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Effects of plant- versus animal-based proteins on muscle protein synthesis: A systematic review with meta-analysis

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ABSTRACT

From 2014 to 2020, plant-based proteins rose from the top ten to the top three in global food trends, driven by ethical, health, economic, and environmental concerns. As interest in plant-based diets continues to grow, it is essential to determine whether plant-based proteins can stimulate muscle protein synthesis (MPS) as effectively as animal-based proteins. To investigate this, we conducted a systematic review with meta-analysis using five electronic databases (PubMed, Web of Science, SPORTDiscuss, Cochrane, and Scopus) to identify peer-reviewed studies (randomized controlled trials or non-controlled trials) published up to October 2024, that directly compared the effects of plant- and animal-based proteins on MPS in healthy adults (aged 18–85). Twelve studies met the eligibility criteria. Based on 26 effect sizes from these studies, animal-based proteins showed a modest advantage for fractional synthesis rate (FSR $\%\cdot h^{-1}$), though with a negligible effect size ($ES_{Plant:Animal}$ = 0.004 [95%CrI: -0.002 to 0.011]; $p(>0)$ = 0.899). Based on the imprecision of the pooled effect size estimate and substantial between-study variability, the certainty of evidence favouring animal-based proteins was judged as low. Subanalysis of data indicated that animal-based proteins showed a more pronounced effect on MPS in older adults, whereas younger individuals exhibited similar MPS responses irrespective of protein source. Given the limited confidence in current estimates, future research should prioritize larger, well-powered trials with standardized methodologies to improve the precision and reliability of findings in this area.

KEYWORDS: Protein source, resistance exercise, protein synthesis, leucine, vegetal protein, whole food, protein supplements

Key Points

- Animal-based proteins showed a modest advantage in stimulating muscle protein synthesis (MPS) compared to plant-based proteins, though the effect estimate was small and of uncertain practical significance. This difference was more noticeable in older adults, whereas younger individuals exhibited similar MPS responses regardless of protein source.
- In individuals aged 65+ years, animal-based proteins yielded a clearer but still relatively small effect on MPS. This age-related difference may be due

to the 'leucine threshold' theory, which suggests that older adults require higher doses of leucine to stimulate MPS effectively, and animal proteins typically provide higher leucine content.

- The comparative responses to plant- and animal-based proteins were similar, regardless of whether resistance exercise was performed. However, resistance exercise is known to enhance MPS, particularly when combined with protein intake. Data limitations prevent strong conclusions about the interaction of exercise and protein type on MPS.

INTRODUCTION

Skeletal muscle is a highly dynamic tissue. Its plasticity is mediated by the continuous interplay between muscle protein synthesis (MPS) and breakdown, which ultimately determines net muscle protein balance. This balance is influenced by dietary intake, exercise and various pathologies that exacerbate anabolism or catabolism [1-6]. MPS represents the metabolic process that involves the incorporation of amino acids into bound skeletal-muscle proteins [2].

The impact of protein ingestion on MPS is well-documented [7]. Its magnitude is regulated by several factors, including (i) protein digestion, (ii) amino acid absorption, (iii) systemic availability of amino acids (aminoacidemia), (iv) transport and uptake of amino acids into the skeletal muscle, and (v) activity of intramuscular cell signalling proteins known to modulate MPS [8]. After the ingestion of a protein-containing meal, MPS can increase acutely by 30-100%, promoting a positive net muscle protein balance [9].

Amino acids not only act as the "building blocks" of muscle tissue, but also as triggers of MPS. Specifically, the branched-chain amino acid leucine is highly involved in activating the mechanistic target of rapamycin complex 1 (mTORC1), which functions as an intracellular switch that regulates the translation initiation process of MPS at the ribosomal level [10-12]. A recent systematic review found that 55% of the available studies on this topic provide unequivocal evidence that leucine plays a key role in mTORC1 stimulation [8]. According to the authors of that study, this effect may have been dissipated in the remaining analysed studies due to several factors that also modulate the "leucine threshold" (the concept that, after protein consumption, a certain amount of leucine must be present in the bloodstream to initiate an optimal MPS response), such as age, training status, dose and source of ingested protein [8]. Despite this, it should be noted that, while being crucial for initiating MPS, the activation of mTORC1 does not necessarily serve as a reliable predictor of MPS duration following a meal [13,14].

Most experimental studies examining the interaction between nutrition and MPS have used milk protein or its constituents (i.e. whey and casein). Whey protein is known for its rapid digestion and high leucine content, which leads to a more prompt (~3 h) and robust stimulation of MPS post-exercise [15]. In contrast, proteins with lower levels of branched-chain amino acids (e.g. plant-based and caseinate), as well as those that are slowly digested (e.g. micellar casein), generally result in a suboptimal MPS response when compared to that observed with an equal quantity of whey protein [15]. However, recent research suggests that achieving a rapid peak in blood leucine levels (leucinemia) may not be obligatory for post-exercise MPS, especially with consumption of dairy proteins. [16] Some studies have even provided preliminary evidence that the effect of ingesting proteins with suboptimal levels of essential amino acids (EAAs) and/or leucine content can be partially compensated by the consumption of a higher absolute amount of protein [16].

