ORIGINAL RESEARCH & COMPARATIVE REGULATORY ANALYSIS

A Protein's Solubility Is Not Its Digestibility

The 2026 UK Fermentation Guidance, EFSA's Validation Caveat and the Evidence Gap in Next-Generation Protein Hydrolysates

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Executive abstract

The expanding market for enzymatically modified, plant-derived and precision-fermented proteins has exposed a methodological weakness in ingredient qualification: dispersibility, peptide size, simulated gastrointestinal release and nutritional amino-acid availability are frequently discussed as though they measured the same property. They do not. The United Kingdom's March 2026 supplementary guidance for fermentation-derived novel foods recommends a tiered approach centred on digestible indispensable amino acid scoring and in-vitro digestion, whereas EFSA's applicable novel-food guidance explicitly cautions that in-vitro models have not yet achieved general validation for true ileal amino-acid digestibility. New 2026 plant-protein comparisons strengthen the case for calibrated laboratory methods without eliminating matrix-specific exceptions. Against the backdrop of the FDA's October 2026 final guidance on ingredient identity and safety evidence, this article develops a cross-jurisdictional, analytically explicit approach to distinguishing technological performance from nutritional quality, exposure and lawful claims. A proposed validation programme for hydrolysed proteins is presented as a research hypothesis, not an established advantage.

KEYWORDS: *protein hydrolysates; amino-acid digestibility; INFOGEST; DIAAS; precision fermentation; nutritional claims; novel foods; regulatory science*

CATEGORY: Biotechnology & Functional Ingredients | Nutrition & Regulatory Affairs

SEO SLUG: protein-solubility-not-digestibility-2026-hydrolysates

META DESCRIPTION: Why soluble protein hydrolysates need validated amino-acid digestibility, matrix testing and market-specific claims under evolving UK, EU and US guidance.

INTERNAL TAGS: Innovative Proteins; Enzymatic Hydrolysis; Protein Quality; Precision Fermentation; INFOGEST; DIAAS; Regulatory Affairs; Emerging Research

01 | The timely signal: three documents, one unresolved measurement problem

On 19 October 2026 the US Food and Drug Administration issued final guidance on the identity and safety evidence supporting notifications for new dietary ingredients (NDIs). The document finalises selected sections of a longer draft rather than creating a new premarket approval system. Its immediate importance for protein innovators lies in the insistence that the substance being marketed, the substance investigated in safety studies and the substance described in manufacturing specifications must be meaningfully connected. A change in process can matter even when the commercial ingredient name remains constant. [1,2]

A different but complementary signal came from the Food Standards Agency (FSA) and Food Standards Scotland in March 2026. Their supplementary guidance for novel foods produced by precision or biomass fermentation places substantial emphasis on protein digestibility, structural characterisation, allergenicity and intended dietary use. In parallel, a January 2026 study involving Spanish and US researchers compared laboratory digestion results with pig ileal data across 17 plant-derived substrates. Read together with EFSA's 2024 novel-food guidance, these sources expose a productive scientific tension: the demand for faster, non-animal evidence is increasing, but a method's convenience does not establish that its numerical output has the same meaning as a validated physiological measurement. [3,4,9]

The issue extends beyond fermentation. It affects enzymatically hydrolysed rice, pea and cereal proteins, protein concentrates, peptide ingredients, protein-enriched beverages, medical nutrition concepts and animal-feed development. The central question is not whether hydrolysis can improve solubility -it often can- but what additional evidence is needed before an industrial operator can assert improved digestibility, superior protein quality or a reduction in the amount of protein required.

02 | Four endpoints routinely mistaken for one another

Solubility describes how much material remains molecularly dissolved or colloidally dispersed under specified conditions. It is sensitive to pH, ionic strength, concentration, temperature, turbidity definition and the separation method used to classify the supernatant. A visually transparent beverage is not necessarily a molecular solution, and a centrifugation-based solubility percentage is not an absorption measurement. Hydrolysis can increase dispersibility by reducing protein size or exposing charged groups, but hydrophobic peptide aggregation and interactions with polyphenols, minerals or polysaccharides can reverse that improvement in a particular food matrix. [13,14]

