Review on human postprandial amino acid kinetic studies


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Background

Measuring postprandial blood amino acid (PBAA) kinetics in humans after intake of a protein source is considered as a proxy for protein digestion and uptake. The method is relatively straightforward and can become the alternative animal-free measure to estimate protein quality. However, further standardisation of the PBAA kinetics method is needed to compare outcomes from separate studies.

Objective

A literature review was performed to gather knowledge on PBAA human trials, summarize data from these studies and to advocate for standardised designs and analysis, improved reporting of results, and to harmonise comparative analysis.

Method

PubMed and Scopus were searched for the following terms: 'protein', 'postprandial', 'amino acid', 'human', 'trial', and 'cross-over'. Based on the set criteria, PBAA human studies were scanned manually and selected. Available food product composition information (macronutrients and amino acids), population characteristics, details on trial design, and PBAA incremental Area Under the Curve (iAUC) data were collected. If numerical PBAA iAUC values were not reported, data were retrieved from presented bar plots or postprandial curves using PlotDigitizer and ImageJ, respectively. Postprandial iAUC values for amino acids or their subsets were computed as a percentage relative to a designated reference. This reference, signifying 100%, was selectively applied to scenarios encompassing whey protein, milk, or beef.

Results

Currently, we identified 65 papers that met our criteria for the review study. Table 1 provides an overview of the study characteristics, categorized by topic. Table 2 shows the ranking of iAUC of TEAA of the test product compared to whey, while Table 3 displays the ranking relative to milk. For studies involving beef, we refer to Table 4. Please note that these rankings are rough estimates due to variations in study designs, populations, reference products, protein concentrations, etc.. Additionally, Table 5 offers a brief summary of studies involving protein hydrolysates and their non-hydrolysed counterparts.

Table 1. *Overview of the current 65 studies included in the database.*

Characteristics	Subgroups		
Composition reported	**macro-nutrients**	**amino acid composition**	
	49%	56%	
Population size (n)	**<10**	**10-20**	**>21**
	20%	63 %	17%
Average Age (year)	**<30**	**30-60**	**>60**
	66%	12%	22%
Population	**healthy**	**obese/MeS**	**(pre)T2D**
	91%	6%	3%
Gender	**male/female**	**only male**	**only female**
	48%	46%	6%
Reference source	**whey**	**milk**	**beef**
	37%	12%	7%
Amount protein provided (g)	**<20**	**20-30**	**>30**
	19%	60%	21%
Collection time (minutes)	**180-239**	**240-299**	**300 and longer**
	37%	25%	34%
Included postprandial iAUC AAs	**(almost) all relevant individual AA**	**Total AA**	**Total EAA**
	23 %	60%	74%

Table 2. *Comparison of test product relative to whey based on % iAUC as tested in the same trial.*

Reference	Product	TEAA % relative to whey in same study	Range
Sharp et al 2019	WPI +io (whey protein isolate plus Ingredient Optimized Protein®)	223.1	
Detzel et al 2016	MyoCHX™ (Essentia Protein Solutions)	216.0	
Gwin et al 2021	EAA+W (EAA-enriched whey protein isolate)	139.3	
King et al 2018	Hydrolysed whey protein (PSNU 28600, Arla Foods) + mixed nutrient breakfast	114.9	
All studies	Whey	100.0	
Hoefle et al 2018	glycomacropeptide (GMP) as part of the whey fraction of bovine milk (90% GMP, Davisco, Eden Prairie)	99.9	
Wegrzyn et al 2022	1:1 soy dairy (48 soy: 32 casein: 20 whey)	95.1	
Wegrzyn et al 2022	1:2 soy dairy (34 soy: 52 casein: 14 whey)	95.1	
Tessari et al 2007	Free AA	91.6	
Detzel et al 2016	BeefISO™ (Essentia Protein Solutions, Ankeny, IA)	79.2	
Thogersen et al 2021	Krill protein hydrolysate (Euphausia superba (INVITM protein, Aker Biomarine Antarctic AS, Lysaker, Norway)	75.3	
Ummels et al 2023	PP (pea protein isolate (NUTRALYS® S85 XF, Roquette, Lestrem, France)	71.0	
Vangoe et al 2018	Insect protein isolate (Experimental Protein Isolate, ~82% protein) from the lesser mealworm (Alphitobius diaperinus) was provided by Proti-Farm R&D BV (Ermelo, Netherlands))	69.3	
Tessari et al 2007, Luiking et al 2016, Juvonen et al 2012, He et al 2013, Gorissen et al 2016, Tang et al 2009	Casein	68.4	39.7 - 78.0
Mes et al 2022	LPC (Lemna protein Concentrate)	66.3	
Sharp et al 2020a	PT-PP (plasma treated pea protein)	64.2	
Tang et al 2009, Vangoe et al 2018, Thogersen et al 2021	Soy protein	63.5	54.9 - 71.8
Lees et al 2021	WBWPH (fish / blue whiting protein hydrolysate)	60.6	
Gorissen et al 2016, Sharp et al 2020a	Wheat protein	59.5	48.4 - 68.3
Ummels et al 2023	BRP (Barley/Rice (ratio on average 70/30) protein isolate (EverPro, EverGrain® by AB InBev, St. Louis, MO, USA)	58.2	
Luiking et al 2016	W320 (20 g whey protein isolate, 3 g total leucine 320kcal, extra fat and carbohydrates))	57.9	
Mensink et al [b]	Luzerne protein isolate	52.5	
Esser et al [c]	CP 85% (corn protein isolate, Cargill, Vilvoorde, Belgium)	51.2	
He et al 2013	HMW (potato protein Solanic 206P)	46.3	
Hoefle et al 2018	MD19 (starch hydrolysate, Berco Arneimittel)	45.0	
Esser et al [c]	BP (Sonac Plasma Powder 70 B, Sonac Loenen BV, Loenen, The Netherlands)	44.5	
He et al 2013	LMW (potato protein Solanic 306P)	20.7	
Sharp et al 2020a	S-PP (standard pea protein)	12.8	
Gwin et al 2021	Meal (protein in mixed-macronutrient meal)	3.1	
Lees et al 2021	NEAA (non-essential AA)	-9.5	