From 2014 to 2020, “plant-based diet” rose from the top ten to the top three in global food trends, reflecting a growing worldwide interest in this dietary approach [17]. This trend is justified by several factors related to ethics, health, economic cost effective and environmental emergency [17,18]. There is strong evidence that the current global food system is unsustainable, due to the pressure on the environment [19,20]. Thus, new strategies to increase planetary sustainability and health have been proposed in the context of food production (e.g. sustainable diets) [19]. Adhering to these dietary patterns implicates increasing the consumption of plant-based products and promoting a proportional reduction in the consumption of animal products [21]. Plant proteins can be derived from various botanical sources, including soybeans, peas, fava beans, mung beans, lentils, algae, and microalgae, each with a unique nutritional profile [18]. Since animal-based foods are the source of protein with the highest nutritional value, it has been discussed if a shift to predominantly plant-based diets might lead to inadequate protein intake or an amino acid imbalance [22-24]. Thus, despite the need to promote more sustainable nutritional strategies (such as via the intake of plant-based proteins), it is essential to ensure that these alternatives provide the full complement of essential amino acids in a digestible form to serve as a viable substitute to animal proteins for supporting skeletal muscle mass [18]. Only then can its consumption be promoted for widespread use across populations.

To address these issues, we conducted a systematic review with meta-analysis to investigate whether plant-based proteins can function as a substitute for animal-based proteins regarding effects on MPS stimulation. This study aimed to 1) compare the MPS response between plant- and animal-based proteins; 2) determine the differential effects of plant- and animal-based proteins on MPS stratified by age group (18-54 years, 55-64 years, or 65-85 years) and post-ingestion time points (2, 4, 6 and 24 h); and 3) explore whether the addition of resistance exercise might mitigate differences between protein sources in MPS stimulation.

METHOD

Approach to the Research Question

This systematic review with meta-analysis is reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [25]. We originally preregistered the study (PROSPERO registration number

CRD42022344599) to include studies that both directly compared plant vs animal protein MPS responses as well as those that compared each condition independently with a placebo control, and to analyse results with a frequentist statistical model. However, after completing the search and expanding the research team, we determined that (1) the indirect comparisons did not add meaningful value to the results and, (2) a Bayesian model would offer greater probabilistic insights. Consequently, prior to analysis, we updated the pre-registration (https://osf.io/9fztm) to focus exclusively on direct comparisons plant- and animal-based proteins using a Bayesian statistical approach. The PICOS (population, intervention, comparison, outcome, and setting) criteria used to define the research question are detailed in Table 1.

Table 1-Population, intervention, comparison, outcome, and settings (PICOS) criteria used to define the research question

Parameter	Description
Population	Healthy adults with a mean age between 18 - 85 years
Intervention	Consumption of plant-based protein, as food or supplement
Comparator	Consumption of animal-based protein, as food or supplement
Outcome	Muscle protein synthesis
Study design	Intervention studies (randomized controlled trials or quasi-experimental trials)
Research question	Are there differences between animal-based protein and plant-based protein for eliciting muscle protein synthesis in healthy adults?

Eligibility Criteria

Only original, peer-reviewed investigations that directly compared the effect of plant- vs animal-based proteins on MPS with similar total protein doses were considered for inclusion. Studies were selected if they: (i) included samples of healthy adults (18-85 years); (ii) had an experimental design (randomized controlled trials or non-controlled trials) and (iii) evaluated MPS as outcome variable. Studies including samples with specific conditions (e.g. diabetes, sarcopenia), reviews, case studies, protocols, published abstracts, and studies published in non-English language journals were excluded from analysis.

Information sources and search strategy

A comprehensive search of peer-reviewed articles was made in April 2024 (including online ahead of print publications) and conducted in five electronic databases: PubMed, Scopus, Cochrane, Sport Discuss and Web of Science. Searches included: i) the target population – healthy adults with mean age between 18 and 85 years, ii) combinations of terms concerning plant-based proteins ("Vegetable protein" OR "Vegetal protein" OR "Plant-based protein" OR "Herbal protein" OR "Plant protein" OR "Soy" OR "Mycoprotein" OR "Potato" OR "Rice" OR "Pea" OR "Peanut" OR "Quinoa" OR "Wheat" OR "Meat substitute" OR "Vegetarian" OR "Vegan" OR "Plant"), iii) terms concerning animal-based proteins ("Animal-based protein" OR "Animal protein" OR "Meat protein" OR "Animal-derived protein" OR "Meat-based protein" OR "Flesh protein" OR "Fish protein" OR "Milk" OR "Whey" OR "Casein" OR "Egg" OR "Meat protein" OR "Beef" OR "Dairy" OR "Chicken" OR "Cheese" OR "Poultry") and iv) the outcome of interest (i.e., MPS: "Myofibrillar protein synthesis" OR "mTOR" OR "MAPK" OR "MyoPS" OR "Fractional synthetic rate” OR “Protein synthesis” OR “Mixed muscle protein synthesis” OR “FSR” OR “Protein synthesis in muscles” OR “Anabolic muscle protein synthesis” OR “Building muscle proteins” OR “Synthesis of muscular proteins” OR “Muscle protein turnover” OR “Myofibrillar protein synthesis” OR “Anabolic response in muscles” OR “Protein accretion in muscles” OR “Protein biosynthesis in muscles” OR “Skeletal muscle protein synthesis” OR “Muscle cell protein synthesis” OR “Myoprotein synthesis” OR “Muscle tissue protein synthesis” OR “Hypertrophic protein synthesis” OR “Protein anabolism in muscles” OR “Muscular protein generation” OR “Synthesis of contractile proteins” OR “Growth of muscle proteins” OR “Leucine” OR “Protein anabolism” OR “Protein metabolism” OR “Intrinsically labelled protein” OR “Translation initiation” OR “Anabolic signalling”). Additionally, manual cross-referencing of retrieved articles and articles cited in prior papers were examined to uncover other studies that might meet inclusion criteria.

