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1CORRELATION BETWEEN GUT MICROBIOME AND THE DEVELOPMENT OF DIABETIC KIDNEY DISEASE

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ABSTRACT

Diabetic kidney disease (DKD) is a major complication of diabetes mellitus characterized by progressive renal damage driven by metabolic, hemodynamic, and inflammatory mechanisms. Recent studies highlight the gut–kidney axis as a crucial pathway linking intestinal dysbiosis to DKD progression. Therefore, this study aims to investigate the association between gut microbiome alterations and the progression of DKD, as well as to explore potential mechanistic pathways linking microbial dysregulation to renal injury. A comprehensive literature review was conducted using PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar up to August 2025. Eligible studies included English-language human and experimental research evaluating the relationship between gut microbiota composition and DKD pathogenesis. From 241 retrieved articles, 22 studies met inclusion criteria. Most demonstrated significant gut dysbiosis in DKD, with decreased Faecalibacterium prausnitzii, Akkermansia muciniphila, and Butyricicoccus, and increased Escherichia-Shigella, Hungatella, and Enterococcus. Reduced short-chain fatty acid (SCFA) production and accumulation of uremic toxins—such as indoxyl sulfate, p-cresyl sulfate, and phenyl sulfate—were strongly associated with inflammation, fibrosis, and renal decline. The analysis was conducted through qualitative synthesis of study methodologies, microbial profiles, and biochemical markers to identify consistent patterns linking gut dysbiosis to DKD progression. These findings suggest that microbial imbalance and altered metabolite profiles play pivotal roles in DKD development. Interventions targeting the gut microbiota, including probiotics, prebiotics, and dietary fiber, may offer renoprotective benefits through restoration of SCFA-producing bacteria and reduction of uremic toxins. Gut dysbiosis in diabetic kidney disease (DKD) disrupts metabolic and immune balance by reducing beneficial short-chain fatty acid–producing bacteria and increasing pathogenic species, leading to inflammation, proteinuria, and progressive renal decline.

Keywords: diabetic kidney disease; dysbiosis; gut microbiome; inflammation; short-chain fatty acids; uremic toxins

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INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia resulting from impaired insulin secretion, insulin action, or both. It is one of the most serious chronic diseases worldwide, associated with increased mortality, disability, and reduced life expectancy. In 2021, approximately 530 million people were living with diabetes, and this number is projected to rise to more than 1.3 billion by 2050. In Indonesia, prevalence continues to increase, reaching 11.7% in 2023 compared with 10.9% in 2018 (American Diabetes Association Professional Practice Committee, 2024; Alam et al., 2021; Ojo et al., 2023; Matoori, 2022; Sun et al., 2022; Antar et al., 2023; GBD 2021, 2023).

Diabetic kidney disease (DKD), previously referred to as diabetic nephropathy, is one of the most common long-term complications of diabetes, affecting around 40% of patients and frequently progressing to end-stage kidney disease (ESKD). Globally, the proportion of ESKD attributable to diabetes increased from 19.0% in 2000 to 29.7% in 2015. However, the precise prevalence of diabetes-related CKD remains uncertain due to overlapping comorbidities and the limited use of renal biopsy for definitive diagnosis. In Indonesia, CKD prevalence is also rising, although specific data on DKD are scarce (Hoogeveen, 2022; Naaman & Bakris, 2023; Hustrini et al., 2022; Koye et al., 2018; Cheng et al., 2021).

The pathophysiology of DKD involves metabolic, hemodynamic, and inflammatory mechanisms triggered by chronic hyperglycemia, leading to glomerulosclerosis and progressive GFR decline (DeFronzo et al., 2021; Qian et al., 2022). The gut microbiome, composed primarily of Firmicutes and Bacteroidetes, plays a crucial role in nutrient metabolism, intestinal barrier integrity, immune modulation, and protection against pathogens. Dysbiosis has been linked to metabolic disorders, including type 2 diabetes mellitus (T2DM). Reduced abundance of beneficial taxa such as Akkermansia and Bifidobacterium, alongside expansion of pro-inflammatory microbes like Escherichia–Shigella and Enterococcus, contributes to impaired short-chain fatty acid (SCFA) production, systemic inflammation, and insulin resistance (Sharma & Tripathi, 2019; Afzaal et al., 2022; Wu et al., 2021; Ahlawat et al., 2021; Rinninella et al., 2019; Chong et al., 2025).

Emerging evidence highlights the gut–kidney axis as a key pathway in DKD progression. Uremic toxins alter gut microbiota composition, while dysbiosis increases intestinal permeability, facilitating endotoxin translocation into systemic circulation. This perpetuates inflammation, oxidative stress, renin–angiotensin system activation, and fibrosis, ultimately accelerating renal injury. Furthermore, loss of SCFA-producing microbes deprives the host of their glucose-stabilizing and renoprotective effects (Cheng et al., 2023; Lin et al., 2022). Therefore, this study aims to investigate the association between gut microbiome alterations and the progression of DKD, as well as to explore potential mechanistic pathways linking microbial dysregulation to renal injury.

METHOD

Table 1.
A detailed search strategy for each database

Database	Searching Strategy (Keyword)	Hits
PubMed (July 29, 2025)	("diabetic nephropathies"[MeSH Terms] OR ("diabetic"[All Fields] AND "nephropathies"[All Fields]) OR "diabetic nephropathies"[All Fields]) AND ("gastrointestinal microbiome"[MeSH Terms] OR ("gastrointestinal"[All Fields] AND "microbiome"[All Fields]) OR "gastrointestinal microbiome"[All Fields])	126
Scopus (July 30, 2025)	(TITLE-ABS-KEY ("diabetic nephropathies") AND TITLE-ABS-KEY ("gastrointestinal microbiome"))	159
Web of science (July 30, 2025)	("diabetic nephropathy" OR "diabetic kidney disease" OR "DKD") (All Fields) and ("gastrointestinal microbiome" OR "gut microbiota" OR "intestinal microbiota" OR "gut flora") (All Fields)	346
Google Scholar (August 01, 2025)	(“intestinal microbiome” OR “gut microbiome” OR “gut microbiota” OR “gut flora” AND “diabetic kidney disease” OR “diabetic nephropathy” OR “diabetes-related kidney disease” AND “correlation” OR “association” OR “risk” OR “development” AND "cohort study" or "experimental study" or "cross sectional" or "case control")	71
Sciencedirect (August 01, 2025)	(“intestinal microbiome” OR “gut microbiome” OR “gut flora” “correlation” OR “association” OR “development” AND “diabetic kidney disease” OR “diabetic nephropathy” AND AND "cohort study" or "experimental study")	646

This study was conducted using a literature review approach. Relevant articles were retrieved from PubMed, Scopus, Web of Science, Google Scholar, and ScienceDirect up to August 2025. The search strategy incorporated a combination of keywords and Boolean operators, including “diabetic kidney disease,” “gut microbiome,” “dysbiosis,” “short-chain fatty acids,” and “uremic toxins.” The search initially yielded 241 articles. After title and abstract screening, removal of duplicates, and application of inclusion and exclusion criteria, 22 primary studies were selected for synthesis. The screening and selection process was performed independently by two reviewers to minimize bias

and ensure methodological rigor. The primary search terms combined concepts of *diabetic nephropathy/diabetic kidney disease* and *gut microbiome/intestinal microbiota*.