Digestibility describes the fraction of protein or individual amino acids digested and made available at a defined anatomical or analytical endpoint. Bioaccessibility usually describes the fraction released from a food matrix under simulated gastrointestinal conditions; bioavailability concerns the fraction reaching systemic circulation or being available for physiological utilisation, depending on the endpoint. Postprandial plasma amino-acid appearance is a kinetic response influenced by gastric emptying, intestinal uptake, first-pass splanchnic extraction and endogenous metabolism. These quantities can be related without being interchangeable. [5–8,11]

Protein quality introduces yet another dimension: the balance of indispensable amino acids relative to human requirements and the digestibility of each amino acid. An ingredient may be highly soluble and rapidly hydrolysed yet remain limited by lysine or another indispensable amino acid. Conversely, a less soluble ingredient may supply a nutritionally valuable amino-acid pattern when incorporated into a suitably processed meal.

03 | Why the degree of hydrolysis is a process variable, not a nutritional multiplier

Degree of hydrolysis (DH) is commonly expressed as the proportion of peptide bonds cleaved under a defined analytical method. It is useful for controlling enzymatic reaction progress, molecular-weight distribution, flavour and functional performance. However, DH does not quantify the fraction of an ingested protein absorbed by a human. Two preparations with similar DH can contain different peptide sequences, free amino-acid fractions, hydrophobicity distributions, enzyme residues and oxidation products. Their gastrointestinal behaviour may therefore differ. [11,14]

Human evidence directly challenges simplistic multipliers. In a controlled study of three whey hydrolysates with different degrees of hydrolysis, all produced more rapid plasma amino-acid appearance than casein, yet increasing

DH within the tested hydrolysates did not significantly increase the measured appearance rate. This finding concerns whey, a specified dose and experimental design; it cannot be mechanically transferred to rice or fermentation-derived proteins. It does, however, refute the general proposition that a larger DH automatically produces proportionally greater human absorption. [11]

Accordingly, an assertion that a hydrolysed ingredient permits one-third the dose of an untreated protein requires a defined comparator, a prespecified endpoint and direct supporting data. It cannot be inferred from peptide size, solubility or an isolated laboratory digestion percentage.

04 | DIAAS measures amino-acid quality, not the speed of a beverage

The Digestible Indispensable Amino Acid Score (DIAAS) was proposed by an FAO expert consultation as a more physiologically relevant protein-quality framework than the older Protein Digestibility-Corrected Amino Acid Score (PDCAAS). In simplified terms, DIAAS compares the amount of each digestible indispensable amino acid in one gram of dietary protein with an age-relevant reference pattern and identifies the limiting ratio. The digestibility coefficients concern individual amino acids at the terminal ileum rather than total nitrogen disappearance in faeces. [5,6]

That definition makes DIAAS conceptually distinct from the time needed for amino acids to appear in plasma. A formulation could produce faster early appearance without materially increasing total ileal digestibility or correcting an indispensable amino-acid deficit. Equally, a score based on amino-acid composition alone is not a DIAAS: it lacks the digestibility correction. The original FAO framework was intended to strengthen nutritional assessment, not to turn a single percentage into a universal clinical efficacy claim. [5,6]

DIAAS must also be interpreted against the population and the role of the ingredient. A protein serving as the principal source in a replacement food poses a different nutritional question from a peptide added at low concentration for foaming, clarity or emulsification. The latter may require safety and allergenicity assessment without requiring the same depth of nutritional replacement evidence. [3,4]

05 | The British guidance is unusually explicit and unusually consequential

The FSA/FSS supplementary guidance published on 20 March 2026 addresses recurring deficiencies in precision- and biomass-fermentation dossiers. It proposes a proportionate approach: low-inclusion techno-functional uses are illustrated at approximately 5% or less, whereas use as a substantive protein source is illustrated at approximately 12% or more. These are examples for evidence planning, not binding concentration cut-offs or statutory definitions. The actual intended function, consumer population and dietary exposure remain decisive. [3]

For nutritional quality, the document favours DIAAS and recommends INFOGEST-based in-vitro digestion as an initial analytical route, with amino-acid analysis, contemporaneous reference proteins and appropriate validation. It also distinguishes nutritional digestion from allergenicity-oriented digestion and calls for consideration of folding, post-translational modifications and host-derived residues. In practice, the guidance encourages applicants to make a coherent, product-specific case rather than assemble unrelated test certificates. [3]

The legal boundary is important. The publication is supplementary technical guidance for applicants; it is not a legislative amendment, a guarantee of authorisation or a mandate that every protein ingredient undergo the same study. Great Britain's competent authorities and ministers retain the relevant statutory roles. An ingredient already lawfully marketed in a different category should not be automatically classified as a new fermentation-derived novel food solely because this guidance exists.