Study selection and data extraction

All titles and abstracts of the studies obtained in the literature search were screened for potential inclusion eligibility by three authors (BM, JMC, and GVM) and exported to Mendeley® Reference Manager version 2.94.0 [26]. Duplicate entries were removed and the full text of relevant articles were then retrieved for review by the same authors. The following information was extracted for each article meeting inclusion criteria: authors, year of publication, participants (i.e., sample size and demographics), study design, intervention characteristics (i.e., methods, protocols, and length of intervention), and outcome of interest. Uncertainties were resolved by consensus among the authors.

Quality Assessment

Study quality was assessed using the Quality Assessment Tool for Quantitative Studies developed by Effective Public Health Practice Project (EPHPP) [27]. Two authors (BM and JMC) independently assigned a subjective level of risk (weak, moderate, or strong) to each study based on six key domains: selection bias, design, confounders, blinding, data collection methods, withdrawals and dropouts. A global rating was calculated based on the scores of each component. The two authors rated the six domains and overall quality independently, and differences were then discussed until a consensus was reached. Inter-rater agreement across categories varied from moderate (Cohen's k = 0.429) to strong (k = 0.739).

For the primary meta-analysis comprising a summary pairwise comparison between plant- and animal-based protein supplementation, an overall assessment for the confidence in the cumulative evidence was made using the GRADE guidelines [28]. Confidence in evidence comprised: 1) overall risk of bias ranked as serious or not serious based on the study quality ratings; 2) inconsistency assessed based on meta-analysis results and comparisons of location and variance parameter estimates; 3) imprecision judged by the number of available data points and the magnitude of uncertainty in the location parameter; 4) indirectness based on the applicability of study populations, interventions, and outcomes to the research question; and 5) small study effects including publication bias assessed by visual inspection of effect size distribution and sampling variance. Overall confidence was recorded as either high, moderate, low, or very low.

Data synthesis and analysis

Meta-analyses were conducted on pairwise comparisons between animal- and plant-based protein supplementation and their effects on MPS, assessed by myofibrillar fractional synthesis rates (FSR). Pre- and post-supplementation FSR expressed the percentage of the total myofibrillar protein synthesized per hour ($\%\cdot h^{-1}$). All analyses were conducted within a Bayesian framework allowing for the inclusion of prior information and probabilistic interpretation of results. Three-level hierarchical random-effects models accounted for variation in study mean effects and the covariance of multiple outcomes reported within the same study.

Point estimates for sampling error of effect sizes were calculated using standard formulae [29], assuming a correlation of 0.7 between pre- and post-supplementation values and 0.5 for crossover designs. A Gaussian error term was incorporated into the Bayesian models to account for uncertainty in these correlation estimates. To improve estimate precision, an informative prior distribution was applied to the between-study variance parameter based on predictive distributions previously developed [30]. To mitigate the influence of outliers, robust meta-analysis models used a Student-T distribution instead of a Gaussian distribution for effect size modelling. Posterior distributions were provided for the between-study variance scale parameter and intraclass correlation coefficient from hierarchical model components. Statistical inferences were based on the posterior distribution of the location parameter, 95% credible intervals and credibility masses calculated from highest density intervals.

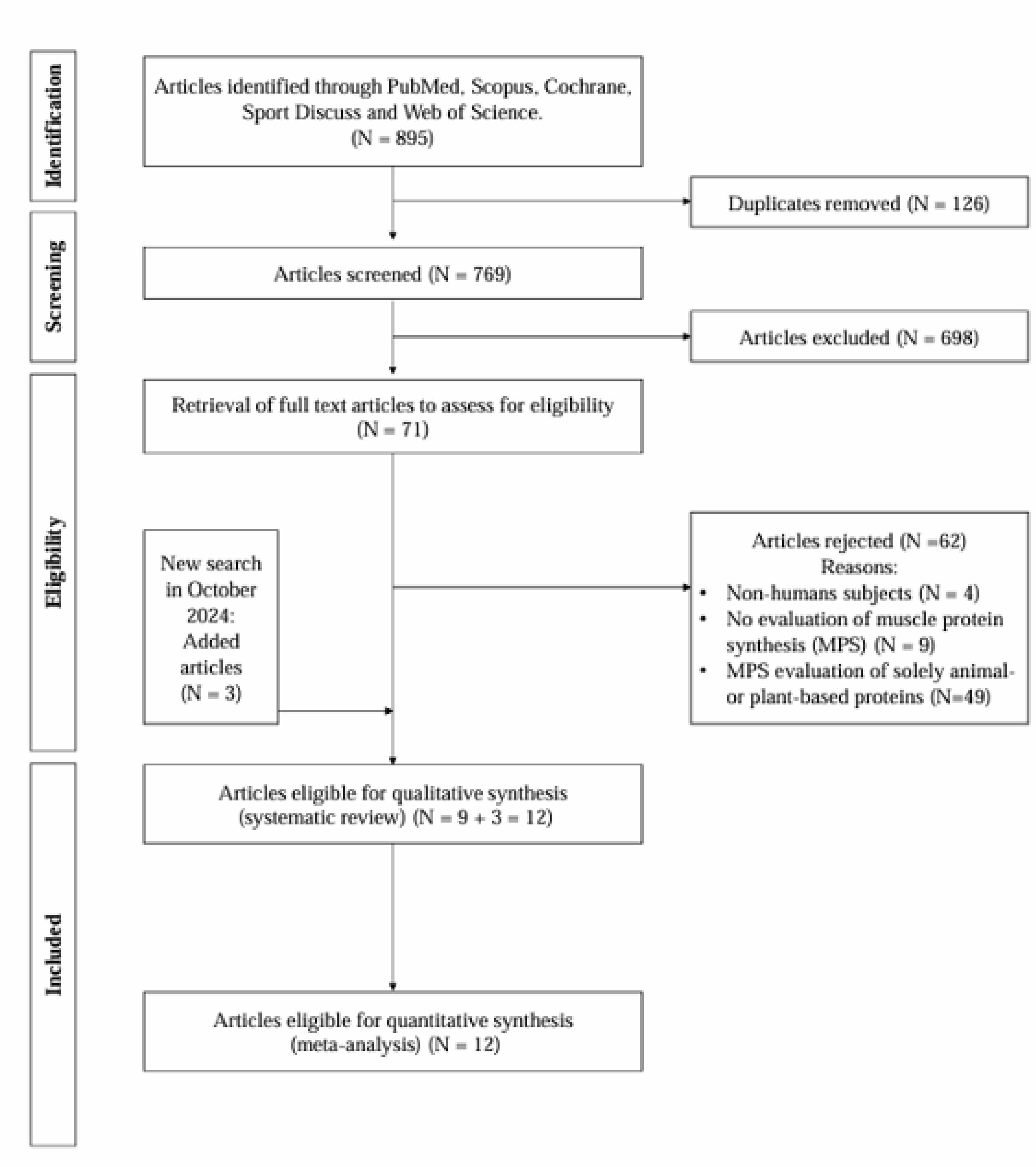
Subgroup analyses examined whether MPS stimulation varied by 1) age (younger < 30, vs. older > 65); 2) presence vs. absence of resistance exercise; and 3) timing of MPS measurement post-protein consumption (0-2 h, > 2-5 h, > 5-24h). Analyses were performed in the R environment (version 4.4.2) using the wrapper package brms interfaced with Stan to perform sampling [31].