RESULT

A total of 241 articles were identified through database searches across PubMed, Scopus, Web of Science, Google Scholar, and ScienceDirect. After title and abstract screening, duplicate removal, and application of inclusion and exclusion criteria, 22 primary studies were included for synthesis. These studies encompassed both human and experimental models exploring the interaction between gut microbiota and diabetic kidney disease (DKD).

Table 2.
Analysis Article

Author (Year)	Study Design / Population	Main Findings	Key Microbiota / Metabolites	Conclusion / Implication
Tao et al., 2019	Cross-sectional; T2DM, DN, and healthy controls (China)	DN group showed increased *Escherichia-Shigella* and decreased *Prevotella_9*; microbial diversity lowest in DN	*Escherichia-Shigella*, *Prevotella_9*	Dysbiosis pattern may distinguish DN from DM and indicate disease progression.
Zhang et al., 2022	Clinical study; 60 DKD vs 60 healthy	DKD patients had increased *Proteobacteria*, *Firmicutes*; reduced SCFA-producing genera	*Faecalibacterium*, *Akkermansia*, *Bifidobacterium*	Gut dysbiosis correlates with renal dysfunction and inflammation.
Lu et al., 2023	Biopsy-proven DN, long-standing diabetes	Increased *Actinobacteria*, *Hungatella*; decreased *A. muciniphila*, *Butyricicoccus*	*Akkermansia*, *Butyricicoccus*	Reduced SCFA producers linked to worsened renal histopathology.
Han et al., 2022	Meta-analysis of 14 studies	Gut microbial richness declines progressively from HC → T2DM → DKD	*Firmicutes*, *Proteobacteria*, *Escherichia-Shigella*	Supports the "microbiome gradient hypothesis" across diabetes stages.
Kikuchi et al., 2019	Human + mouse study	Identified Phenyl sulfate (PS) as marker of albuminuria progression	*Phenyl sulfate*, *L-tyrosine metabolism*	PS induces podocyte injury and inflammatory gene upregulation.
Li et al., 2022	Experimental (mice)	*F. prausnitzii* improved renal injury via butyrate–GPR43 pathway	*F. prausnitzii*, *Butyrate*	SCFA supplementation may attenuate renal inflammation and fibrosis.
Cheng et al., 2023	Review + animal models	Uremic toxins (IS, PCS, TMAO) amplify oxidative stress and fibrosis	*Indoxyl sulfate*, *p-Cresyl sulfate*, *TMAO*	Targeting microbial metabolites could slow DKD progression.
Wu et al., 2017	Human; T2DM before/after metformin	Metformin increased *A. muciniphila*, *Bifidobacterium*, improved glycemia	*Akkermansia*, *Bifidobacterium*	Gut modulation contributes to metformin's anti-diabetic effects.
Niu et al., 2024	Clinical; normal-weight T2DM on metformin	Restored carbohydrate metabolites and SCFA-producing taxa	*Prevotella*, *Megasphaera*, *Anaerostipes*	Reinforces metformin's microbiota-mediated benefits.
Li et al., 2020	Experimental; high-fiber diet in DKD mice	High-fiber diet increased *SCFA* levels and *GPR43/GPR109a* activation	*Acetate*, *Propionate*, *Butyrate*	Dietary fiber mitigates DKD via SCFA–GPR axis.
Cani et al., 2008	Animal; high-fat diet–induced diabetes	High-fat diet increased LPS and inflammation, reduced *Bifidobacterium*	*LPS*, *Bifidobacterium*	Supports "metabolic endotoxemia" concept in DKD.
Desai et al., 2016	Experimental; fiber-deprived mice	Fiber-free diet depleted mucus barrier, expanded pathogens	*Mucus-degrading bacteria*	Fiber deprivation exacerbates leaky gut and systemic inflammation.
Smith et al., 2024	Mice; high-glycemic diet + antibiotics	Severe dysbiosis, *Bacteroides* depletion, early mortality	*Bacteroides*, *Firmicutes*	Antibiotic–diet interaction aggravates gut barrier damage.
González-Correa et al., 2024	Hypertensive rats	ACEi/ARB therapy increased acetate-producing bacteria	*Acetate-producing anaerobes*	Antihypertensives exert gut-protective effects.
Wu et al., 2019	Candesartan-treated rats	Elevated SCFAs (acetate, propionate, butyrate) after therapy	*Anaerobes*, *SCFAs*	Gut–cardiorenal improvement via SCFA pathway.

The gut microbiome is made up of a diverse array of bacteria, fungi, and viruses that play important roles in the human body, affecting metabolic, immune, and neurobehavioral functions (Gomaa, 2020; Tsuji et al., 2024). The intestine is essential for nutrient absorption and the production of various substances, including vitamins, amino acids, and enzymes, as well as short-chain fatty acids (SCFAs) (Martin-Gallausiaux et al., 2021). Acetate, butyrate, and propionate are types of SCFAs that result from the fermentation of carbohydrates by bacteria and serve as an energy source in the large intestine (Louis & Flint, 2017; Stavropoulou et al., 2021). Additionally, SCFAs have an impact on metabolic processes, such as the regulation of glucose and lipid metabolism, by interacting with peripheral tissues through signaling pathways that affect insulin sensitivity and lipid management (He et al., 2020). Butyrate, in particular, provides energy to colon cells, promotes gut health and the intestinal barrier, reduces inflammation, defends against pathogens, and reduces the risk of systemic infections (Tsuji et al., 2024; Ullah et al., 2023; Hodgkinson et al., 2023).