06 | EFSA’s qualification: in-vitro ileal estimates remain method-dependent

EFSA's updated scientific guidance for novel-food applications, applicable to submissions from February 2025, recognises the relevance of protein quality when a novel food replaces conventional protein sources or could disadvantage consumers nutritionally. It identifies established in-vivo approaches for true ileal amino-acid digestibility and explicitly states that in-vitro models have been developed but have not yet been generally validated. When applicants submit in-vitro data, the suitability of the particular method is evaluated during risk assessment. [4]

This is not a formal legal conflict with the British guidance. The FSA recommends a pragmatic starting point and describes the type of validation expected; EFSA warns against treating a simulated result as automatically equivalent to a physiological measurement. Both positions can be reconciled by specifying the measurand, reference data, applicability domain and uncertainty. What cannot be defended is to present every INFOGEST-derived number as a universally validated human DIAAS without disclosing the modelling assumptions. [3,4,7–9]

The regulatory lesson is that analytical comparability must be earned at the matrix level. An assay validated on dairy isolates, for example, cannot be presumed equally accurate for high-fibre cereal concentrates, heavily hydrolysed peptide mixtures or products containing inhibitors of digestive proteases.

07 | What the 2023 and 2026 validation studies actually establish

A 2023 Food Chemistry study by Sousa and colleagues integrated INFOGEST digestion with an analytical workflow for amino-acid-specific measurements. Across the selected substrates, the investigators reported a strong correlation between in-vitro and in-vivo DIAAS estimates ($r = 0.96$) and a small average difference. This is important evidence that well-designed laboratory methods can be predictive within a defined test set; it does not establish universal interchangeability across all proteins and processing histories. [8]

The January 2026 study by Gómez-Marín and colleagues broadened the question to 17 plant-based substrates, comparing an INFOGEST-based workflow with pig ileal measurements. The authors reported absolute percentage errors below 20% for most tested substrates, with corn flakes as a notable exception. Rapeseed samples also demonstrated that trypsin inhibitors and the enzyme-to-substrate ratio can distort laboratory results; adjustments to the assay conditions improved correspondence. This is evidence of both promise and an applicability boundary. [9]

The most defensible conclusion is therefore neither that in-vitro methods are useless nor that they are already universally equivalent to in-vivo DIAAS. They are increasingly valuable for screening, mechanistic comparison and targeted dossier support, provided the tested food, method and reference materials are disclosed and method-specific bias is characterised.

08 | A result without a measurement model is not a reliable claim

A laboratory may report '92% protein digestibility' without explaining whether the value derives from nitrogen solubilisation, free amino groups, soluble peptides, amino-acid recovery, a simulated intestinal fraction or true ileal disappearance. These are different operational definitions. An OPA colorimetric assay can respond to newly exposed amino groups without identifying which indispensable amino acids are available. Likewise, size-exclusion chromatography can describe peptide distribution without quantifying absorption. [3,7–9]

A credible report should identify the exact substrate mass and protein input, the digestive enzyme activities, pH programme, ionic composition, digestion time, quenching conditions, fractionation and analytical recovery. For a proposed in-vitro DIAAS, it should also state how endogenous nitrogen is handled, how individual amino-acid digestibilities are estimated and which reference pattern is used. Method precision and interlaboratory reproducibility must be distinguished from agreement with a physiological comparator. [5–9]

For industrial qualification, the decision should be tied to the claim. A beverage formulator seeking clarity needs a validated solubility and stability protocol; a clinical nutrition developer seeking nutritional equivalence needs a much stronger nutritional evidence package. One laboratory endpoint should not be asked to certify both.

