Available Online: 22 April 2026 DOI: 10.54254/3029-0821/2026.32933

Research progress on the role of ellagic acid in improving glucose homeostasis by regulating gut microbiota

Boya Zhang[1], Yan Dong[1], Naige Zhang[1], Yujia Fu[1], Mengdi Sun[1], Ruimeng Liu[1], Jiayun Li[1], Shengquan Mi[1,2*]

[1]College of Biochemical Engineering of Beijing Union University, Beijing, China
[2]Key Laboratory of Bioactive Substances and Functional Foods, Beijing Union University, Beijing, China

*Corresponding Author. Email: msq65@buu.edu.cn

Abstract. Ellagic Acid (EA) needs to be metabolized by intestinal flora to urolithin active products, or directly regulates the composition and function of intestinal flora, and maintains blood glucose homeostasis by regulating insulin secretion, improving insulin sensitivity and activating multiple organ regulatory pathways. Animal experiments and clinical studies have confirmed that EA can reduce fasting blood glucose and improve insulin resistance. This article reviews the two-way interaction between EA and gut microbiota, the core pathway of gut microbiota regulating blood glucose, the specific regulatory mechanism of EA and related in vitro and in vivo studies, so as to provide a new perspective for the intervention of glucose metabolism diseases. In the future, it is necessary to focus on the transformation mechanism, dosage form optimization and large sample clinical research to promote its clinical transformation.

Keywords: ellagic acid, intestinal flora, urolithin, blood glucose homeostasis, regulation of glucose metabolism

1. Introduction

Ellagic Acid (EA) is a type of natural polyphenolic compound widely present in fruits and nuts such as pomegranates, walnuts, and raspberries. Due to its polyphenolic hydroxyl structure, EA possesses various physiological activities such as antioxidant, anti-inflammatory, and potential anti-tumor properties, and has attracted much attention in the field of nutrition and health [1, 2]. However, EA has poor water solubility and extremely low oral bioavailability. Only a small amount can be directly absorbed by the small intestine, and most need to enter the colon and be metabolized by intestinal flora into urolithin-like substances. These metabolites are the key substance basis for EA to exert its physiological effects in the body [3, 4].

The gut microbiota, as the core regulator of the host's metabolic homeostasis, can deeply participate in the regulation of blood glucose homeostasis through generating short-chain fatty acids, maintaining the integrity of the intestinal barrier, and regulating inflammatory responses, etc. Imbalance of the microbiota is prone to induce insulin resistance and glucose metabolism disorders [5-8]. Moreover, there is a bidirectional interaction between EA and the gut microbiota: EA can regulate the structure and diversity of the microbiota, and the

Copyright: © 2026 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

microbiota mediates the metabolic activation of EA. This interplay relationship provides a new direction for the intervention of abnormal glucose metabolism by EA.

At present, the specific mechanism by which EA improves blood sugar through the gut microbiota, the in vivo and in vitro experimental evidence, and the clinical translational value have not been systematically clarified. This article will focus on the bidirectional interaction between EA and the gut microbiota, the core mechanism by which the gut microbiota regulates blood sugar, the specific regulatory mechanism of EA, in vivo experiments and clinical research, as well as existing problems and prospects. The aim is to provide theoretical references for the application of EA in the intervention of metabolic diseases.

2. The bidirectional interaction between EA and the intestinal microbiota

2.1. The regulatory effect of EA on the composition and diversity of intestinal flora

EA can significantly regulate the composition and diversity of the intestinal microbiota. In the C57BL/6J mouse experiment, the intake of 0.3% EA supplement significantly reduced the number of Escherichia coli in the jejunal contents, while increasing the number of lactic acid bacteria, and had no significant effect on the overall abundance of the Bacteroidetes and Firmicutes phyla, indicating that it can specifically inhibit harmful bacteria and promote the proliferation of beneficial bacteria [9]. The in vitro simulation of human colon fermentation experiment showed that the raspberry tannin-enriched component (containing EA and its precursor ellagic tannin) could significantly increase the relative abundance of beneficial bacteria such as Faecalibacterium prausnitzii, Butyricicoccus pulmoneus, Ruminococcus flaviestinctus, and Enterobacteriaceae in feces, although gastrointestinal digestion would reduce its improvement effect on bifidobacteria, it could still promote the growth of acid-producing bacteria and maintain the intestinal microecological balance [10]. In the SD rat experiment, continuous intragastric administration of EA for 28 days could significantly increase the diversity of the intestinal microbiota (with an increase in Shannon index and a decrease in Simpson index), the abundance of Bacteroidetes phylum increased at the phylum level, the abundance of Proteobacteria phylum (including pathogenic bacteria such as Escherichia coli) decreased, and the proportions of Bacteroidales S24-7 genus, Lachnospiraceae NK4A136 genus and Bacteroides genus increased significantly at the genus level, further confirming the optimization effect of EA on the structure of the intestinal microbiota [11].