SCFAs benefit the immune system in a variety of ways. By inhibiting histone deacetylases (HDACs) and activating G protein-coupled receptors (GPRs), including GPR43, GPR41, and GPR109A, they encourage Treg development in the intestine (Sumida & Kovesdy, 2019; Huang et al., 2017). HDAC inhibition suppresses nuclear factor-kappa beta (NF-κB) in the mucosal immune system, which impacts the transcription of genes linked to inflammation, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). Furthermore, by inhibiting NF-κB expression and encouraging colonic Treg development, GPR activation may help control the inflammatory process (Tsuji et al., 2024; Sumida & Kovesdy, 2019). An imbalance between pathogenic and beneficial bacteria in the gut microbiota, also known as dysbiosis, can result from both internal and environmental sources (Carías Domínguez et al., 2024; Tourountzis et al., 2022).

Immune activation and systemic inflammation in CKD are significantly influenced by gut dysbiosis. Reduced expression of tight junction proteins (ZO-1, claudin, and occludin) in the intestinal epithelium caused by gut dysbiosis allows endotoxins, such as lipopolysaccharides (LPS), to pass into the circulation, increasing intestinal permeability and contributing to “leaky gut” (Sumida & Kovesdy, 2019; Huang et al., 2022; Chelakkot et al., 2018; Horowitz et al., 2023; Tsuji et al., 2024). LPS is one of the metabolites produced by bacteria that can pass through the intestinal barrier. Vascular inflammation and blood vessel damage are caused by pro-inflammatory cytokines like TNF-α and IL-6, which are produced by immune cells when LPS enters the bloodstream (Tsuji et al., 2024; Huang et al., 2022). Because inflammatory mediators encourage the production of plaque, this immune activity also raises the risk of cardiovascular disease (Huang et al., 2022). Kidney damage is directly caused by cytokine-induced inflammation, which exacerbates glomerulosclerosis and fibrosis (Tsuji et al., 2024). The gut microbiota changes quite significantly in CKD patients, especially in terms of the gut microbiome’s balance. While other bacteria, which are typically found in modest quantities, can multiply up to 100 times in CKD patients, the normal colonic microbiota is drastically diminished (Tourountzis et al., 2022; Chelakkot et al., 2018).

Although the exact mechanisms of dysbiosis in CKD are unknown, a number of variables are believed to be involved. CKD patients frequently experience constipation, decreased dietary fiber intake, and impaired bowel function. These factors also include metabolic acidosis, the buildup of uremic toxins as a result of kidney dysfunction, and the effects of chelating agents like oral iron, potassium, and phosphorus supplements (Huang et al., 2022; Sumida et al., 2017). The uremic environment itself, medications, and dietary factors (such as reduced fiber consumption) all have an impact on these alterations in the gut microbiota (Afzaal et al., 2022). Urea along with other uremic toxins builds up in the bloodstream as kidney function deteriorates, with the potential to enter the intestine and damage the intestinal barrier (Tsuji et al., 2024). Endotoxins in CKD cause oxidative stress and a number of pro-inflammatory responses by stimulating Toll-like receptors (TLRs) on kidney cells (Kadatane et al., 2023). This includes increased immune cell infiltration in the kidneys due to the overexpression of cytokines and chemokines. Oxidative stress, a condition in which an

excess of reactive oxygen species (ROS) damages cellular components and exacerbates inflammation, further aggravates this process (Kadatane et al., 2023). Toxins from the gut can contribute to oxidative stress, which can damage renal tubular cells directly, resulting in fibrosis and a decline in kidney function (Cheng et al., 2020). Endotoxemia and oxidative stress work together to create a harmful feedback loop that progressively impairs kidney function and exacerbates the clinical signs of chronic kidney disease (Tsuji et al., 2024). Furthermore, intestinal edema, uremia, and ischemic gut alterations all worsen leaky gut in CKD. In comparison to healthy people, CKD patients have greater levels of circulating endotoxins, which suggests that their gut barrier is weakened. The progression of kidney disease is accelerated by a vicious cycle that is perpetuated by leaky gut in CKD, where inflammation further disturbs the gut microbiota (Tsuji et al., 2024).

Renal and systemic damage becomes worse due to reduced toxin clearance caused by impaired kidney function in CKD. Proteolytic gut bacteria, which are more prevalent in CKD, create harmful chemicals like ammonia, urea, amines, thiols, phenols, and indoles (Nallu et al., 2017). Increased urea influx into the gastrointestinal tract due to blood urea buildup in CKD raises ammonia production (Hobby et al., 2019). By raising pH, high ammonia levels disturb the surrounding environment, compromising the gut barrier and harming epithelial cells (Hobby et al., 2019). It has been discovered that ammonia compromises the integrity of intestinal tight-junction proteins such as occludin and ZO-1 (Yokoo et al., 2021). A “leaky gut” problem results from this disruption of tight junctions. High ammonia can also cause epithelial damage, which can set off a series of immunological reactions that increase the production of inflammatory cytokines like TNF-α and IL-6 and worsen the chronic inflammation linked to CKD. Moreover, urease-producing proteolytic bacteria may proliferate due to the changed gut environment brought on by ammonia, releasing more toxins that are detrimental to the kidneys and other tissues. This can lead to an endless loop where ammonia aggravates the progression of renal disease by causing systemic inflammation in addition to direct damage to intestinal epithelial cells (Tsuji et al., 2024). Uremic toxins, including indoxyl sulfate, p-cresyl sulfate, and trimethylamine N-oxide (TMAO), which significantly contribute to the progression of CKD and its vascular complications, are derived from dietary components and metabolized by gut bacteria (Tsuji et al., 2024; Pan et al., 2023; Hsu et al., 2022). These uremic toxins are present in the bloodstream and are primarily bound to proteins, such as albumin, rather than in the free state (Opdebeeck et al., 2020). This protein binding limits their removal during dialysis and contributes to their accumulation and toxicity in CKD (Tsuji et al., 2024).

Indoxyl sulfate increases oxidative stress and inflammation in kidney tissue by stimulating the production of ROS and increasing the expression of pro-fibrotic genes, accelerating tubular injury and interstitial fibrosis, and contributing to the development of CKD (Tsuji et al., 2024). P-cresyl sulfate also induces oxidative stress and has pro-inflammatory effects on the kidneys and vascular system, contributing to endothelial dysfunction and triggering atherosclerosis (Tsuji et al., 2024; Gryp et al., 2017). TMAO increases vascular inflammation and enhances platelet aggregation and macrophage activation, further exacerbating cardiovascular complications (Pan et al., 2023). TMAO may also worsen kidney damage by affecting inflammatory pathways (Tsuji et al., 2024; Tang et al., 2014).