Results

Study Selection

The literature search identified 895 studies (Figure 1). After removing 126 duplicates, 71 studies were selected for full-text screening with nine meeting the eligibility criteria. A follow-up search in October 2024 added three additional studies, resulting in a total of 12 eligible studies included in the systematic review with meta-analysis.

Figure 1 - PRISMA Flow-chart



Study Characteristics

The characteristics of the included studies are summarised in Table 2. Eleven studies were double-blind randomized controlled trials and 1 study used a quasi-experimental design [32], with group sample sizes ranging from 7 to 15 (median: n = 12). The mean participant age ranged from 18 to 72 years. One study included a mix population (8 men and 2 woman), while the remaining 11 studies included only men. Nine studies included untrained participants, two included resistance-trained participants, and one included recreationally active participants.

Quality Assessment

Table 2 details the methodological quality of each study. Overall, 4 studies were rated “strong”, 8 were rated “moderate”, and none were rated “weak”. For selection bias, all studies were rated “strong” as participants were representative of the target population. For study design, 10 studies were rated “strong”, while 2 were rated “moderate” due to unclear randomisation methods. For confounder control, 11 studies were rated “strong”, indicating proper adjustment for confounders. For blinding, 11 studies were rated “strong”, while 1 was rated “moderate” because full blinding was not feasible. All data collection methods were rated “strong” based on use of validated tools. For withdrawal and dropouts, 10 studies were rated “strong”, 1 “moderate” (dropouts reported but values missing), and 1 “weak” (no details provided).

Table 2 - Quality assessment using the Quality Assessment Tool for Quantitative Studies

Study	Selection Bias	Study Design	Confounders	Blinding	Data Collection Method	Withdrawals	Global
Yang et al. 2012	2	2	1	2	1	3	Moderate
Gorissen et al. 2016	2	1	1	1	1	1	Strong
Monteyne A. et al. 2020	2	2	1	1	1	1	Moderate
Kouw. et al, 2021	3	1	1	1	1	1	Moderate

Pinckaers et al. 2021	3	1	1	1	1	1	Moderate
Pinckaers et al. 2022	3	1	1	1	1	1	Moderate
Pinckaers et al. 2022 (b)	3	1	1	1	1	1	Moderate
Heijden et al. 2024	2	1	2	1	1	1	Strong
Lim et al. 2024	3	1	1	1	1	2	Moderate
McKendry et al. 2024	1	1	1	1	1	1	Strong
Pinckaers et al. 2024	3	1	1	1	1	1	Moderate
Pinckaers et al. 2024 (b)	2	1	1	1	1	1	Strong

