Protein Quality

Why does it matter?

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Proteins play a crucial role in the growth, maintenance and physiological functions of the human body.[1] All amino acids are important in the synthesis and functioning of muscles and organs, as well as in enzymes, hormones and the immune system.[2] Protein quality plays a significant role in muscle protein synthesis and influences how the body effectively uses dietary protein to build and repair muscle tissue.

Essential amino acids

Amino acids are categorised as essential (EAA) or non-essential (NEAA), depending on whether the body can synthesise them or not. NEAA can be synthesised by the human body, whereas EAA cannot, and must be obtained from dietary protein. Therefore, it is necessary to ensure an adequate intake of EAA through the diet.[3]

In addition, some NEAA, such as arginine, cysteine, glutamine, glycine, proline and tyrosine, can become conditionally essential (CEAA), e.g. for premature neonates and in some clinical conditions.[4] In these cases, the body cannot produce sufficient amounts of these amino acids and they need to be consumed through dietary protein to compensate for insufficient synthesis during these stages of life or clinical conditions.[4, 5, 6] To meet the metabolic demand and to assure proper functioning of the human body, consumption of adequate amounts of protein is therefore vital to meet both total protein and EAA requirements.[7]

In addition to total protein requirements, specific EAA requirements have also been established.[3, 6] The requirements for EAA have been defined by the Food and Agriculture Organization of the United Nations (FAO)[3, 6] and the European Food Standards Authority (EFSA),[4] and are presented in **Table 1**. Considering the requirements for EAA and the fact that protein is the only dietary source of EAA, the Recommended Daily Amount (RDA) for protein does not only contain a quantitative aspect but also a qualitative aspect. For example, if we consider that the RDA for protein in adults is 0.8 g protein/kg bodyweight/day, this amount is only sufficient to meet the requirements for this target population, if the intake also provides the levels of EAA outlined in **Table 1**. Such aspects are central to the concept of protein quality,[8] and demonstrates the need to consume either complete protein sources, or a combination of protein sources to provide all EAA.

Table 1: Recommended intake of EAA (in mg/kg body weight/day) for humans in different age groups[8]

Age (Years)	Histidine	Isoleucine	Leucine	Lysine	SAA*	AAA**	Threonine	Tryptophan	Valine
0.5-1	22	36	73	64	31	59	34	9.5	49
1-2	15	27	54	45	22	40	23	6.4	36
3-10	12	23	44	35	18	30	18	4.8	29
11-14	12	22	44	35	17	30	18	4.8	29
15-18	11	21	42	33	16	28	17	4.5	28
>18	10	20	39	30	15	25	15	4.0	26

*SAA = Sulphur-containing amino acids (Cysteine + Methionine) **AAA = Aromatic amino acids (Phenylalanine + Tyrosine)

When consuming low-quality proteins (based on EAA content), an individual may need to consume a higher total amount of protein to compensate for the lower levels of amino acids.[9] For example, if 60 g of protein is required to meet an individual's protein needs, these needs will only be met if the proteins consumed are high enough quality to meet EAA and CEAA requirements. If EAA and CEAA requirements are not met within the 60 g of protein consumed, further protein may be required over and above the 60 g requirements.

Protein digestion

Protein digestion is a complex, multistage process that involves hydrolysing proteins into free amino acids and small peptides for absorption into the bloodstream.[10] The process begins with chewing, which mechanically breaks down the food matrix, increasing the protein's surface area and enhancing its exposure to digestive enzymes.[10, 11] Digestion of starch by salivary amylase, further breaks down the food structure, making protein more accessible to digestive enzymes. After the brief oral phase, food enters the stomach, where gastric juice (pH 1-2) and pepsin begin breaking down proteins into polypeptides.[8]

Chyme is transferred to the duodenum, where it mixes with pancreatic enzymes[11] that, along with intestinal brush border enzymes, break down proteins and peptides into amino acids and smaller peptides. Pancreatic proteases and peptidases are more potent than pepsin, and most protein digestion occurs in the small intestine.[8]

Amino acids and peptides released during digestion are absorbed across the small intestinal mucosa, typically nearing full absorption by the terminal ileum. Any unabsorbed amino acids and peptides pass into the large intestine, where absorption is minimal despite the presence of amino acid transporters. Instead, these substances may be digested and fermented by the microbiota.[8]