DISCUSSION

Akkermansia muciniphila is considered one of the most promising next-generation probiotics and has been found to help strengthen and protect the gut barrier. Research using cell and animal models shows that its effects depend on the specific strain, as each strain can influence tight junctions differently. In addition, certain genes — COG0438, COG0463, and COG2244 — and surface proteins of A. muciniphila play important roles in supporting and maintaining intestinal barrier integrity (Liu et al., 2023). However, the overall abundance of gut microorganisms in the DKD group was lower than that of healthy controls. Additionally, the DKD group showed an increased

presence of Actinobacteria, Hungatella, Escherichia, and Lactobacillus, while beneficial genera such as Butyricicoccus, Faecalibacterium, and Lachnospira were reduced. Notably, elevated levels of Hungatella and Escherichia were distinctive features of gut microbiota changes in DKD (Han et al., 2022).

Short-chain fatty acid (SCFA) levels decline following gut microbiota imbalance. SCFAs — including butyrate, acetate, propionate, valerate, and isocaproic acid — are metabolites produced by microbial fermentation of dietary polysaccharides in the intestine. Faecalibacterium prausnitzii is one of the most abundant bacteria in the human gut microbiome, but its abundance decreases in DKD. This reduction lowers SCFA production, disrupts energy absorption, impairs intestinal anti-inflammatory and immune-regulatory functions, and contributes to kidney injury (Li et al., 2022). DKD is linked to gut microbiota dysbiosis. A Chinese study involving biopsy-confirmed DN patients, T2DM patients without renal disease, and healthy controls found that individuals with diabetes had higher levels of Firmicutes and Proteobacteria compared to both healthy controls and T2DM individuals. The authors noted that Proteobacteria may elevate circulating LPS, contributing to chronic inflammation. Gut microbial richness, based on OTUs, was markedly lower in DN than in T2DM, with distinct compositional differences among HC, DM, and DN groups. Notably, Escherichia–Shigella was elevated and Prevotella_9 reduced in DN, suggesting these genera may help distinguish DN from DM (Tao et al., 2019).

A study on CKD reported that higher levels of Escherichia–Shigella species were associated with disease progression. These bacteria were enriched in the feces of patients with advanced CKD and contributed to renal dysfunction by producing excess indoxyl sulfate. Escherichia–Shigella are opportunistic pathogens capable of breaching the intestinal barrier and worsening gut permeability (Tao et al., 2019; Wu et al., 2020). People with type 2 diabetes have higher levels of bacteria such as Enterobacteriaceae, Collinsella, Streptococcus, Lactobacillus, and Ruminococcus compared to healthy individuals. These bacteria may trigger chronic low-grade inflammation and impair insulin signaling (Remely et al., 2016; Candela et al., 2016). Gut microbiota also influence the host through the production of various metabolites. Phenyl sulfate (PS), a byproduct of dietary L-tyrosine metabolism in the gut, has been strongly linked to baseline and predicted two-year progression of albuminuria in DKD patients. In db/db mice, PS treatment led to foot process effacement, glomerular basement membrane thickening, and increased renal expression of Tnfa, Ccl2, Emr1, and Fn1. PS-treated mice also showed higher albuminuria levels than controls. In vitro, PS exhibits toxicity to human podocytes, contributing to podocyte damage, renal inflammation, and fibrosis in diabetes (Kikuchi et al., 2019).

Hyperglycemia is a key factor in regulating the integrity of the gut barrier. Elevated blood glucose levels significantly disrupt the normal structure and function of the intestinal epithelial cell (Tang et al., 2024; Thaiss et al., 2018). A study revealed that excess glucose entered intestinal epithelial cells from the bloodstream via the GLUT2 transporter, leading to transcriptional reprogramming, impaired tight junctions, and barrier dysfunction (Thaiss et al., 2018). Metagenomic analysis showed that, although overall microbial diversity and richness did not differ significantly among healthy controls, T2DM, and DN groups, the beneficial and butyrate-producing bacteria were significantly reduced in both T2DM and DN patients (L. Zhang et al., 2022). Other researchers also observed that several butyrate-producing species, such as Faecalibacterium, Clostridium, Alistipes, Oscilibacter, and A. muciniphila, were depleted in individuals with prediabetes or T2D (Allin et al., 2018; H. Wu et al., 2020). This imbalance in gut microbiota was found to be significantly associated with abnormal clinical markers, including impaired glucose and lipid metabolism, and declining kidney function (L. Zhang et al., 2022).

Hyperglycemia not only alters the gut microbiota, but high-fat feeding can also induce dysbiosis, which contributes to the development of metabolic diseases. The coexistence of these factors may

establish a self-perpetuating cycle that exacerbates disease progression. In high-fat diet-fed mice, gut microbiota changes were associated with elevated lipopolysaccharide and increased expression of inflammatory markers (PAI-1, IL-1, TNF-α, and F4/80) in both visceral and subcutaneous adipose deposits. High-fat diet-fed mice were found to have reduced Lactobacillus, Bifidobacterium, and Bacteroides-Provotella, yet lowered circulating lipopolysaccharide (LPS) levels and attenuated inflammation. This inhibition of endotoxin improved glucose tolerance and decreased both visceral and subcutaneous fat mass (Cani et al., 2008). Xiong, Le et al. established that a high-fat diet promotes the expansion of Enterococcus galinarum in both the ileum and colon, a bacterium known to impair tight-junction expression and reduce intestinal mucus. Conversely, beneficial species such as Anaerobutyricum hallii and Lactobacillus gasseri, which produce short-chain fatty acids (SCFAs) essential for gut homeostasis, were significantly decreased in the high-fed diet group (Xiong et al., 2025).

Long-term high-salt diet-fed rats resulted in a reduction in Ruminococcus species (71%), which aligns with decreased insulin levels, elevated blood pressure, and liver inflammation, implicating that intestinal dysbiosis is a potential mediator of metabolic and hepatic dysfunction (X. Zhang et al., 2025). The beneficial Lactobacillus spp. and the level of SCFA butyrate were also found to decrease after mice were fed a high-salt diet (Miranda et al., 2018; Wilck et al., 2017). These changes impaired gut immune homeostasis and exacerbated vulnerability to intestinal inflammation (Miranda et al., 2018).

Patients with kidney disease often follow dietary restrictions such as reducing protein intake and avoiding foods high in potassium and phosphorus, which can attenuate the gut microbiota. However, research shows that a high-fiber diet corrected the gut imbalance seen in diabetic mice and increased the number of SCFA-producing bacteria. In the molecular mechanism, SCFAs activate specific receptors (GPRs), cell proliferation, apoptosis, and histone acetylation. They act as signalling molecules and gene regulators to maintain cell health and modulate immune and inflammatory responses (Li et al., 2020). Desai et al. provided evidence that mice maintained on a fiber-free diet exhibited an expansion of mucus-degrading bacterial populations along with increased expression of mucin-degrading enzymes. Consequently, the colonic mucus barrier was reduced to one-fifth or one-sixth of its normal thickness compared to fiber diet controls. This erosion allowed greater pathogen access to the epithelium, leading to amplified morbidity and mortality upon infection, thereby exacerbating disease outcomes (Desai et al., 2016).

