



## Dietary metabolites and blood pressure regulation in dietary feeding interventions: a systematic review

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Hypertension, characterised by elevated blood pressure (BP), continues to be a major global public health problem. It is defined as systolic blood pressure (SBP)  $\geq 140$  mmHg and/or diastolic BP (DBP)  $\geq 90$  mmHg<sup>(1)</sup> and is the leading risk factor for cardiovascular diseases<sup>(2)</sup>. Nutritional metabolomics (Nutrimetabolomics) presents an objective approach to explore the interplay between diet and health outcomes<sup>(3)</sup>. Through analysis of intermediate molecules and metabolic byproducts, metabolomic profiles can objectively reflect an individual's dietary intake and assess variations in metabolism<sup>(3)</sup>. To date, no review has been conducted that investigates the relationship between diet, metabolites and BP regulation. This systematic review aimed to identify and synthesise findings of human dietary feeding intervention studies that have examined the role of metabolites in BP regulation. A comprehensive search was conducted in November 2022 across EMBASE, Medline, CINAHL, PsychINFO, Scopus and Cochrane databases. Search terms were defined using a combination of keywords, including “metabolome”, “diet”, and “blood pressure”. All included intervention studies explored the dietary metabolome from food provision, meals or supplements to a comparator or control intervention and, examined the relationship between dietary-related metabolites and BP in humans and published in English. The initial search identified 1,109 studies, with a final six studies meeting all eligibility criteria and included in the final review. Metabolites were identified in urine (n = 4), plasma (n = 2), or faeces (n = 1). Various analytical techniques were employed, including H-NMR, LC-MS, and GC-MS, while majority of studies used untargeted metabolomics (n = 4). Among included studies, five reported a significant association between individual metabolites and BP or change in BP. These investigations emphasised dietary patterns as the primary focus of analysis. In contrast, one study revealed no relationship between the investigated metabolites and BP. However, this particular study evaluated the impact of a single food product rather than dietary patterns. In total, 39 metabolites were linked to BP, with 36 associated with SBP and 25 with DBP. Several super-pathways involved in blood pressure regulation were identified, across metabolism of amino acids, carbohydrates, cofactors, vitamins, lipids, nucleotides, peptides, and xenobiotics. Within these, 17 distinct sub-pathways were delineated. The only metabolite found to have a significant relationship with BP measures across multiple studies was N-Acetylneuraminic acid. In one study, it showed a relationship with DBP, while another study linked it to a decrease in both 24-hour DBP and SBP. No other metabolites were consistently replicated between studies. Nutrimetabolomics appears to be a promising field in evaluation of diet and BP reduction. However, further research is required to understand which metabolites influence BP regulation.

**Keywords:** metabolome; diet; blood pressure; hypertension

### Ethics Declaration

Yes

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