2.2. The metabolic transformation effect of gut microbiota on EA

Although EA possesses various biological activities such as antioxidant and anti-inflammatory properties, its bioavailability is relatively low. Approximately 90% to 95% of EA cannot be digested and absorbed in the human small intestine. It needs to be metabolized and transformed by the intestinal microbiota to exert its physiological functions [12]. In the colon, the intestinal microbiota first remove the lactone ring of EA and dehydrate it to form pentahydroxy uricosine, and then undergo a series of dehydroxylation reactions to ultimately convert it into easily absorbable active products such as uricosine A and uricosine B, among which uricosine A has the strongest activity [12]. The key transforming bacterial genera that have been discovered are mainly concentrated in the Actinobacteria phylum, such as Gordonia bacteria, pseudo-clostridium bifidus, etc. [12]. In addition, Bacillus coagulans BC2000 can further promote the production of uricosine A by increasing the relative abundance of the bacteria involved in the transformation of EA in the intestinal tract [12]. In vitro studies have also confirmed that the UM-A type human intestinal microbiota can achieve the in vitro transformation of EA, providing direct evidence for the intestinal microbiota-mediated EA metabolism [13].

3. The core mechanism by which the gut microbiota regulates glucose homeostasis

3.1. The gut microbiota regulates blood glucose homeostasis through metabolites.

The gut microbiota can regulate glucose homeostasis by producing metabolites such as SCFAs and secondary bile acids. Among them, SCFAs are the core protective metabolites, such as acetic acid, propionic acid, and butyric acid, which can activate the G Protein-Coupled Receptors (GPCRs) of intestinal L cells, promoting the secretion of Glucagon-like Peptide-1 (GLP-1) and peptide YY (PYY) to improve insulin sensitivity, and also activating the G Protein-coupled Receptor 41/43 (GPR41/43) - Adenosine Monophosphate-activated Protein Kinase (AMPK) signaling pathway in skeletal muscle to promote the translocation of Glucose Transporter Type 4 (GLUT-4) for enhanced glucose uptake [14]. Some hypoglycemic drugs can exert their effects by regulating the microbiota that produces SCFAs. For example, metformin can increase the abundance of Blautia, Bacteroides, etc., which produce SCFAs, and SCFAs can stimulate the secretion of GLP-1 by regulating the expression of free fatty acid receptor genes [15]. After liraglutide treatment, the levels of acetic acid, propionic acid, and butyric acid in the feces and plasma of patients significantly increased. These SCFAs can improve insulin sensitivity, inhibit liver fat synthesis and regulate liver glucose metabolism to maintain blood glucose stability [16].

3.2. The gut microbiota-immune axis regulates glucose homeostasis

The dynamic interaction between the gut microbiota and the host's immune system constitutes the key defense line for glucose regulation. Their imbalance is an important trigger for inducing glucose metabolism disorders. Normal microbiota can activate the host's innate immunity through their components and metabolic signals, such as stimulating the expression of pattern recognition receptors on intestinal epithelial cells, regulating the differentiation and function of immune cells, maintaining immune tolerance and defense balance, and avoiding abnormal inflammation from interfering with glucose regulation [17]. When the microbiota is imbalanced, it will disrupt this balance: harmful bacteria proliferate excessively and release substances such as lipopolysaccharides, causing intestinal barrier damage and endotoxemia, activating systemic inflammatory responses, and thereby inhibiting insulin signaling pathway transmission, exacerbating insulin resistance [18]. Beneficial bacteria can alleviate glucose metabolism abnormalities by regulating intestinal immunity, such as promoting the secretion of anti-inflammatory factors, reducing the level of pro-inflammatory factors, improving the immune microenvironment, and indirectly enhancing insulin sensitivity to maintain blood glucose stability [18].

