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Effects of Different Processing Methods on the Protein Quality of Microalgae and their Metabolomic Profile Responses: A Systematic Review and Meta-Analysis

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Abstract

Background/Aim: A growing global population is projected to drive a 32-78% increase in dietary protein demand over the next few decades, intensifying pressure on environmental resources [1]. Microalgae have emerged as promising sustainable protein sources due to their high productivity and lower greenhouse gas emissions, land and freshwater requirements compared with conventional proteins [2]. Many microalgal species exhibit high protein content and well-balanced essential amino acid profiles [3], however, protein digestibility, bioaccessibility, and bioavailability are low in many species due to structural barriers such as rigid cell walls and associated biochemical constraints [4]. To address these limitations, various processing strategies have been explored to enhance protein quality [4], though findings remain inconclusive due to heterogeneity in microalgae species, processing conditions, and experimental models. Furthermore, metabolomic profile changes following the consumption of processed microalgae remain unexplored and have not been systematically assessed. Therefore, this systematic review and meta-analysis aimed to evaluate the effects of different processing methods on the protein quality of microalgae and associated metabolomic profile responses.

Methods: A database search from five online databases was conducted, and a total of 56 studies were included for systematic review, comprising 33 *in vitro* studies, 19 animal studies, 3 studies involving both *in vitro* and animal models, and 1 human clinical trial. Of these, meta-analysis was conducted using data extracted from 36 studies, including 19 *in vitro*, 14 animal, and 3 mixed-model studies. Processing methods were broadly categorised as physical (e.g. high-pressure homogenisation, bead milling), chemical (e.g. solvent or lipid extraction), biological (e.g. enzymatic treatment, fermentation) or combined approaches. A total of 16 microalgal genera were identified, with the most commonly studied being the eukaryotic Chlorella and Nannochloropsis, and the prokaryotic Arthrospira.

Results: Overall, processing improved protein quality in *in vitro* studies, as evidenced by increased *in vitro* protein digestibility (Hedges' g = 2.46, 95% CI [1.58; 3.33]) and degree of hydrolysis (Hedges' g = 5.42, 95% CI [3.45; 7.39]), alongside improvements in digestible protein content and *in vitro* Protein Digestibility-Corrected Amino Acid Score (PDCAAS). Animal studies also showed that processing enhanced apparent digestibility coefficients for both whole diets (Hedges' g = 1.30, 95% CI [0.65; 1.95]) and single microalgal ingredients (Hedges' g = 1.82, 95% CI [0.97; 2.66], coupled with improvements in true digestibility coefficient, protein efficiency ratio, biological value, net protein utilization, protein retention efficiency, and PDCAAS. As for clinical studies, limited evidence indicated increases in the incremental area under the curve (iAUC) of total, essential, and non-essential amino acids following consumption of processed microalgae. Among processing methods, physical approaches, particularly high-pressure homogenisation, showed consistent improvements across multiple protein quality outcomes. No studies were identified to have evaluated the metabolomic profile responses following the consumption of processed microalgae.

Conclusion: Processing improved the protein quality of microalgae, though the magnitude of improvement may vary according to the processing method. The limited number of clinical studies, as well as the absence of metabolomic evidence, highlights critical research gaps and underscores the need for clinical trials and integrated omics approaches in future studies.

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