09 | The matrix can reverse the ingredient-level ranking

A protein ingredient is rarely consumed as an isolated powder in water. Acidic fruit beverages, heat-treated shakes, extruded snacks and emulsified sauces create different physical and chemical environments. Low pH may alter charge and solubility; thermal processing can generate aggregation or Maillard reactions; polyphenols can form complexes; calcium or other minerals can change precipitation and gelation; and fat or fibre can influence gastrointestinal disintegration. A technically successful hydrolysate at bench scale may behave differently after industrial pasteurisation and storage. [7,12,13]

In a human crossover study published in 2024, high-moisture extrusion of a mycoprotein–pea blend delayed postprandial plasma amino-acid availability relative to a non-extruded comparator, while in-vitro measurements revealed differences in gastric-phase digestion. The finding illustrates that process-induced structure can alter kinetics even when nominal protein content is held constant. It is not proof that all extrusion reduces total digestibility. [12]

A 2025 study on pea and rice protein texturisation found that processing could improve some in-vitro digestibility measures while reducing the bioaccessibility of certain indispensable amino acids, including lysine. This is precisely why total protein release and amino-acid-specific quality should be reported separately. [13]

10 | Hydrolysis can create new technological liabilities

Proteolysis can improve solubility, reduce sedimentation and broaden formulation options, especially for plant proteins whose native structure resists aqueous dispersion. Yet greater hydrolysis may also release bitter hydrophobic peptides, change foam and emulsion behaviour, reduce viscosity, increase hygroscopicity or alter shelf-life stability. The optimum hydrolysis degree for clarity is not necessarily the optimum for taste, nutritional quality or production yield. [14,28,29]

Manufacturing can introduce additional qualification questions. Protease identity, microbial production strain, processing aids, residual enzyme activity, cleaning agents, microbial control and any reaction by-products should be documented. When the ingredient is derived from rice, source-related chemical contaminants, including inorganic arsenic and cadmium where applicable, require matrix- and category-specific consideration. A reduction in molecular size does not itself remove elemental contaminants. [4,20]

The appropriate design objective is multi-criteria optimisation. It should weigh soluble-protein recovery, peptide profile, indispensable amino-acid retention, taste, stability, contaminant profile, water and energy use, and the actual consumer exposure. A single high solubility percentage cannot stand in for that industrial balance.

11 | A simple arithmetic example exposes the false equivalence

Consider two hypothetical ingredients added at 3 g protein per 100 mL beverage. Ingredient A disperses 98% of its measured protein under a specified centrifugation protocol; ingredient B disperses 60%. If both supply the same indispensable amino-acid profile and the same fraction is truly digested and absorbed, the greater dispersibility of A improves formulation performance but does not create extra grams of absorbed amino acids. The missing 38 percentage points in B's dispersibility assay are not, by definition, 38 percentage points of nutritional loss.

Now suppose ingredient A has an in-vitro digestibility estimate of 90% and ingredient B an estimate of 75%. The ratio 90/75 is 1.20, not 3.00; even that ratio does not prove a 20% improvement in human absorption without a validated correspondence between the assay and the physiological endpoint. The example is deliberately hypothetical and is not a claim about any commercial ingredient.

In the EU, a beverage containing 3 g protein per 100 mL derives 12 kcal per 100 mL from protein using the statutory 4 kcal/g energy factor. If the beverage's total energy is 60 kcal per 100 mL, 20% of its energy comes from protein, potentially meeting the Annex condition for the 'high protein' nutrition claim, subject to all other applicable requirements. That calculation says nothing about whether the protein is absorbed three times better than a comparator. [18,19]

12 | Human evidence: kinetics, utilisation and clinical relevance

A study measuring plasma amino acids after ingestion can establish a postprandial response under its experimental conditions. It may compare peak concentration, time to peak or area under the curve. Yet those endpoints are influenced by the distribution and clearance of amino acids, not merely by intestinal absorption. Stable-isotope techniques and carefully designed tracer studies can help separate exogenous appearance from endogenous kinetics, while true ileal measurements answer a different question. [5,6,11]

Even improved amino-acid appearance does not automatically prove improved muscle protein synthesis, reduced malnutrition risk, better clinical outcomes or a proportional reduction in the dose required. Such claims require their own endpoints, adequate statistical power and appropriate populations. A study in healthy young adults

cannot simply be extrapolated to infants, older adults or patients with impaired digestion. The same distinction applies to animal nutrition: digestibility evidence in a growing pig can inform methodology but does not automatically confer a human health benefit. [6,12]

The evidentiary ladder should therefore be explicit: physical characterisation, in-vitro mechanistic testing, physiological validation when justified, and clinical outcome testing only for claims that genuinely require it.