Antibiotic treatment markedly reshaped the intestinal microbial composition. There are risks when antibiotics interact with certain diets, like high-glycemic (HG) diets. Smith KM et al identified a lethal interaction between high-glycemic (HG) diets and antibiotic exposure, characterized by severe dysbiosis, including a loss of Firmicutes and Bacteroides. Bacteroides are crucial for maintaining the health of goblet cells and the integrity of the epithelial barrier. The depletion of this bacterium led to colonic gland hyperplasia and early mortality (Smith et al., 2024). Maintaining Bacteroides abundance protects the mucus barrier, supports epithelial function, and improves host survival during antibiotic stress (Zafar & Saier, 2021). These findings suggest that careful consideration of diet and microbiota composition is essential when using antibiotics to avoid detrimental effects on host metabolism and gut integrity.

Accumulating evidence indicates that commonly prescribed therapies for type 2 diabetes and hypertension not only cure the underlying disease but also modulate the gut microbiota, thereby influencing host metabolism and cardiovascular health. A common type 2 diabetes treatment, metformin, significantly lowered hemoglobin A1c (hbA1c) and fasting blood glucose levels, while enriching beneficial microbes such as Akkermansia muciniphila and Bifidobacterium bifidum. Additional taxa, including Prevotella, Megasphaera, and Anaerostipes, with some evidence for Butyvibrio, were also more abundant in metformin users. These bacteria are associated with the

production of short-chain fatty acids (SCFAs) such as butyrate, propionate, and acetate, which support intestinal health and glucose metabolism (de la Cuesta-Zuluaga et al., 2016; Niu et al., 2024; H. Wu et al., 2017). Moreover, metformin treatment restored the levels of xylulose, xylose, and ribulose, which were decreased in normal-weight T2DM patients, and this restoration was associated with improvements in glycemic metabolism and inflammation (Niu et al., 2024).

First-line anti-hypertensive drugs, such as captopril and amlodipine, have been proven to affect the gut microbiota in hypertensive rats. Both drugs were found to reduce gut leakiness and structural damage to the intestinal wall and restore the production of α-defensive peptides that help protect the intestinal barriers. In addition, these drugs increased the levels of strict anaerobic and acetate-producing bacteria, which are associated with healthy blood pressure regulation (González-Correa et al., 2024). Notably, acetate is one of the major short-chain fatty acids (SCFAs), alongside butyrate and propionate, and plays a crucial role in gut and cardiovascular health.(González-Correa et al., 2024; Nogal et al., 2021). Wu et al. also found that long-term treatment with candesartan may help restore gut microbiota's capacity to produce SCFAs, potentially contributing to both its blood pressure-lowering and gut-protective effects. The study shows that 14-week treatment substantially increases acetic, propionic, and butyric acid, which are the main types of short-chain fatty acids (SCFAs) produced in the colon by bacterial fermentation (D. Wu et al., 2019).

CONCLUSION

The gut microbiome, composed of bacteria, fungi, and viruses, is crucial for metabolism, immunity, and gut health through the production of short-chain fatty acids (SCFAs). In DKD, gut dysbiosis occurs with a reduction in beneficial bacteria and an increase in pathogenic species, contributing to proteinuria and declining eGFR.

REFERENCES

Afzaal, M., Saeed, F., Shah, Y. A., Hussain, M., Rabail, R., Socol, C. T., et al. (2022). Human gut microbiota in health and disease: Unveiling the relationship. Frontiers in Microbiology, 13, 999001. https://doi.org/10.3389/fmicb.2022.999001

Ahlawat, S., Asha, & Sharma, K. K. (2021). Gut-organ axis: A microbial outreach and networking. Letters in Applied Microbiology, 72(6), 636–668. https://doi.org/10.1111/lam.13333

Alam, S., Hasan, M. K., Neaz, S., Hussain, N., Hossain, M. F., & Rahman, T. (2021). Diabetes mellitus: Insights from epidemiology, biochemistry, risk factors, diagnosis, complications and comprehensive management. Diabetology, 2(2), 36–50. https://doi.org/10.3390/diabetology2020004

Allin, K. H., Tremaroli, V., Caesar, R., Jensen, B. A. H., Damgaard, M. T. F., Bahl, M. I., et al. (2018). Aberrant intestinal microbiota in individuals with prediabetes. Diabetologia, 61(4), 810–820. https://doi.org/10.1007/s00125-018-4550-1

American Diabetes Association Professional Practice Committee. (2024). 2. Diagnosis and classification of diabetes: Standards of care in diabetes—2024. Diabetes Care, 47(Suppl. 1), S20–S42. https://doi.org/10.2337/dc24-S002

Antar, S. A., Ashour, N. A., Sharaky, M., Khattab, M., Ashour, N. A., Zaid, R. T., Roh, E. J., Elkamhawy, A., & Al-Karmalawy, A. A. (2023). Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. Biomedicine & Pharmacotherapy, 168, 115734. https://doi.org/10.1016/j.biopha.2023.115734

Candela, M., Biagi, E., Soverini, M., et al. (2016). Modulation of gut microbiota dysbioses in type 2 diabetic patients by macrobiotic Ma-pi 2 diet. British Journal of Nutrition, 116, 80–93. https://doi.org/10.1017/S0007114516001045

Cani, P. D., Bibiloni, R., Knauf, C., Waget, A., Neyrinck, A. M., Delzenne, N. M., et al. (2008). Changes in gut microbiota control metabolic endotoxemia-induced inflammation in high-fat

diet–induced obesity and diabetes in mice. Diabetes, 57(6), 1470–1481. https://doi.org/10.2337/db07-1403

Carías Domínguez, A. M., de Jesús Rosa Salazar, D., Stefanolo, J. P., Cruz Serrano, M. C., Casas, I. C., & Zuluaga Peña, J. R. (2024). Intestinal dysbiosis: Exploring definition, associated symptoms, and perspectives for a comprehensive understanding—A scoping review. Probiotics and Antimicrobial Proteins, 17(1), 440. https://pmc.ncbi.nlm.nih.gov/articles/PMC11832579/

Chelakkot, C., Ghim, J., & Ryu, S. H. (2018). Mechanisms regulating intestinal barrier integrity and its pathological implications. Experimental & Molecular Medicine, 50(8), 1–9. https://pubmed.ncbi.nlm.nih.gov/30115904/