3.3. The gut microbiota regulates glucose homeostasis through multi-organ axes (the gut-brain axis, the gut-liver axis)

3.3.1. Gut-brain axis: bidirectional regulation of neuroendocrine signals

The gut microbiota can regulate blood sugar through the interaction between metabolites and neural signals. The active substances such as SCFAs produced by fermentation can stimulate intestinal endocrine cells to secrete hormones like GLP-1 that lower blood sugar, while activating the vagus nerve pathway to transmit signals to the central nervous system, regulating appetite and glucose perception. The central nervous system regulates intestinal peristalsis and the colonization environment of the microbiota through efferent nerves, forming a "perception-regulation" loop to maintain blood sugar homeostasis [19].

3.3.2. Gut-liver axis: cross-organ transmission of metabolic signals

The metabolites produced by the gut microbiota directly reach the liver through the portal vein to regulate glucose metabolism. The SCFAs produced by beneficial bacteria can inhibit the activity of liver gluconeogenesis enzymes and reduce endogenous glucose production; while when the microbiota is imbalanced, the lipopolysaccharides released by harmful bacteria enter the bloodstream through damaged intestinal barriers and activate the liver inflammatory pathways, exacerbating insulin resistance [20]. The bile acids secreted by the liver can also reverse the composition of the microbiota, forming a bidirectional regulatory network.

3.3.3. Two-axis synergy: multi-dimensional steady-state maintenance network

The gut-brain axis and the gut-liver axis achieve coordinated regulation through common metabolic mediators. SCFAs not only participate in the neural signal transmission of the gut-brain axis but also act as key metabolites of the gut-liver axis to regulate liver function, and the central nervous system's regulation of liver glucose metabolism further strengthens the network connectivity [19-24]. The coordinated operation of the two axes constitutes the core network for the microbiota to regulate blood sugar, and their imbalance is an important cause of glucose metabolism disorders. The gut microbiota can coordinate regulate blood sugar through three core pathways: metabolic products, immune axis, and multi-organ axis, as shown in Figure 1.

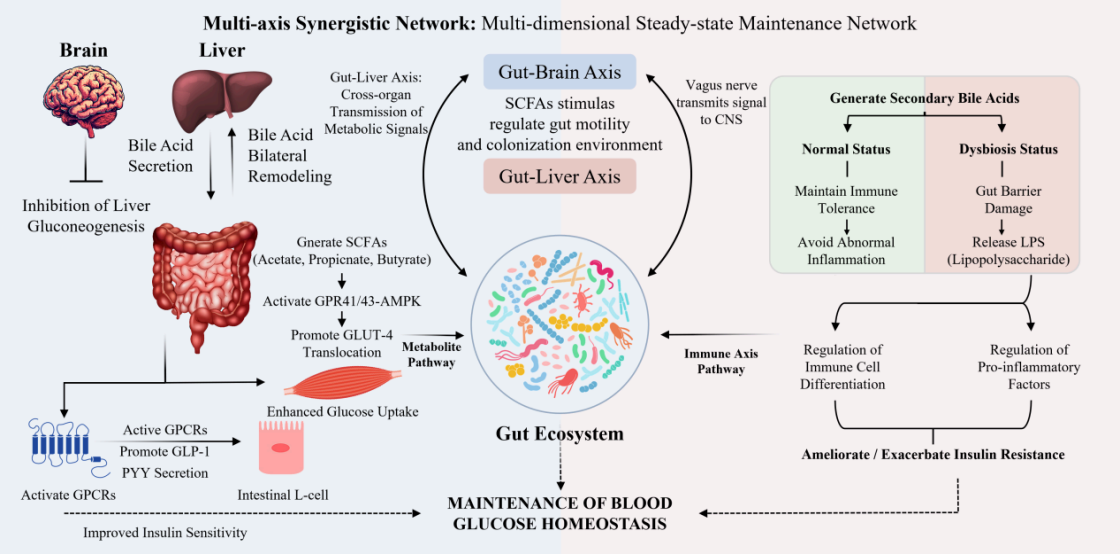

Figure 1. Research progress on the role of ellagic acid in improving glucose homeostasis by regulating the intestinal microbiota

4. The mechanism by which EA improves blood sugar through the intestinal microbiota

4.1. The intestinal microbiota metabolizes EA to produce urolithin. Urolithin regulates insulin secretion and insulin sensitivity, thereby improving glucose homeostasis

The bioavailability of EA is relatively low. It needs to be metabolized by intestinal flora into urolithin-like substances to fully exert its role in regulating blood sugar. This biological transformation process is a key prerequisite for improving blood sugar homeostasis [25-28]. Among them, urolithins A, B, and C, as the main metabolites, participate in blood sugar regulation by regulating insulin sensitivity or secretion function.