13 | EU law: a protein claim is not a bioavailability claim

Regulation (EC) No 1924/2006 governs nutrition and health claims made on foods in the European Union. Its Annex permits 'source of protein' when at least 12% of the food's energy is provided by protein and 'high protein' when at least 20% is provided by protein. These are energy-composition criteria; they do not authorise statements that a specific hydrolysate is absorbed at a multiple of a conventional protein or confers a therapeutic effect. A comparative or health claim must satisfy its own legal requirements and evidence standard. [18]

Regulation (EU) No 1169/2011 governs mandatory food information and defines protein for nutrition labelling by reference to total Kjeldahl nitrogen multiplied by 6.25, subject to the applicable framework. This convention does not itself distinguish intact protein, peptides, free amino acids and non-protein nitrogen for every scientific purpose. Consequently, analytical protein declarations and research measures of amino-acid availability should be reconciled rather than conflated. [19]

For ingredients involving genuinely new sources or production processes, Regulation (EU) 2015/2283 and the Union list established by Implementing Regulation (EU) 2017/2470 require an independent assessment of novel-food status and the specific authorised identity and uses. Hydrolysis of a familiar raw material is not automatically novel, but neither does familiarity of the source guarantee that every substantially modified preparation shares its regulatory status. [16,17]

14 | Spain: substantiation, traceability and technical dossier discipline

The EU framework applies directly in Spain, with enforcement by the competent national and autonomous-community authorities under the general food-law and official-control architecture. The food business operator must ensure that ingredient identity, safety, traceability and labelling are defensible for the intended application. AESAN's guidance on contaminants is relevant where rice or other agricultural sources create additional analytical risks. [20,21]

A practical dossier for a hydrolysed plant protein should document botanical source and origin, process flow, enzyme identity and inactivation, batch specifications, nitrogen-to-protein calculation, amino-acid profile, molecular-weight distribution, microbiology, relevant contaminants, intended food categories, stability and the precise method supporting each performance claim. If the ingredient is sold as a preparation rather than a chemically pure substance, the distinction should appear in technical documentation and customer specifications.

For a Spanish manufacturer supplying multiple countries, one laboratory report should not be labelled generically 'EU/UK/US compliant'. The legal status, claims rules, exposure assumptions and product categories must be reviewed separately for each destination.

15 | Great Britain and Northern Ireland: similar science, distinct market decisions

Great Britain has its own novel-food authorisation framework and public register. The FSA/FSS guidance supports the preparation of dossiers, but an EU novel-food authorisation adopted after the United Kingdom's withdrawal is not automatically a Great Britain authorisation. Northern Ireland requires separate consideration under the applicable EU-linked arrangements and movement rules. Operators must verify the relevant register, conditions of use and current legal instruments before market entry. [3,22,23]

The British 2026 guidance is particularly useful for its emphasis on a tiered evidence strategy, the distinction between nutritional and allergenicity digestibility tests, and the requirement to evaluate protein structure and host-derived impurities in fermentation products. However, it would be a category error to treat its illustrative 5% and 12% inclusion examples as binding legal thresholds for every protein hydrolysate, including products not produced by precision or biomass fermentation. [3]

A UK commercial dossier should therefore specify whether the product is a novel food, a conventional ingredient, a food supplement ingredient or a substance with another regulated function, and then identify which guidance applies.

16 | United States: a different protein-quality calculation and a new NDI signal

US conventional-food labelling under 21 CFR 101.9(c)(7) retains a protein-quality correction linked to PDCAAS for relevant percentage-Daily-Value declarations, particularly when a protein claim is made. It is not interchangeable with the EU's energy-percentage conditions or with the FAO's preferred DIAAS research framework. Supplement Facts protein declarations follow additional provisions in 21 CFR 101.36. The correct calculation depends on product classification, consumer age and claim type. [24,25]

The FDA's 19 October 2026 final NDI guidance concerns dietary supplements containing new dietary ingredients, not all protein-containing foods. Under section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 190.6, qualifying notifications generally must be submitted at least 75 days before interstate marketing unless a statutory exception applies. The guidance is non-binding and finalises selected recommendations about identity, history of use and safety reasoning; it is not an automatic marketing authorisation. [1,2,26,27]

For a peptide ingredient, the practical question is whether manufacturing changes, altered peptide distributions, impurities or intended intake mean that historical safety evidence genuinely describes the proposed product. A supplement dossier may need a different legal route from a conventional beverage, and neither route should be inferred from a supplier's marketing category.