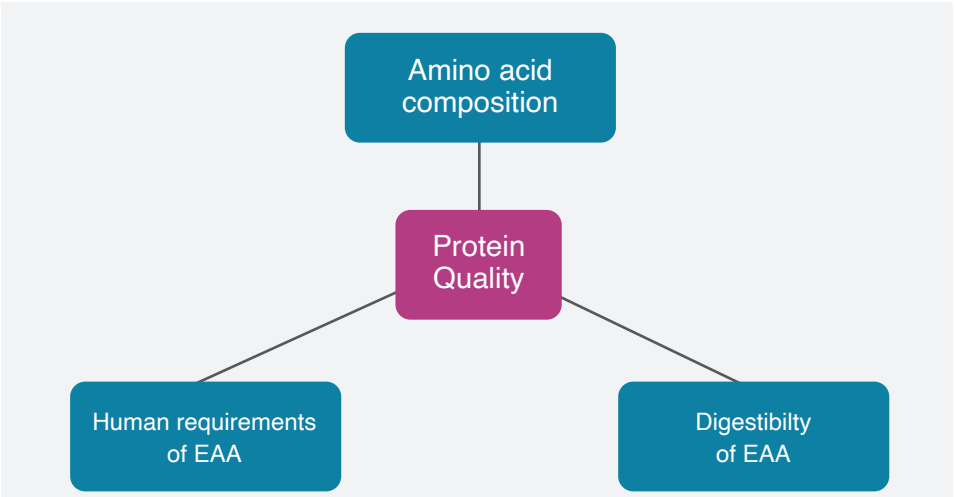
Protein quality measurement

Protein quality is generally determined by its amino acid composition, particularly the content of EAA and the bodies' ability to digest and absorb it. It can be defined by considering the following principles (**Figure 1**):

- **Amino acid composition** – A high-quality protein contains all EAA in the necessary amounts for human health. Low quality proteins have lower levels of, or lack one or more EAA, these are often referred to as limiting amino acids.[3, 12]
- **Digestibility** – Refers to the ease with which a protein can be broken down and absorbed by the body. Digestibility of protein is typically defined as the proportion of ingested protein that is hydrolysed into amino acids, di- and tripeptides, which are available for absorption.[13] Proteins that are consumed in a hydrolysed form have a higher digestibility and are typically more easily absorbed than whole proteins. Conversely whole proteins will take longer to digest and are absorbed more slowly.[14]
- **EAA Requirements** – EAA requirements can be population specific, for example, adults, children and specific clinical conditions such as sepsis.

Although there are several, 3 main methods are used to assess protein quality based on amino acid digestibility (**Table 2**). The methods, however, do have limitations and offer only theoretical measures of protein quality. Food processing can alter amino acid composition and digestibility, so protein quality assessments of raw materials may not accurately represent the final food products.[8]

Figure 1: Elements required to quantitively define protein quality†[8]



†Adapted from Adhikari *et al* 2022.[8]

Table 2: Main methods used to assess protein quality

Method	Protein Digestibility-Corrected Amino Acid Score (PDCAAS)	Digestible Indispensable Amino Acid Score (DIAAS)	Biological Value (BV)
What it measures	PDCAAS assesses the amino acid profile of a protein and its digestibility.	DIAAS evaluates the digestibility of individual EAA in specific parts of the digestive tract (small intestine).	BV measures how efficiently the body utilises protein consumed in the diet.
How it works	The amino acid content of the protein is compared to a reference pattern (usually based on human needs), and the result is adjusted based on how well the protein is digested. A PDCAAS score of 1.0 means the protein meets all essential amino acid needs and is highly digestible (e.g. eggs and milk).[15]	It provides a more precise assessment of how much of each indispensable amino acid is absorbed by the body, using ileal digestibility rather than whole-tract digestibility, making it more accurate than PDCAAS.[15]	Foods with a high value correlate to a high supply of EAA. Animal sources typically have a higher BV than vegetable sources due to most vegetable source's lack of one or more of the EAA. It does however not consider digestibility.[15]

How digestible a protein is depends on the form – intact proteins, peptides or free amino acids. Whole food proteins require more digestion, leading to slower absorption of EAAs into circulation compared to simpler EAA formats.[16]

Protein quality and muscle protein synthesis (MPS)

A protein source that lacks EAA will limit the body's ability to efficiently synthesise muscle protein.[16] Therefore, it is important to ensure that protein consumed provides a good source of EAA and any required CEAA, when compared to the amino acid reference ranges, and not just total protein requirements. Proteins that are incomplete (i.e. do not contain all EAA) have been shown to be less effective at stimulating MPS, if a protein is lacking or has low amounts of an EAA (referred to as the 'limiting amino acid'), it can restrict the body's ability to synthesise new muscle proteins effectively.[17]

Leucine, an EAA and branched chain amino acid (BCAA), has been identified as a trigger for MPS by activating the mammalian target of rapamycin (mTOR) pathway, a central regulator of muscle growth. When leucine levels are high, mTOR signalling is activated, leading to increased protein synthesis.[18] Whilst the exact dose of leucine needed to stimulate MPS is unclear, and may be population specific, 1.2 g of leucine has been shown to induce a robust stimulation of MPS.[19] Ongoing research is required to determine the optimum leucine content to stimulate MPS in specific populations, with studies showing variable effects on MPS with supplementation >6 g per day in older adults with sarcopenia.[20] It is important to note that leucine is a key trigger for MPS but works synergistically with other essential amino acids. Thus, consuming sufficient high-quality protein with optimal EAA levels is crucial for maximizing MPS and muscle growth.