Ursolic acid exerts its main mechanism of action by improving insulin sensitivity. It can regulate the mitochondrial functions of the liver and skeletal muscles, reduce the serum levels of free fatty acids, alleviate diet-induced insulin resistance, and simultaneously enhance adiponectin expression and the insulin-mediated glucose clearance capacity [29]. Ursolic acid B improves insulin sensitivity through anti-inflammatory pathways. In models of insulin resistance induced by Tumor Necrosis Factor alpha (TNF-α), it can inhibit the abnormal signaling pathways mediated by inflammatory factors, reduce the interference of inflammation on insulin signal transduction, and thereby restore the response ability of target tissues to insulin [29]. Ursolic acid C focuses on insulin secretion regulation. Its effect has a glucose-dependent characteristic. By binding to the Cav1.2 L-type calcium channel (Cav1.2 L-type Ca2+ channel) of pancreatic β cells, it promotes channel opening and calcium ion influx, and only enhances insulin secretion under glucose stimulation conditions. This effect can be reversed with a decrease in glucose concentration [30].

The three elements work together to form a glucose regulation network for EA after it is metabolized by the intestinal microbiota. They maintain glucose homeostasis from the perspectives of secretion activation and sensitivity enhancement.

4.2. EA directly regulates the composition and function of the intestinal microbiota. It maintains blood sugar stability by improving the intestinal microecology and the insulin target organ signaling pathway

EA can directly regulate the composition and function of the intestinal microbiota, optimize the intestinal microecology to establish the basic environment for maintaining blood sugar stability. Studies have shown that EA can significantly increase the abundance of beneficial bacteria such as Lactobacillus and Bifidobacterium in the intestinal tract, reduce the proportion of potential harmful bacteria such as Escherichia coli, and at the same time promote the production of SCFAs such as propionic acid by the intestinal microbiota, enhance the integrity of the intestinal barrier, reduce the inflammatory response caused by the entry of endotoxins into the bloodstream, and eliminate interference at the microecological level in the subsequent blood sugar regulation [31].

This improvement in the intestinal microecology can also have an indirect effect on the insulin target organ signaling pathways, especially in adipose tissue, with significant effects observed. The experiment found that EA, through the aforementioned regulatory effects on the intestinal microecology, can correct the insulin signaling disorder in adipose tissue of type 2 diabetic mice, significantly upregulate the expression of insulin receptor substrate 1 (Insulin Receptor Substrate 1, IRS-1), phosphorylated protein kinase B (phosphorylated protein kinase B, p-Akt), and GLUT-4, enhance insulin-mediated glucose uptake and utilization, and simultaneously reduce serum free fatty acid levels and the insulin resistance index of adipose tissue. This helps maintain blood sugar stability at the target organ level [32]. To visually present the dual core mechanism of EA improving blood sugar through the intestinal microbiota (direct regulation of the microbiota and the generation of urolithin regulation), and clearly display the logical connections of each link.

5. In vivo and clinical studies on the effect of EA on improving blood sugar through the intestinal microbiota

5.1. Progress in in vivo animal experiment research

EA can be metabolized by the intestinal microbiota to form active products and exert its effects. In an experimental model of autoimmune encephalomyelitis in mice, dietary EA can reshape the structure of the

intestinal microbiota, significantly increase the abundance of SCFAs-producing bacteria such as Alloprevotella, and promote the production of propionic acid. Although the research focuses on central immunity, the changes in the metabolic products of the intestinal microbiota lay a microecological foundation for subsequent regulation of glucose metabolism [33]. Studies on metabolic health further confirm this pathway. In experiments with mice induced by a high-fat and high-sugar diet to develop insulin resistance, EA metabolized by the intestinal microbiota to form urushiol A can lower fasting blood glucose and increase adiponectin levels. When used in combination with EA, it can significantly improve the insulin-mediated hypoglycemic effect. The mechanism is related to the regulation of mitochondrial functions in the liver and skeletal muscles [34].