17 | Precision fermentation adds a second identity problem

For proteins produced by engineered or selected microorganisms, sequence identity with a familiar protein is informative but may not resolve all safety or nutritional questions. Host-cell proteins, residual DNA, post-translational modifications, folding, aggregation, fermentation metabolites and downstream purification can alter the final ingredient. The 2026 FSA/FSS guidance explicitly addresses these issues and recommends process-specific verification, including production-organism characterisation and appropriate evidence of removal or inactivation. [3,22]

A recombinant protein's amino-acid sequence may match a conventional counterpart while its glycosylation, tertiary structure or impurity profile differs. Conversely, a well-purified product may be sufficiently characterised to support a proportionate safety assessment without every conceivable experimental test. The correct response is neither to presume equivalence nor to demand an identical exhaustive dossier for all fermentation products. [3,4]

Where the product is intended to replace a major dietary protein, nutritional adequacy and potential allergenicity require separate analyses. The existence of a high-quality production process cannot substitute for proof that the intended consumer obtains an appropriate indispensable amino-acid supply.

18 | Prior art: enzymatic rice peptides are not a newly discovered technology

Published research and patent applications have long described enzymatic hydrolysis of rice protein to improve dispersibility, functionality and processing performance. US patent publication US20220024974A1, for example, discloses a multi-stage route for rice protein peptides involving proteolysis, separation, membrane treatment and drying. US20160128356A1 addresses rice-bran hydrolysates and the trade-off between solubility, degree of hydrolysis and bitterness. These are public technical disclosures, not proof that every claimed performance figure has been independently reproduced or that any later process infringes a patent. [28,29]

A 2025 study on enzymatic modification of rice proteins likewise investigated structural and functional changes, confirming that the scientific field is active rather than unexplored. A 2026 review of alternative proteins identifies persistent gaps connecting extraction, structure, nutrition and industrial functionality. The relevant opportunity is thus not to claim invention of hydrolysis, peptide profiling or in-vitro digestion. It is to test whether a rigorously integrated, matrix-specific validation protocol improves the quality of development decisions and reduces unsupported nutritional claims. [14,15]

Any proposed proprietary process would require a separate patentability and freedom-to-operate review based on claims, jurisdictions and current legal status. A publication or patent title alone cannot establish novelty, commercial exclusivity or technical freedom to operate.

19 | A fit-for-purpose industrial evidence package

The first stage is identity and composition: botanical or microbial origin, manufacturing history, peptide molecular-weight distribution, free amino-acid content, indispensable amino-acid pattern, nitrogen conversion method, relevant contaminants and batch variability. The second is technological function: solubility at the target pH, turbidity, sedimentation, rheology, sensory profile and stability after the intended heat treatment. The third is nutritional evidence: a prespecified digestion method with reference proteins, amino-acid-specific analysis, recovery checks and transparent uncertainty. [3,4,7–9]

For products that make stronger claims, a fourth stage may be needed: physiological comparison with a relevant intact protein or established benchmark, designed to measure the actual proposed advantage. This may require in-vivo or human studies where ethically justified, but the purpose should be to resolve a defined uncertainty, not to produce an impressive number detached from the commercial claim. [5,6,11,12]

Each stage should have its own release criteria and claim vocabulary. A product can be 'highly dispersible' on robust formulation evidence without being called 'three times more bioavailable'. A nutrient-quality claim should not be inferred from a solubility assay, and a novel-food safety dossier should not be replaced by a nutritional marketing study.