A recent study combined data from 4 previous studies to investigate how changes in peripheral EAA after ingesting different types of protein and free amino acids altered muscle and whole-body protein synthesis.[15] The findings demonstrated that ingestion formats with a high proportion of EAA relative to total protein content represent a viable means of improving muscle and whole-body protein responses. Additionally, EAA sources that produce a large and rapid increase in peripheral EAA concentrations are recommended to improve muscle and whole-body protein synthesis.[16] This highlights the importance of protein quality – EAA content and digestibility, in choosing protein sources to support MPS.

Conclusion

Protein quality significantly influences the effectiveness of dietary protein in supporting MPS. EAA content and digestibility of proteins should be given consideration when meeting total protein requirements, including, for example, combining protein sources to provide all EAA.

> "A protein source that lacks EAA will limit the body's ability to efficiently synthesise muscle protein.[16]"

References: **1.** BoyeJ, Wijesinha-Bettoni R, Burlingame B. (2012). Protein quality evaluation twenty years after the introduction of the protein digestibility corrected amino acid score method. Br J Nutr.; 108(Suppl 2): S183–S211. **2.** Wu G. (2009). Amino acids: Metabolism, functions, and nutrition. Amino Acids.; 37(1): 1–17. **3.** FAO (2013). Dietary Protein Quality Evaluation in Human Nutrition: Report of an FAO Expert Consultation; FAO: Auckland, New Zealand. **4.** EFSA. (2012). Panel on Dietetic Products; Nutrition and Allergies (NDA). Scientific Opinion on Dietary Reference Values for protein. EFSA J.; 10: 2557. **5.** IoM. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients); National Academies Press: Washington, DC, USA. 2005. **6.** Joint WHO/FAO/UNU. Expert Consultation Protein and Amino Acid Requirements in Human Nutrition; WHO: Geneva, Switzerland, 2007. **7.** Gilani GS. Lee N. (2003). Protein Quality. In Encyclopedia of Food Sciences and Nutrition, 2nd ed.; Caballero, B., Ed.; Academic Press: Oxford, UK, pp. 4847–4854. **8.** Adhikari S, *et al.* (2022). Protein Quality in Perspective: A Review of Protein Quality Metrics and Their Applications. Nutrients.; 14(5): 947. **9.** Van-Vilet S, Burd NA, Van-Loon LJC. (2015). The Skeletal Muscle Anabolic Response to Plant-Versus Animal Based Protein Consumption. J Nutr.; 145(9): 1981–1991. **10.** Trommelen J, Tomé D, van Loon LJC. (2021). Gut amino acid absorption in humans: Concepts and relevance for postprandial metabolism. Clin Nutr Open Sci.; 36: 43–55. **11.** Singh H, Gallier S. (2014). Chapter 2-Processing of Food Structures in the Gastrointestinal Tract and Physiological Responses. In Singh Digestion and Health; Boland M, Golding M, Eds.; Academic Press: San Diego, CA, USA, pp. 51–81. **12.** Mathai JK, Liu Y, Stein HH. (2017). Values for digestible indispensable amino acid scores (DIAAS) for some dairy and plant proteins may better describe protein quality than values calculated using the concept for protein digestibility-corrected amino acid scores (PDCAAS). Br J Nutr.; 117(4): 490–499. **13.** Sá AGA, Moreno YMF, Carciofi BAM. (2019). Food processing for the improvement of plant proteins digestibility. Crit Rev Food Sci Nutr.; 60(20): 3367–3386. **14.** Koopman R, *et al.* (2009). Ingestion of a protein hydrolysate is accompanied by an accelerated in vivo digestion and absorption rate when compared with its intact protein. Am J Clin Nutr.; 90(1): 106–115. **15.** Boye J, Wijesinha-Bettoni R, Burlingame B. (2012). Protein quality evaluation twenty years after the introduction of the protein digestibility corrected amino acid score method. Br J Nutr.; 108(2): S183–211. **16.** Church DC, *et al.* (2020). Essential Amino Acids and Protein Synthesis: Insights into Maximising the Muscle and Whole-Body Response to Feeding. Nutrients.; 12(12): 3717. **17.** Wolfe RR. (2002). Supplement: Protein Metabolism in Response to Ingestion Pattern and Composition of Proteins. Am Society of Nutr Sc.; 3219s–3224s. **18.** Atherton PJ, *et al.* (2010). Distinct anabolic signalling responses to amino acids in C2C12 skeletal muscle cells. Amino Acids.; 38(5): 1533–1539. **19.** Bukahari S, *et al.* (2015). Intake of low-dose leucine-rich essential amino acids stimulates muscle anabolism equivalently to bolus whey protein in older women at rest and after exercise. Am J Physiol Endocrinol Metab.; 308(12): E1056–E1065. **20.** Martinez-Arnau FM, *et al.* (2020). Effects of leucine administration in sarcopenia: a randomized and placebo-controlled clinical trial. Nutrients.; 12(4): 932.