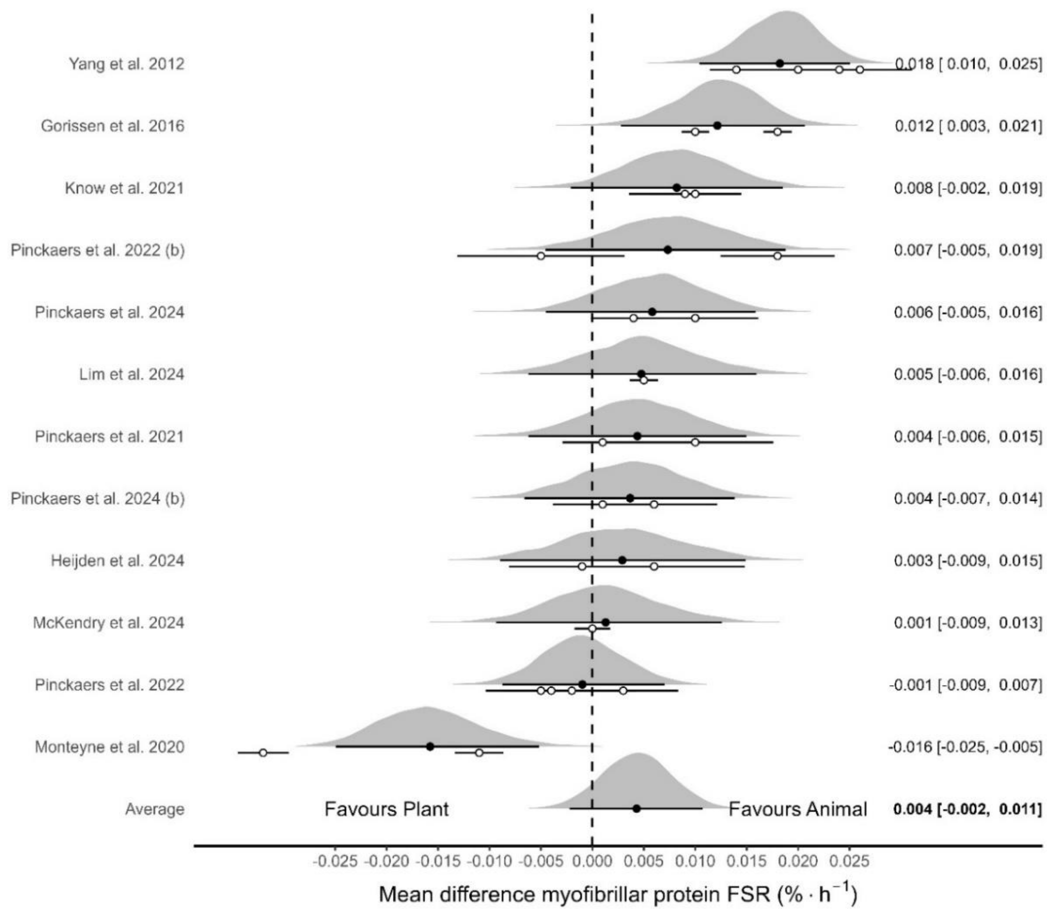
1: strong; 2: moderate; 3: weak

Effects of Plant- vs. Animal-based Proteins on Muscle Protein Synthesis

Twelve studies that directly compared plant- and animal-based proteins were included in this review. Nine studies (75%) [33-41] reported no significant differences in MPS, and three studies (25%) [32,42,43] reported lower MPS with plant-based proteins. Across the 12 studies, a total of 26 comparisons were made. For animal-based proteins, 14 used milk protein, 9 used whey protein, two used chicken meat and one used casein. Greater variety of sources were used for plant-based proteins including blended protein (n=7), isolated wheat protein (n=4), isolated potato protein (n=4), isolated soy protein (n=4), isolated pea protein (n=3), mycoprotein (n=2), and isolated corn protein (n=2).

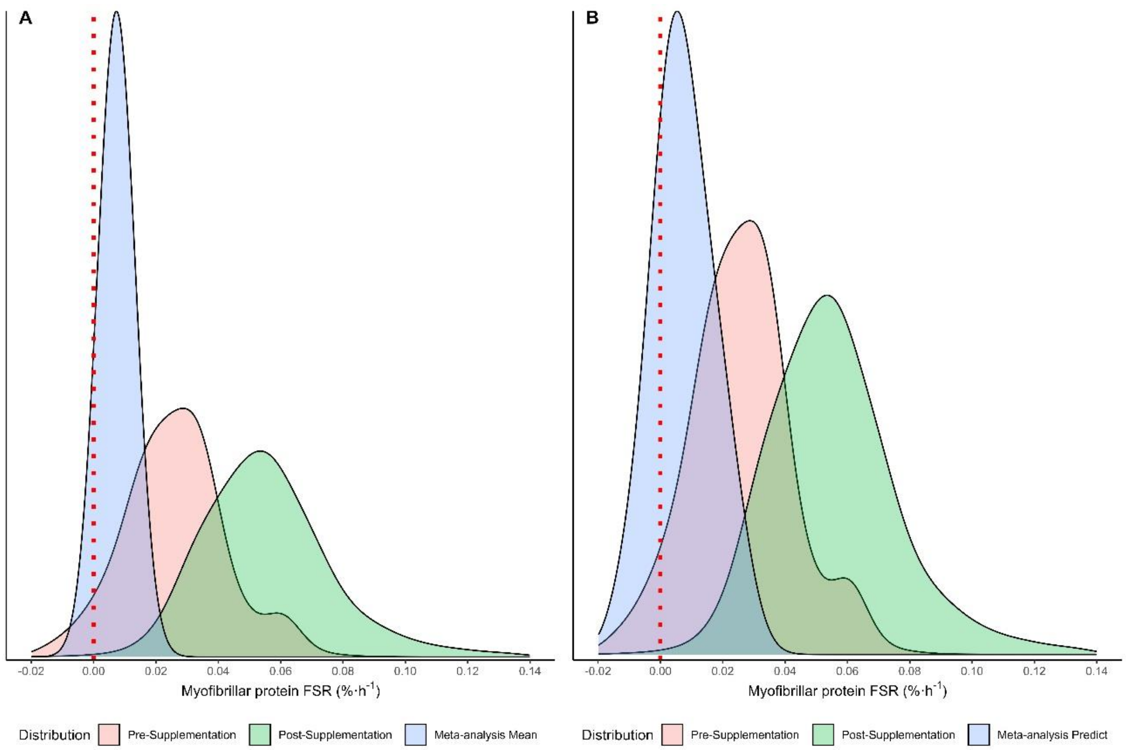
The primary meta-analysis incorporated a total of 26 comparative effect sizes from 12 studies and provided evidence that favoured animal-based protein ($ES_{Plant:Animal}$ = 0.004 [95%CrI: -0.002 to 0.011 FSR $\%\cdot h^{-1}$]; $p(>0) = 0.899$; Figure 2). Full model details are presented in Table 4. A visual comparison of pooled pre- and post-supplementation FSR %·h^{-1} contextualizes the effect size. Using both uncertainty in the mean effect size, and predicted difference (accounting for between-study variance), the plot highlights the effect sizes are towards the lower end of pre-supplementation MPS. More precisely, the central measure of the mean effect size aligned with the 0.08-quantile of the pre-supplementation distribution and 0.0035-quantile of the post-supplementation distribution.