Cheng, H.-T., Xu, X., Lim, P. S., & Hung, K.-Y. (2021). Worldwide epidemiology of diabetes-related end-stage renal disease, 2000–2015. Diabetes Care, 44(1), 89–97. https://doi.org/10.2337/dc20-1913

Cheng, T. H., Ma, M. C., Liao, M. T., Zheng, C. M., Lu, K. C., Liao, C. H., et al. (2020). Indoxyl sulfate, a tubular toxin, contributes to the development of chronic kidney disease. Toxins, 12(11), 684. https://www.mdpi.com/2072-6651/12/11/684

Cheng, X., Zhou, T., He, Y., Xie, Y., Xu, Y., & Huang, W. (2023). The role and mechanism of the gut microbiota in the development and treatment of diabetic kidney disease. Frontiers in Physiology, 14, 1166685. https://doi.org/10.3389/fphys.2023.1166685

Chong, S., Lin, M., Chong, D., Jensen, S., & Lau, N. S. (2025). A systematic review on gut microbiota in type 2 diabetes mellitus. Frontiers in Endocrinology, 15, 1486793. https://doi.org/10.3389/fendo.2024.1486793

de la Cuesta-Zuluaga, J., Mueller, N. T., Corrales-Agudelo, V., Velásquez-Mejía, E. P., Carmona, J. A., Abad, J. M., et al. (2016). Metformin is associated with higher relative abundance of mucin-degrading Akkermansia muciniphila and several short-chain fatty acid–producing microbiota in the gut. Diabetes Care, 40(1), 54–62. https://doi.org/10.2337/dc16-1324

DeFronzo, R. A., Reeves, W. B., & Awad, A. S. (2021). Pathophysiology of diabetic kidney disease: Impact of SGLT2 inhibitors. Nature Reviews Nephrology, 17, 319–334. https://doi.org/10.1038/s41581-021-00393-8

Desai, M. S., Seekatz, A. M., Koropatkin, N. M., Kamada, N., Hickey, C. A., Wolter, M., et al. (2016). A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility. Cell, 167(5), 1339–1353.e21. https://doi.org/10.1016/j.cell.2016.10.043

Gomaa, E. Z. (2020). Human gut microbiota/microbiome in health and diseases: A review. Antonie van Leeuwenhoek, 113(12), 2019–2040. https://pubmed.ncbi.nlm.nih.gov/33136284/

González-Correa, C., Moleón, J., Miñano, S., Robles-Vera, I., Toral, M., Barranco, A. M., et al. (2024). Differing contributions of the gut microbiota to the blood pressure lowering effects induced by first-line antihypertensive drugs. British Journal of Pharmacology, 181(18), 3420–3444. https://doi.org/10.1111/bph.16410

Gryp, T., Vanholder, R., Vaneechoutte, M., & Glorieux, G. (2017). p-Cresyl sulfate. Toxins, 9(2), 52. https://www.mdpi.com/2072-6651/9/2/52

Han, S., Chen, M., Cheng, P., Zhang, Z., Lu, Y., Xu, Y., et al. (2022). A systematic review and meta-analysis of gut microbiota in diabetic kidney disease: Comparisons with diabetes mellitus, non-diabetic kidney disease, and healthy individuals. Frontiers in Endocrinology, 13, 1018093. https://doi.org/10.3389/fendo.2022.1018093

He, J., Zhang, P., Shen, L., Niu, L., Tan, Y., Chen, L., et al. (2020). Short-chain fatty acids and their association with signalling pathways in inflammation, glucose and lipid metabolism. International Journal of Molecular Sciences, 21(17), 6356. https://www.mdpi.com/1422-0067/21/17/6356

Hobby, G. P., Karaduta, O., Dusio, G. F., Singh, M., Zybailov, B. L., & Arthur, J. M. (2019). Chronic kidney disease and the gut microbiome. American Journal of Physiology–Renal Physiology, 316(6), F1211–F1217. https://doi.org/10.1152/ajprenal.00298.2018

Hodgkinson, K., El Abbar, F., Dobranowski, P., Manoogian, J., Butcher, J., Figeys, D., et al. (2023). Butyrate's role in human health and the current progress towards its clinical application to treat gastrointestinal disease. Clinical Nutrition, 42(2), 61–75. https://www.clinicalnutritionjournal.com/action/showFullText?pii=S0261561422003843

Hoogeveen, E. K. (2022). The epidemiology of diabetic kidney disease. Kidney and Dialysis, 2(3), 433–442. https://doi.org/10.3390/kidneydial2030038

Horowitz, A., Chanez-Paredes, S. D., Haest, X., & Turner, J. R. (2023). Paracellular permeability and tight junction regulation in gut health and disease. Nature Reviews Gastroenterology & Hepatology, 20(7), 417–432. https://www.nature.com/articles/s41575-023-00766-3

Hsu, B. G., Wang, C. H., Lin, Y. L., Lai, Y. H., & Tsai, J. P. (2022). Serum trimethylamine N-oxide level is associated with peripheral arterial stiffness in advanced non-dialysis chronic kidney disease patients. Toxins, 14(8), 539. https://pubmed.ncbi.nlm.nih.gov/36006188/

Huang, W., Guo, H. L., Deng, X., Zhu, T. T., Xiong, J. F., Xu, Y. H., et al. (2017). Short-chain fatty acids inhibit oxidative stress and inflammation in mesangial cells induced by high glucose and lipopolysaccharide. Experimental and Clinical Endocrinology & Diabetes, 125(2), 98–105. https://pubmed.ncbi.nlm.nih.gov/28049222/

Huang, Y., Xin, W., Xiong, J., Yao, M., Zhang, B., & Zhao, J. (2022). The intestinal microbiota and metabolites in the gut–kidney–heart axis of chronic kidney disease. Frontiers in Pharmacology, 13. https://pubmed.ncbi.nlm.nih.gov/35370631/

Hustrini, N. M., Susalit, E., & Rotmans, J. I. (2022). Prevalence and risk factors for chronic kidney disease in Indonesia: An analysis of the National Basic Health Survey 2018. Journal of Global Health, 12, 04074. https://doi.org/10.7189/jogh.12.04074

Kadatane, S. P., Satariano, M., Massey, M., Mongan, K., & Raina, R. (2023). The role of inflammation in CKD. Cells, 12(12), 1581. https://www.mdpi.com/2073-4409/12/12/1581

Kikuchi, K., Saigusa, D., Kanemitsu, Y., et al. (2019). Gut microbiome-derived phenyl sulfate contributes to albuminuria in diabetic kidney disease. Nature Communications, 10, 1835. https://doi.org/10.1038/s41467-019-09735-4