20 | Research & Innovation Opportunity

Unresolved problem. Ingredient developers lack a widely standardised cross-matrix method for translating peptide size and in-vitro digestion data into reliable, uncertainty-qualified predictions of indispensable amino-acid availability after real beverage or food processing. Existing methods and published comparisons are promising, but validation domains remain narrow and exceptions persist for complex plant matrices, protease inhibitors and process-induced aggregation. [4,8,9,12,13]

What is established. Enzymatic hydrolysis can modify plant-protein solubility; INFOGEST provides a harmonised laboratory digestion framework; amino-acid-specific in-vitro scoring workflows have been compared with in-vivo data; and processing can alter digestion kinetics. Patent literature already covers multiple rice-protein hydrolysis routes. None of these components is claimed as newly invented here. [7–9,11–14,28,29]

Proposed hypothesis, not established fact. A 'Matrix-Calibrated Protein Evidence Ladder' that combines (i) peptide and amino-acid profiling, (ii) matched process-condition stability tests, (iii) in-vitro digestion with concurrent reference proteins, (iv) a model trained only on independently validated physiological comparators and (v) a jurisdiction-specific claim rulebook will predict clinically relevant differences more reliably than a single degree-of-hydrolysis or soluble-protein specification. Whether it does so remains to be tested.

Validation pathway. Select at least three protein families -rice hydrolysate, pea concentrate and a fermentation-derived protein- and three applications: an acidic beverage, a heat-treated neutral beverage and an extruded food. Predefine matched protein doses, amino-acid patterns, peptide distributions and process histories. Measure solubility and stability; conduct blinded INFOGEST assays with validated enzyme activities and contemporaneous reference proteins; quantify indispensable amino acids by a validated chromatographic method; compare a justified subset against existing high-quality ileal or human kinetic reference data; and preregister prediction errors, confidence intervals and failure criteria. External laboratories should repeat key analyses.

Regulatory constraints and industrial relevance. The model would not replace legally required novel-food authorisation, allergenicity assessment, protein-claim rules or appropriate clinical substantiation. Research should protect personal data where human trials are undertaken and should avoid extrapolating results to vulnerable groups without evidence. If independently validated, the framework could improve ingredient selection, avoid unnecessary testing, support credible R&D claims and make reformulation decisions more reproducible. Those benefits are prospective, not established performance.

21 | Evidence classification and limits of inference

Established legal facts: the EU's nutrition-claim energy thresholds, food-information duties and novel-food framework are in force; the US protein-quality labelling rules and NDI statutory notification pathway are distinct; and Great Britain operates a separate regulated-products authorisation system. [16–19,23–27]

Established scientific evidence: solubility, DH, in-vitro digestion, true ileal amino-acid digestibility and plasma appearance measure different properties. Hydrolysis and food processing can alter physical behaviour and digestion, but their effects depend on substrate and matrix. [5–14]

Emerging evidence: 2023 and 2026 comparisons support calibrated INFOGEST-derived estimates for selected foods while identifying limitations. These results do not constitute universal validation across hydrolysed, fermented and high-complexity ingredients. [8,9]

Expert interpretation: a multi-endpoint, claims-specific qualification dossier is more defensible than relying on a single attractive percentage. Research hypothesis: an integrated matrix-calibrated protocol may improve prediction and regulatory efficiency; this remains to be prospectively demonstrated.

22 | Conclusions: the useful distinction is not academic, it is commercial

The market for alternative and hydrolysed proteins is moving faster than the vocabulary used to evaluate them. Solubility is a valuable technological property, but it is not a digestibility score. A digestibility score is not a direct measure of absorption kinetics. A faster amino-acid response is not proof that a consumer needs proportionally less protein, and a nutrition claim based on statutory composition thresholds is not a clinical efficacy claim. These distinctions determine which experiments are necessary, which labels are lawful and which customer promises can withstand scrutiny.

The 2026 British fermentation guidance and new plant-protein validation studies provide a credible route toward more efficient, less animal-dependent assessment. EFSA's caution and the FDA's renewed emphasis on ingredient identity reinforce the same obligation: every number must be connected to a defined material, method, use and decision. For food biotechnology, the next competitive advantage may come not from reporting the highest digestibility percentage but from producing evidence that remains valid when the ingredient moves from the laboratory into the actual food, consumer population and legal market.

Related Knowledge Areas

Biotechnology; Nutrition; Functional Ingredients; Processing Technologies; Food Safety; Regulatory Affairs; Emerging Research; AI & Food.

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