Figure 2- Forest plot illustrating pairwise comparative mean differences in muscle protein synthesis between animal-based and plant-based protein supplementation.



Positive values indicate change in MPS that favours animal-based protein sources and negative values indicate a change in MPS that favours plant-based protein sources. Distributions represent "shrunken estimates" based on all effects sizes included, the random effects model fitted and borrowed information across studies to reduce uncertainty. Black circles and connected intervals represent the median value and 95% credible intervals for the shrunken estimates. White circles and intervals represent the raw estimates and sampling variance calculated directly from study data. Bottom distribution illustrates uncertainty in the pooled mean.

Figure 3 - Density plots of muscle protein synthesis pre-supplementation, post-supplementation and from meta-analysis providing effect size context



Plot A (left) illustrates uncertainty from posterior distribution of the meta-analysis mean. Plot B (Right) illustrates uncertainty from posterior predictions of study values using estimated model parameters without additional sampling error. Density for pre- and post-supplementation were created by combining data from animal- and plant-based groups and applying normal distributions using sample means and standard deviations. For plot A, 50% credibility mass lies between 0.065- and 0.095-quantiles of the pre-supplementation distribution, and 0.003- and 0.004-quantiles of the post-supplementation distribution. For plot B, 50% credibility mass lies between 0.030- and 0.12-quantiles of the pre-supplementation distribution, and 0.001- and 0.005-quantiles of the post-supplementation distribution.

Moderation Analysis

Evidence of moderation effects were obtained for mean participant age (Table 4). For younger participants, the pairwise difference was close to zero ($ES_{Plant:Animal}$ = 0.001 [95%CrI: -0.007 to 0.009 FSR $\%\cdot h^{-1}$]; $p(>0)$ = 0.653). Stronger evidence favouring animal-based protein supplementation was obtained for older participants ($ES_{Plant:Animal}$ = 0.012 [95%CrI: 0.000 to 0.026 FSR $\%\cdot h^{-1}$]; $p(>0)$ = 0.977). Only a single effect size was obtained for more than five hours post-supplementation, and subgroup analyses showed similar meta-analysis results between other time points, and whether supplementation was combined or not with exercise (Table 4).

Certainty assessment

Table 5 presents the certainty assessment for MPS outcome. No concerns were raised following risk of bias assessment. In contrasts, serious concerns were raised for inconsistency and imprecision due to the relatively large between study variation estimate, and wide credible interval for the effect size estimate. No concerns were raised regarding directness of the evidence or risk of publication bias based on visual analysis of study effect size estimates and their sampling variance (supplementary file S1).

Table 3- Included study characteristics.

Study	Study design	Participants	Protocol	Control Group (n)	Intervention Group (n)
Yang et al., 2012	Quasi-experimental D-B	30 older men (71±5y)	Unilateral Rex or No Rex + protein ingestion MPS evaluation at 0 and 4h	Whey isolate 20g 2.4g leucine Or 40g 4.8g leucine (10)	Soy isolate 20g 1.6g leucine Or 40g 3.2g leucine (10)
Gorissen et al., 2016	RCT D-B	48 older men (71±1y)	MPS evaluation at 0 and 4h	Casein 35g 3.2g leucine (12)	Wheat hydrolysate 35g 2.5g leucine (12)
Monteyne et al., 2020	RCT D-B	20 resistance-trained young men (22±1y)	Unilateral Rex or no Rex + protein ingestion MPS evaluation at 0 and 3h	Milk protein 26.2g 2.5g leucine (9)	Mycoprotein 31.5g 2.5g leucine (10)
Kouw et al., 2021	RCT D-B	24 active young men (18-35y)	MPS evaluation at 0 and 5h	Chicken 40g 0.93g leucine (12)	Plant meat substitute 40g 0.84g leucine (Lysine-enriched) (12)

Pinckaers et al., 2021	RCT D-B	36 young men (23±3y)	MPS evaluation at 0 and 5h	Milk protein 30g 2.4g leucine (12)	Wheat protein 30g 2.1g leucine (12)
Pinckaers et al., 2022	RCT D-B	24 young men (24±4y)	Unilateral Rex or no Rex + protein ingestion MPS evaluation at 0 and 5h	Milk protein 30g 1g leucine (12)	Potato protein 30g 0.9g leucine (12)
Pinckaers et al., 2022 (b)	RCT D-B	24 young men (24±4y)	MPS evaluation at 0and 5h	Milk protein 30g 2.4g leucine (12)	Plant protein blend 30g 2.4g leucine (12)
Heijden et al. 2024	RCT D-B	10 resistance-trained young adults (26±6y)	Bilateral Rex + protein ingestion MPS evaluation at 0, 2 and 4h	Whey 32g PRO 3.2g leucine (10)	Plant blend 32g PRO 2.1g leucine (10)
Lim et al. 2024	RCT D-B Cross-over	15 young men (25±4y)	MPS evaluation at 0 and 5h	Whey 21.3g PRO 3g leucine (7)	Plant blend 23.2g PRO 1.5g leucine (8)
McKendry et al. 2024	RCT D-B	30 older men (72±4y)	MPS evaluation at 0 and 24h	Whey 50g PRO 5.4g leucine (15)	Pea protein 50g PRO 4.1g leucine (15)
Pinckaers et al., 2024	RCT D-B	36 young men (26±4y)	MPS evaluation at 0 and 5h	Milk protein 30g 2.4g leucine (12)	Corn Protein 30g 4.1g leucine (12)

