Supplementary material 1

A comprehensive literature search was conducted to identify studies relevant to the gut-liver-kidney axis in chronic kidney disease (CKD). Electronic databases including PubMed/MEDLINE (pubmed.ncbi.nlm.nih.gov/), Web of Science (webofscience.com/) and Scopus (scopus.com/) were systematically searched for articles published from January 2000 to October 2025. The search strategy combined controlled vocabulary terms (MeSH) and free-text keywords, namely: 'gut-liver-kidney axis', 'gut-kidney axis', 'chronic kidney disease', 'diabetic kidney disease', 'intestinal dysbiosis', 'gut microbiota', 'intestinal barrier', 'uremic toxins', 'trimethylamine N-oxide', 'short-chain fatty acids', 'bile acids', 'hepatic signaling', 'non-alcoholic fatty liver disease', 'microbiome,' 'endotoxemia', 'systems biology', 'multi-organ crosstalk', and 'metabolic signaling'.

Studies were screened based on titles and abstracts, followed by full-text evaluation where appropriate. Priority was given to mechanistic studies, clinical investigations and high-quality review articles that provided insight into interorgan communication between the gut, liver, and kidney. Reference lists of relevant reviews were manually examined to identify additional pertinent publications.

Articles were included if they met ≥1 of the following criteria: i) Mechanistic evidence linking gut-liver and kidney-derived signals; ii) clinical relevance to CKD progression or associated metabolic complications; iii) interorgan crosstalk using experimental, translational or clinical approaches; or iv) systems-level perspectives integrating multiple pathways or organs.

Studies were excluded if they were limited to single-organ phenomena without relevance to interorgan communication, lacked mechanistic or clinical context or focused exclusively on unrelated disease entities. Non-peer-reviewed sources, conference abstracts without full data and articles with insufficient methodological detail were also excluded.

The enzymes, hormones, and metabolites were selected based on predefined prioritization criteria to ensure representativeness and relevance within the gut-liver-kidney axis. Specifically, priority was given to molecules that have been implicated in CKD-associated gut-liver-kidney interactions across multiple independent studies, are supported by both mechanistic and clinical evidence, serve a key regulatory role in metabolic, inflammatory or barrier-related signaling pathways and have potential diagnostic or therapeutic relevance.