Table 3. *Comparison of test product relative to milk based on % iAUC as tested in the same trial.*

Reference	Product	TAA % relative to ref	TEAA % relative ref
Wijzen et al 2021	FAA (Free Amino Acids)		152.1
Dunlop et al 2017	MYC 80, 80 g mycoprotein	119.8	105.0
Milan et al 2021	Sheep milk	115.2	132.4
Wilkinson et al 2006	Soy (drink based on isolated soy protein (GeniSoy, Fairfield, CA))	113.9	
de Hart et al 2021	Cheddar cheese		108.0
Dunlop et al 2017	MYC 60, 60 g mycoprotein	109.2	101.8
Burke et al 2012	Liquid meal power bar protein Plus	101.3	101.5
Burke et al 2012	Skim milk	100.0	100.0
Dunlop et al 2017	MLK 20, 20 g milk protein	100.0	100.0
Milan et al 2021	Cow milk	100.0	100.0
Pinckaers et al 2022	Milk	100.0	100.0
Wilkinson et al 2006	Milk (non fat skim milk powder based drink)	100.0	
de Hart et al 2021	2% fair life milk		100.0
Wijzen et al 2021	PRO (intact milk protein)		100.0
Dunlop et al 2017	MYC 40, 40g mycoprotein	99.6	96.4
Dunlop et al 2017	MYC 20, 20 g mycoprotein	92.2	89.1
Burke et al 2012	Soy milk	79.7	82.3
Burke et al 2012	Beef steak	72.8	95.8
Pinckaers et al 2022	Plant-blend (2:1:1 wheat:corn:pea)	69.0	52.3
Burke et al 2012	Eggs	66.3	95.6

Table 4. *Comparison of test product relative to beef based on % iAUC as tested in the same trial.*

Reference	Product	TAA % relative to ref	TEAA % relative to ref
Pham et al 2022	Lamb (pasture-raised lamb as wrap with canned vegetable, tomato salsa, seasonings in flour tortilla)	118.3	133.5
Pham et al 2022	Grain (grain-finished beef as wrap with canned vegetable, tomato salsa, seasonings in flour tortilla)	116.0	127.9
Neacsu et al 2022	Lupin (flour)	100.4	86.5
Pennings et al 2013	Minced beef		102.1
Agergaard et al 2021	Minced (chopped steak)	100.0	100.0
Neacsu et al 2022	Beef (Meat)	100.0	100.0
Pham et al 2022	Pasture (Pasture-raised beef as wrap with canned vegetable, tomato salsa, seasonings in flour tortilla)	100.0	100.0
Pennings et al 2013	Beef steak		100.0
Neacsu et al 2022	Green pea (flour)	98.6	83.9
Agergaard et al 2021	Steak (beef)	98.2	102.3
Agergaard et al 2021	HMP (hydrolysed meat protein)	97.3	96.7
Neacsu et al 2022	Hemp (flour)	88.6	65.6
Neacsu et al 2022	Fava bean (flour)	81.0	64.5
Pham et al 2022	BB (Beyond Burger as wrap with canned vegetable, tomato salsa, seasonings in flour tortilla)	66.7	57.3
Neacsu et al 2022	Buckwheat (flour)	47.2	25.2

Table 5. *Effect of hydrolysed and non-hydrolysed forms of the same protein sources on PBAA kinetics.*

Reference	Product	TEAA % relative to ref		
		non hydrolysed	hydrolysed	diff
Farnfield et al 2009	WPI	100	85.7	-14.3
Gorissen et al 2016	Wheat protein	57.2	48.4	-8.9
Fleddermann et al 2013	Canola protein (CPI)	96.2	96.0	-0.2
King et al 2018	Whey protein concentrate	100.0	114.9	14.9
Skov et al 2019	Collagen	100.0	123.8	23.8
Horner et al 2019	Casein	100.0	126.6	26.6
Koopman et al 2009	Casein	100.0	146.0	46.0

Advise for trial design and reporting

- Balanced amounts of protein (20-30g) in comparing arms of a cross-over trial
- Using whey (WPC 80 MILEI-LEUTKIRCH), or milk (Refit MPC 80 Lactose reduced FC-DMV) or minced beef (Black Angus, low fat paddies) as referent in at least one arm of the trial
- Blood collection for 240-360 min after protein intake with minimum of 10 sampling points
- Report composition of test product including amino acid composition (preferable in mg/g protein) in numerical values
- Calculate iAUC (preferable use R codes[a]) for individual AA, TEAA, and TAA and provide numerical values for each individual person
- Include T_0 values for each person at each trial day in the database

Conclusion

- A first dataset was generated on published PBAA kinetic studies with 65 studies and information on 192 tested products
- The dataset can be used for different type of analysis (including a proxy for DIAAS) overarching individual trials
- Our aim is to make this dataset publicly available and create an open database, where researchers can upload their PBAA results, derived from studies with a high degree of similar methodology
- PBAA trials, when further standardised, can be used as measure for *in vivo* relative protein quality analysis

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[a] Wehrens *et al*. in submission (https://github.com/Biometris/aaresponse).
[b] Mensink *et al.* in preparation
[c] Esser *et al*. in press Current Research in Food Science