Pinckaers et al., 2024	RCT D-B	24 young men (24±3y)	MPS evaluation at 0 and 5h	Milk Protein 30g 2.4g Leucine (12)	Pea Protein 30g 1.8g Leucine (12)

Table 4- Meta-analysis model details including sub-group analyses

Model	**Main (all data)**	**Mean age (younger)**	**Mean age (older)**	**Time post-supplementation (0-2 hours)**	**Time post-supplementation (>2-5 hours)**	**Without Exercise**	**With Exercise**
Included data	26 effect sizes 12 studies	19 effect sizes 9 studies	7 effect sizes 3 studies	8 effect sizes 7 studies	17 effect sizes 11 studies	19 effect sizes 11 studies	7 effect sizes 4 studies
Pooled mean effect size (95% CrI)	0.004 (-0.002 to 0.011)	0.001 (-0.007 to 0.009)	0.012 (0.000 to 0.026)	0.005 (-0.005 to 0.015)	0.004 (-0.003 to 0.012)	0.004 (-0.003 to 0.011)	0.004 (-0.009 to 0.017)
***p(*Pooled mean effect size>0)**	0.899	0.653	0.977	0.857	0.872	0.852	0.720
50% Credibility mass	(0.002, 0.007)	(-0.001, 0.005)	(0.008, 0.017)	(0.002, 0.009)	(0.002, 0.007)	(0.001, 0.006)	(-0.000, 0.008)

75% Credibility mass	(0.000, 0.008)	(-0.003, 0.006)	(0.005, 0.020)	(-0.001, 0.011)	(-0.000, 0.009)	(-0.000, 0.008)	(-0.004, 0.010)
85% Credibility mass	(0.000, 0.009)	(-0.004, 0.007)	(0.003, 0.022)	(-0.001, 0.013)	(-0.001, 0.010)	(-0.001, 0.009)	(-0.005, 0.013)
Between-study standard deviation (τ) (75% CrI)	0.010 (0.007 to 0.014)	0.010 (0.008 to 0.011)	0.009 (0.008 to 0.010)	0.010 (0.008 to 0.011)	0.010 (0.009 to 0.011)	0.010 (0.009 to 0.011)	0.010 (0.009 to 0.011)
ICC (75% CrI)	0.29 (0.17 to 0.43)	0.30 (0.18 to 0.85)	0.31 (0.13 to 0.60)	0.12 (0.01 to 0.47)	0.38 (0.23 to 0.56)	0.25 (0.09 to 0.47)	0.24 (0.02 to 0.67)

Positive values for pooled mean effect size favour animal-based proteins. ICC: Intra-class correlation coefficient. CrI: Credible interval.

Table 5- GRADE Summary of findings table

Outcome	Certainty assessment							№ of participants		Effect		Certainty
	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Plant-based	Animal-Based	Relative (95% CrI)	Absolute (95% CrI)	
Muscle Protein Synthesis	12	N= 11 RCT	Not serious [a]	Serious [b]	Not serious [c]	Serious [d]	None	136	136		MD 0.004 **$\%\cdot h^{-1}$ higher** (0.002 lower to 0.011 higher) Animal-based	⊕⊕◯◯ Low

CrI: Credible interval; MD: Mean difference; a. Low risk of Bias, no serious limitations; b. Substantial heterogeneity (τ_0.5=6.1 [75%CrI: 1.9 to 12.2]).; c. All studies directly compare plant proteins to animal proteins except one, which used the animal MPS values of other study by the same author; d. Substantial range that stretches across zero.

Discussion

This is the first systematic review with meta-analysis to compare the effects of ingesting plant- vs. animal-based proteins on MPS. The primary analysis indicated greater MPS activation when consuming animal-based proteins. Effect sizes from ten of the twelve included studies favoured animal-based proteins to varying extents, although modelled results showed equivocal differences between conditions for most studies. The overall pooled effect favouring animal-based proteins was relatively modest, but potentially meaningful as discussed in the following sections.

Age-Related Differences in MPS Response

Subgroup analysis suggested that age could be a key determinant of MPS differences between protein sources. In older individuals aged 65+ years, animal-based proteins yielded a more pronounced effect on MPS across the studied time periods. In contrast, younger individuals (aged 18-54 years) displayed similar MPS increases between conditions, with pairwise differences in effects sizes close to zero. Conceivably, the differential responses between age groups can be explained by the "leucine threshold" theory, which suggests that a given amount of leucine is required to trigger a robust MPS response [8,44]. There is some evidence that older adults require a higher dose of leucine to achieve the desired effect compared to younger individuals, likely due to the phenomenon of "muscle anabolic resistance", which diminishes the capacity of amino acids and proteins to stimulate MPS [16,45-48]. The quality of a protein source largely determines the anabolic response in older people [46-48]. Some authors have argued that doses of at least 2.5 g of leucine per meal, distributed over three daily meals (approximately 7.5 g in total), are necessary to stimulate MPS in older adults [49]. Others have proposed a 3 g bolus of leucine to acutely stimulate MPS in individuals over 65 years [50]. Alternatively, the quantity of leucine and the protein source appear to be less critical for MPS stimulation in younger adults, with total daily protein intake and nutrient-dense foods playing a more prominent role [51,52].

