximately 10 g of IAAs is proposed to maximize MPS and maintain muscle mass in the elderly, with higher intakes being energetically inefficient, because the excess is oxidized.[218] Intake of >30 g per meal may be required in a diet to compensate for lower protein density in vegan diets, although more evidence is required.[59] However, poorer digestibility of high-fiber PSFs, coupled with reduced appetite in old age, make this an undesirable option. Appropriately balanced meal and snack compositions throughout the day can help vegan older adults achieve sufficient IAA thresholds and maintain elevated levels before the next protein-dense meal without consuming excessive food volumes

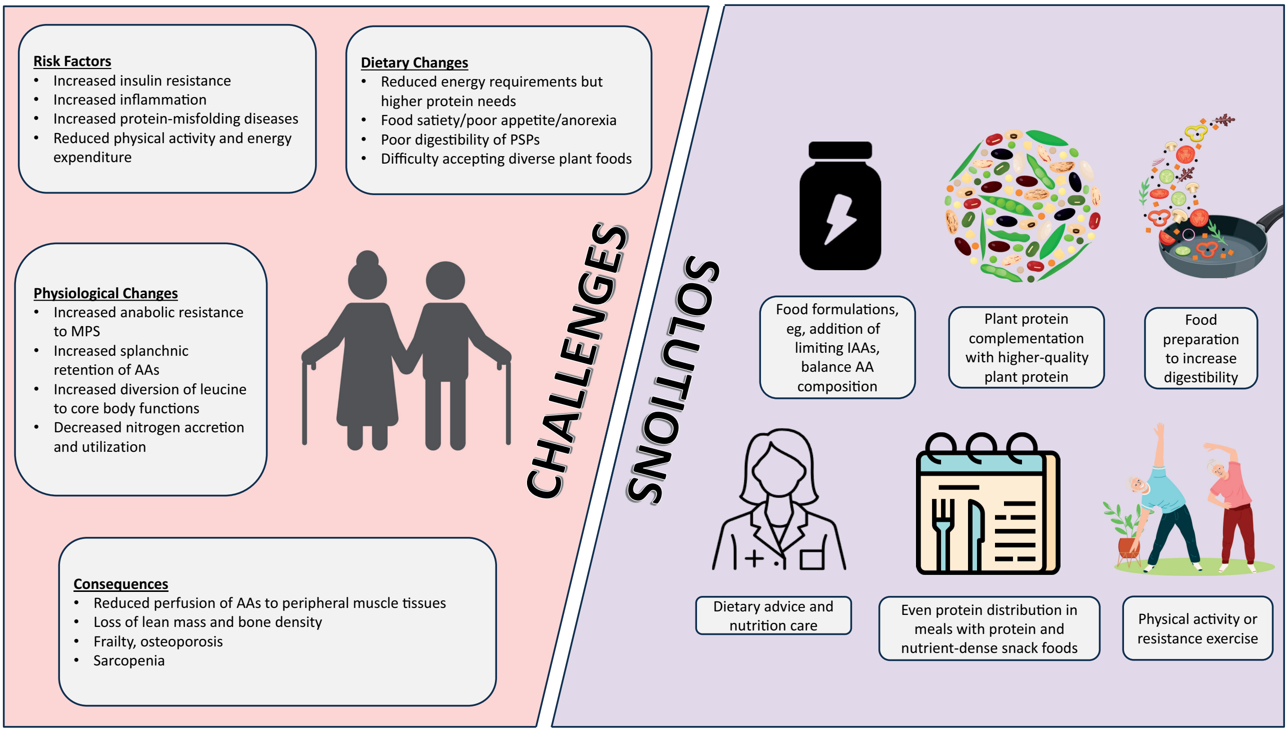

Figure 2. Challenges and Practical Solutions for Protein Intake by Vegan Older Adults. Abbreviations: AA, amino acid; IAA, indispensable amino acid; MPS, muscle protein synthesis; PSP, plant-sourced protein. This figure was created on the basis of relevant literature discussed in this report. (Design created with images from a Paid Canva Pro account and PowerPoint.)

(Figure 2). The intake of complementary plant proteins (eg, legumes with cereals), fortified PB alternatives, and supplementation with beverages and snacks that are enriched with limiting IAAs in appropriate concentrations are practical options for the elderly.[60] Appropriate cooking methods to increase palatability and digestibility of plant proteins are other effective measures.[219] Food formulations by industry partners, dietetic advice, and guidance on physical activity would optimize nutritional intake and support the maintenance of body composition and overall health.

CONCLUSION AND PERSPECTIVES

The PB diet transition is gaining significant attention as part of the solution to achieve healthy and sustainable food systems. However, nutrient adequacy, such as protein quality, should not be overlooked. Overall, this review provides insight into the associated challenges of following a vegan diet, as outlined in Figure 1.

Both ASFs and PSFs provide unique and complementary nutrients.[23,220] Plant-based alternatives are a convenient option, as evidenced by their gaining popularity in high-income countries that do not traditionally or culturally adopt PB diets.[19,221] Although the use of protein isolates in these products may provide protein quantity comparable to ASFs, studies evaluating the overall AA digestibility of these foods are limited and are ingredient-dependent, with soy isolates being superior.[222] Varied fortification strategies in novel alternatives further complicate assessments of how these products compare with ASFs and traditional plant foods.

Although a diet rich in plant foods undeniably provides several health benefits, there is insufficient evidence that the complete absence of ASFs is necessary to achieve these benefits. Old-age frailty is associated with reduced whole-body protein synthesis and a persistent catabolic state that drives increased muscle protein breakdown.[223] High-quality protein foods are especially valuable for the elderly to supply digestible IAAs and certain micronutrients, but these options are reduced in a vegan diet. Meal- and snack-based approaches to evenly distribute diverse protein sources throughout the day are viable solutions to address intolerance to high food volumes at 1 meal.

The current understanding of the long-term feasibility of vegan diets, especially in vulnerable populations, is hampered by limited studies determining the effects of prolonged vegan diets on the metabolic functions in these populations.[16,28] Several studies conflate results with less restrictive PB diets (eg, vegetarian diets), which are unlikely to have similar metabolic repercussions as vegan diets. Future research should aim to understand the implications of the food matrix (other macronutrients and antinutritional compounds), surplus and limiting AAs in various plant protein combinations,[224] and meal protein distribution patterns. Incorporating such analyses will further the understanding of protein adequacy in vegan diets, especially for populations who are most at risk of nutrient deficiencies from restrictive diets.

Author Contributions

All authors were responsible for the research design, critical analysis, and review of the manuscript. B.X.P.S. analyzed the results and wrote the manuscript. All authors read and approved the final manuscript.

Supplementary Material

Supplementary Material is available at *Nutrition Reviews* online.

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Conflict of Interest

None declared.

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