Koye, D. N., Magliano, D. J., Nelson, R. G., & Pavkov, M. E. (2018). The global epidemiology of diabetes and kidney disease. Advances in Chronic Kidney Disease, 25(2), 121–132. https://doi.org/10.1053/j.ackd.2017.10.011

Li, H.-B., Xu, M.-L., Xu, X.-D., Tang, Y.-Y., Jiang, H.-L., Li, L., et al. (2022). Faecalibacterium prausnitzii attenuates CKD via butyrate–renal GPR43 axis. Circulation Research, 131, e120–e134. https://doi.org/10.1161/CIRCRESAHA.122.320184

Li, Y. J., Chen, X., Kwan, T. K., Loh, Y. W., Singer, J., Liu, Y., et al. (2020). Dietary fiber protects against diabetic nephropathy through short-chain fatty acid–mediated activation of G protein–coupled receptors GPR43 and GPR109A. Journal of the American Society of Nephrology, 31(6), 1267–1282. https://journals.lww.com/jasn/fulltext/2020/06000/dietary_fiber_protects_against_diabetic.17.aspx

Lin, J. R., Wang, Z. T., Sun, J. J., et al. (2022). Gut microbiota and diabetic kidney diseases: Pathogenesis and therapeutic perspectives. World Journal of Diabetes, 13(4), 308–318. https://doi.org/10.4239/wjd.v13.i4.308

Liu, Y., Liu, Q., Zhang, C., Zhao, J., Zhang, H., Chen, W., & Zhai, Q. (2023). Strain-specific effects of Akkermansia muciniphila on the regulation of intestinal barrier. Food Science and Human Wellness, 12(5), 1526–1537. https://doi.org/10.1016/j.fshw.2023.02.022

Louis, P., & Flint, H. J. (2017). Formation of propionate and butyrate by the human colonic microbiota. Environmental Microbiology, 19(1), 29–41. https://pubmed.ncbi.nlm.nih.gov/27928878/

Lu, X., Ma, J., & Li, R. (2023). Alterations of gut microbiota in biopsy-proven diabetic nephropathy and a long history of diabetes without kidney damage. Scientific Reports, 13, 12150. https://doi.org/10.1038/s41598-023-39444-4

Martin-Gallausiaux, C., Marinelli, L., Blottière, H. M., Larraufie, P., & Lapaque, N. (2021). SCFA: Mechanisms and functional importance in the gut. Proceedings of the Nutrition Society, 80(1), 37–49. https://pubmed.ncbi.nlm.nih.gov/32238208/

Matoori, S. (2022). Diabetes and its complications. ACS Pharmacology & Translational Science, 5(8), 513–515. https://doi.org/10.1021/acsptsci.2c00122

Miranda, P. M., De Palma, G., Serkis, V., Lu, J., Louis-Auguste, M. P., McCarville, J. L., et al. (2018). High salt diet exacerbates colitis in mice by decreasing Lactobacillus levels and butyrate production. Microbiome, 6, 57. https://doi.org/10.1186/s40168-018-0433-4

Naaman, S. C., & Bakris, G. L. (2023). Diabetic nephropathy: Update on pillars of therapy slowing progression. Diabetes Care, 46(9), 1574–1586. https://doi.org/10.2337/dci23-0030

Nallu, A., Sharma, S., Ramezani, A., Muralidharan, J., & Raj, D. (2017). Gut microbiome in chronic kidney disease: Challenges and opportunities. Translational Research, 179, 24–37. https://www.translationalres.com/action/showFullText?pii=S1931524416300330

Niu, X., Wang, Y, Huang, L., Guo, P., Zhang, S., Sun, Y., et al. (2024). Effect of oral metformin on gut microbiota characteristics and metabolite fractions in normal-weight type 2 diabetic mellitus patients. Frontiers in Endocrinology, 15. https://www.frontiersin.org/articles/10.3389/fendo.2024.1397034

Nogal, A., Louca, P., Zhang, X., Wells, P. M., Steves, C. J., Spector, T. D., et al. (2021). Circulating levels of the short-chain fatty acid acetate mediate the effect of the gut microbiome on visceral fat. Frontiers in Microbiology, 12. https://www.frontiersin.org/articles/10.3389/fmicb.2021.711359

Ojo, O. A., Ibrahim, H. S., Rotimi, D. E., Ogunlakin, A. D., & Ojo, A. B. (2023). Diabetes mellitus: From molecular mechanism to pathophysiology and pharmacology. Medicine in Novel Technology and Devices, 19, 100247. https://doi.org/10.1016/j.medntd.2023.100247

Ong, K. L., et al. (2023). Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: A systematic analysis for the Global Burden of Disease Study 2021. The Lancet, 402(10397), 203–234.

Opdebeeck, B., D'Haese, P. C., & Verhulst, A. (2020). Molecular and cellular mechanisms that induce arterial calcification by indoxyl sulfate and p-cresyl sulfate. Toxins, 12(1), 58. https://pubmed.ncbi.nlm.nih.gov/31963891/

Pan, S., Zhao, D., Duan, S., & Chen, X. (2023). The role of gut-dependent molecule trimethylamine N-oxide as a novel target for the treatment of chronic kidney disease. International Urology and Nephrology, 55(7), 1747–1756. https://pubmed.ncbi.nlm.nih.gov/36797553/

Qian, N., Li, Y., Liu, Z., Chen, X., & Xie, J. (2022). Molecular mechanisms and therapeutic targets for diabetic kidney disease. International Review of Cell and Molecular Biology, 371, XX–XX. https://doi.org/10.1016/S0085-2538(22)00436-7

Remely, M., Hippe, B., Zanner, J., Aumueller, E., Brath, H., & Haslberger, A. G. (2016). Gut microbiota of obese, type 2 diabetic individuals is enriched in Faecalibacterium prausnitzii, Akkermansia muciniphila and Peptostreptococcus anaerobius after weight loss. Endocrine, Metabolic & Immune Disorders – Drug Targets, 16, 99–106. https://doi.org/10.2174/1871530316666160831093813

Rinninella, E., Raoul, P., Cintoni, M., et al. (2019). What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms, 7(1), 14. https://doi.org/10.3390/microorganisms7010014

Sharma, S., & Tripathi, P. (2019). Gut microbiome and type 2 diabetes: Where we are and where to go? Journal of Nutritional Biochemistry, 63, 101–108. https://doi.org/10.1016/j.jnutbio.2018.10.003

Smith, K. M., Francisco, S. G., Zhu, Y., LeRoith, T., Davis, M. L., Crott, J. W., et al. (2024). Dietary prevention of antibiotic-induced dysbiosis and mortality upon aging in mice. FASEB Journal, 38(23), e70241. https://doi.org/10.1096/fj.202402262R

Stavropoulou, E., Kantartzi, K., Tsigalou, C., Konstantinidis, T., Romanidou, G., Voidarou, C., et al. (2021). Focus on the gut–kidney axis in health and disease. Frontiers in Medicine, 7, 620102.