Inspection of the individual studies provides explanatory support that the age-related differences in MPS response may be related to the leucine content of the respective protein sources. All three included studies that employed a sample of older adults employed greater amounts of leucine in the animal- vs. plant-based protein conditions. Yang et al [32] compared 20 and 40 g doses of whey and soy isolate in a cohort of older men; the leucine content in these conditions equated to 2.4 vs. 1.6 g and 4.8 vs. 3.2 g, respectively. Gorissen et al. [42] compared a 35 g dose of casein and wheat hydrolysate in a cohort of older men, with a leucine content equating to 3.2 vs. 2.5 g, respectively. Notably, these two studies had the largest effect sizes favouring animal-based proteins of all interventions included in our analysis. In contrast, McKendry et al [39] compared a 50 g dose of whey and pea protein in a cohort of older men, with a leucine content equating to 5.4 vs. 4.1 g, respectively. The magnitude of effect between conditions in this study was similar, conceivably because the leucine dose exceeded the critical threshold for initiating MPS. When viewing the data collectively, the results suggest that the leucine threshold for older adults may be higher than what has been speculated by some researchers [49,50]. Alternatively, the similar observed MPS responses between plant- vs animal-based protein sources in younger individuals align with evidence that the leucine threshold is less relevant in this population [53].

Effects of Resistance Exercise on MPS

Plant- and animal-based proteins elicited similar MPS responses, regardless of whether the resistance exercise was performed. These results are consistent with previous reports showing no disparities in MPS between plant- and animal-based proteins, either with or without exercise [34,37,43,54]. Resistance exercise is crucial for influencing MPS, particularly at relative loads greater than 60% of one-repetition maximum [55]. This seemingly is due to a reduced leucine threshold required to initiate MPS, which results from improved efficiency in utilizing essential amino acids for muscle anabolism [55]. However, only three studies [33,35,3] examined the effects of vegetable proteins (mycoprotein, potato protein, and soy protein) versus animal proteins (milk protein and whey protein) following resistance exercise, limiting the ability to draw strong inferences on the topic.

Time-Dependent Effects & Protein Absorption

Pooling data across multiple post-ingestion time points revealed no substantive difference in MPS between protein sources. However, it should be noted that the included studies used a variety of protein sources for both animal- (whey, casein, milk and chicken) and plant-based (pea, wheat, corn, soy and blends) conditions, and there were insufficient data to sub analyse the potential interaction between these sources and timing of assessment. Thus, we cannot exclude the possibility that the type of protein might influence findings when testing the effect of animal- vs. plant-based sources at segmented time windows. For example, whey is a “fast-acting” protein, with an absorption rate estimated at ~ 10 g per hour, while cooked egg protein has a much slower absorption rate of ~ 3 g per hour [56]; these differences in absorption rate could conceivably elicit differential effects on MPS over time. Moreover, whole-plant proteins contain components that reduce their digestibility, such as a high fibre content, protease inhibitors, and "anti-nutritional" factors like phytates, lectins and polyphenols, which are not present when the protein is isolated [57-60]. Thus, when ingested in their natural form (with more fibre, phytates and several other components), the digestion and absorption of plant-based proteins may be different compared to that seen with animal-based proteins [61].

Certainty of Evidence

The overall certainty of evidence of this meta-analysis is rated as "low", requiring cautious interpretation. The evidence used in this review was from higher quality RCTs with no serious concerns regarding indirectness. The best estimate from the meta-analysis suggested that animal-based proteins result in a 0.004%.h^{-1} higher MPS compared to plant-based proteins. However, the credible interval (95%CrI: -0.002 to 0.011 %.h^{-1}) was relatively wide and the between-study variation (0.010; 75%CrI: 0.007 to 0.014 %.h^{-1}) large such that observed values from study to study could be expected to generate meaningfully different conclusions. As a result, it is likely that a series of larger RCTs will be required for estimates to stabilise and create greater certainty in a summary finding. Results from this review suggesting that effect sizes may be different based on participant age indicates that further research is required at both ends of the age spectrum to increase certainty in findings.

Limitations

This systematic review and meta-analysis has some important limitations. First, all of the included studies involved males limiting generalisability to females. Moreover, only three studies involved older adults, limiting the inferences that can be drawn from sub analysis of age-related effects between conditions. Future research should focus on studying more diverse populations to determine what, if any, differences may exist when consuming animal- vs. plant-based proteins. Second, only one of the included studies assessed MPS beyond 5-hours post protein consumption; thus, we cannot draw relevant conclusions as to MPS responses outside of this relatively short window. Third, acute measures of MPS are not necessarily indicative of long-term changes in muscle mass [62]; thus, caution is warranted when drawing conclusions on how consumption of plant- vs. animal-based proteins influences skeletal-muscle hypertrophy. Finally, all included studies provided protein as a supplement, in isolation of other nutrients. Thus, the results cannot necessarily be extrapolated to the consumption of various protein sources in combination with traditional dietary regimens.

Practical Implications and Conclusions

The present findings provide limited evidence that animal-based proteins can stimulate MPS to a modestly greater extent compared to plant-based proteins. However, sub analyses suggest that the benefits could be largely age-dependent. Older adults seem to derive greater MPS stimulation from animal-based proteins. This may be specific to the leucine content of the protein source, as differences between conditions appear to dissipate at a higher leucine intake. Hence, either consuming higher amounts of plant-based proteins or supplementing these sources with additional leucine conceivably could negate the beneficial effects of animal-based proteins in an older population. On the other hand, animal- and plant-based proteins seem to promote relatively similar MPS increases in younger individuals, suggesting that leucine content may not be as critical in this population. Further investigation is warranted in diverse populations across longer time-point MPS assessments to draw stronger conclusions on the anabolic effects of plant- and animal-based protein consumption.

Author Contributions

All authors made substantial contributions to the conception and design of the work. BM, JMC, IS and GM made substantial contributions to the acquisition, analysis and interpretation of data. BM drafted the work and IS, BJS, GM, revised it critically for important intellectual content. All authors gave approval of the final manuscript.

Conflict of interest

The authors report no competing interests.

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Data and Supplementary Material Accessibility

Data and supplementary material are available on the Open Science Framework project page: https://osf.io/yjbfx/

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