Sumida, K., & Kovesdy, C. P. (2019). The gut–kidney–heart axis in chronic kidney disease. Physiological International, 106(3), 195–206. https://akjournals.com/view/journals/2060/106/3/article-p195.xml

Sumida, K., Molnar, M. Z., Potukuchi, P. K., Thomas, F., Lu, J. L., Matsushita, K., et al. (2017). Constipation and incident CKD. Journal of the American Society of Nephrology, 28(4), 1248–1258. https://pubmed.ncbi.nlm.nih.gov/28122944/

Sun, H., Saeedi, P., Karuranga, S., et al. (2022). IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Research and Clinical Practice, 183, 109119. https://doi.org/10.1016/j.diabres.2021.109119

Tang, W. H. W., Wang, Z., Kennedy, D. J., Wu, Y., Buffa, J. A., Agatisa-Boyle, B., et al. (2014). Gut microbiota–dependent trimethylamine N-oxide (TMAO) pathway contributes to both development of renal insufficiency and mortality risk in chronic kidney disease. Circulation Research, 116(3), 448–455. https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.116.305360

Tang, X., Chen, X., Ferrari, M., Walvoort, M. T. C., & de Vos, P. (2024). Gut epithelial barrier function is impacted by hyperglycemia and secondary bile acids in vitro: Possible rescuing effects of specific pectins. Molecular Nutrition & Food Research, 68(11), 2300910. https://doi.org/10.1002/mnfr.202300910

Tao, S., Li, L., Li, L., et al. (2019). Understanding the gut–kidney axis among biopsy-proven diabetic nephropathy, type 2 diabetes mellitus and healthy controls: An analysis of the gut microbiota composition. Acta Diabetologica, 56, 581–592. https://doi.org/10.1007/s00592-019-01316-7

Thaiss, C. A., Levy, M., Grosheva, I., Zheng, D., Soffer, E., Blacher, E., et al. (2018). Hyperglycemia drives intestinal barrier dysfunction and risk for enteric infection. Science, 359(6382), 1376–1383. https://doi.org/10.1126/science.aar3318

Tourountzis, T., Lioulios, G., Fylaktou, A, Moysidou, E., Papagianni, A., & Stangou, M. (2022). Microbiome in chronic kidney disease. Life, 12(10), 1513. https://pmc.ncbi.nlm.nih.gov/articles/PMC9604691/

Tsuji, K., Uchida, N., Nakanoh, H., Fukushima, K., Haraguchi, S., Kitamura, S., et al. (2024). The gut–kidney axis in chronic kidney diseases. Diagnostics, 15(1), 21. https://www.mdpi.com/2075-4418/15/1/21

Ullah, H., Arbab, S., Tian, Y., Liu, C. Q., Chen, Y., Qijie, L., et al. (2023). The gut microbiota–brain axis in neurological disorder. Frontiers in Neuroscience, 17. https://pubmed.ncbi.nlm.nih.gov/37600019/

Wilck, N., Matus, M. G., Kearney, S. M., Olesen, S. W., Forslund, K., Bartolomaeus, H., et al. (2017). Salt-responsive gut commensal modulates TH17 axis and disease. Nature, 551(7682), 585–589. http://dx.doi.org/10.1038/nature24628

Wu, D., Tang, X., Ding, L., Cui, J., Wang, P., Du, X., et al. (2019). Candesartan attenuates hypertension-associated pathophysiological alterations in the gut. Biomedicine & Pharmacotherapy, 116, 109040. https://www.sciencedirect.com/science/article/pii/S0753332219309035

Wu, H., Esteve, E., Tremaroli, V., Khan, M. T., Caesar, R., Mannerås-Holm, L., et al. (2017). Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug. Nature Medicine, 23(7), 850–858. https://doi.org/10.1038/nm.4345

Wu, H., Tremaroli, V., Schmidt, C., Lundqvist, A., Olsson, L. M., Krämer, M., et al. (2020). The gut microbiota in prediabetes and diabetes: A population-based cross-sectional study. Cell Metabolism, 32(3), 379–390.e3. https://doi.org/10.1016/j.cmet.2020.06.011

Wu, I. W., Lin, C. Y., Chang, L. C., et al. (2020). Gut microbiota as diagnostic tools for mirroring disease progression and circulating nephrotoxin levels in chronic kidney disease: Discovery and validation study. International Journal of Biological Sciences, 16(3), 420–434. https://doi.org/10.7150/ijbs.37421

Wu, J., Wang, K., Wang, X., Pang, Y., & Jiang, C. (2021). The role of the gut microbiome and its metabolites in metabolic diseases. Protein & Cell, 12(5), 360–373. https://doi.org/10.1007/s13238-020-00814-7

Xiong, L., Diwakarla, S., Chatzis, R., Artaiz, O., Macowan, M., Zhang, S., et al. (2025). Acute exposure to high-fat diet impairs ILC3 functions and gut homeostasis. Immunity, 58(5), 1185–1200.e8. https://doi.org/10.1016/j.immuni.2025.03.017

Yokoo, K., Yamamoto, Y., & Suzuki, T. (2021). Ammonia impairs tight junction barriers by inducing mitochondrial dysfunction in Caco-2 cells. FASEB Journal, 35(11), e21968. https://pubmed.ncbi.nlm.nih.gov/34597422/

Zafar, H., & Saier, M. H. (2021). Gut Bacteroides species in health and disease. Gut Microbes, 13(1), 1–20. https://doi.org/10.1080/19490976.2020.1848158

Zhang, L., Wang, Z., Zhang, X., Zhao, L., Chu, J., Li, H., et al. (2022). Alterations of the gut microbiota in patients with diabetic nephropathy. Microbiology Spectrum, 10(4), e00324-22.

Zhang, X., Gaballa, M. M. S., Hasan, A. A., Liu, Y., Hocher, J.-G., Chen, X., et al. (2025). Effects of high salt intake on glucose metabolism, liver function, and the microbiome in rats: Influence of ACE inhibitors and angiotensin II receptor blockers. American Journal of Physiology–Cell Physiology, 328(4), C1366–C1382. https://doi.org/10.1152/ajpcell.01036.2024