The functions of the members of the urolithin family are specific. In the type 1 diabetes model, the intestinal metabolite of EA, urolithin C, exhibits glucose-dependent activation activity for insulin secretion and can directly alleviate pancreatic β-cell dysfunction. It improves glucose homeostasis by targeting the regulation of the core Section of insulin secretion [35]. Urolithin A can also exert its effects by bidirectionally regulating the relationship between the intestinal microbiota and blood glucose. Studies on type 2 diabetic mice have found that urolithin A can optimize the composition of the intestinal microbiota and simultaneously alleviate glucose metabolism disorders by improving insulin sensitivity, confirming the glucose-regulating value of the tannic acid-intestinal microbiota-urolithin axis [36]. Tannic acid can also directly regulate the intestinal microbiota to improve blood glucose. In insulin-resistant mice induced by high-fat diet, the combined intervention of Clostridium concisum BC2000 and tannic acid can significantly increase the abundance of Actinobacteria and Lactobacillus genera, and reduce the level of Desulfurococcus, through improving the intestinal microecological barrier function and down-regulating inflammatory factors, ultimately reducing the insulin resistance index [37].

5.2. Current status and evidence of clinical research

At present, clinical studies on the effect of EA on improving blood sugar through the intestinal microbiota have accumulated some evidence-based data, providing support for its clinical application. In the randomized double-blind controlled trial conducted by Ghadimi et al., 44 patients with type 2 diabetes were randomly divided into the intervention group (180 mg EA per day) and the placebo group. After 8 weeks of intervention, the fasting blood sugar, insulin levels, and insulin resistance index (Homeostatic Model Assessment of Insulin Resistance, HOMA-IR) in the intervention group significantly decreased, while the serum silent information regulator factor-related enzyme 1 (Sirtuin 1, SIRT1) level increased and fetuin-A decreased. This suggests that EA can improve blood sugar homeostasis by regulating the molecular pathways related to sugar metabolism, and its effect may depend on the regulation of metabolic signals by the intestinal microbiota [38]. Wang et al.'s Meta-analysis further integrated the data of 10 Randomized Controlled Trials (RCTs) involving a total of 419 patients, finding that EA can significantly reduce fasting blood sugar, triglycerides, and low-density lipoprotein, enhance insulin secretion function and improve resistance. The effects are more significant when the intervention time is ≥ 8 weeks and the dose is ≥ 180 mg/day. This further confirms its clinical value and suggests that the optimization of the intestinal microbiota structure may be an important intermediary mechanism for improving blood sugar metabolism [39]. To systematically summarize the in vitro and in vivo research evidence of EA regulating blood sugar through the intestinal microbiota, and to clarify the intervention schemes and core outcomes of different studies, the key research information is presented in Table 1.

Table 1. Summary of EA-Mediated blood glucose regulation studies

Study Type	Key Interventions	Core Outcomes	References
Animal study (Mouse)	EA monotherapy; EA + Urolithin A combination	Reduced fasting blood glucose, improved insulin sensitivity, enhanced insulin-mediated glucose-lowering effect	[34]
Animal study (Mouse)	Urolithin C (EA metabolite) intervention	Improved pancreatic β-cell function, enhanced glucose-dependent insulin secretion	[35]
Animal study (Mouse)	Urolithin A monotherapy	Alleviated glucose metabolism disorder, reduced insulin resistance	[36]
Animal study (Mouse)	Weizmannia coagulans BC2000 + EA combination	Reduced insulin resistance index, enhanced intestinal barrier function	[37]
Clinical study (RCT)	EA (180 mg/day) for 8 weeks	Reduced fasting blood glucose, insulin level and HOMA-IR	[38]
Clinical study (Meta-analysis)	EA (≥ 180 mg/day) for ≥ 8 weeks	Reduced fasting blood glucose, TG, LDL and insulin resistance	[39]

6. Conclusion

EA can improve glucose homeostasis through bidirectional interactions with the gut microbiota. The core mechanism lies in the fact that gut microorganisms metabolize EA into urinary stone-like active products, or EA directly regulates the microbial community structure to optimize the intestinal microecology, activate the intestinal-brain axis, intestinal-liver axis and other multi-organ glucose regulation pathways, providing a new perspective for the natural polyphenol intervention of sugar metabolism diseases. However, there are still key bottlenecks in current research: Firstly, the mechanism of individual differences in the conversion of EA into urinary stones is unclear, and the detailed metabolic regulation of key microorganisms (such as Gordonia bacteria) needs to be further analyzed; Secondly, the sample size of clinical studies is small, the intervention period is short, and the long-term application effects and safety data are still insufficient; Thirdly, EA has poor water solubility and low oral bioavailability, and the problem has not been effectively solved through formulation optimization.

Therefore, future research should focus on three aspects: Firstly, analyze the metabolic pathways of key transforming bacteria and develop bacterial regulators to enhance the efficiency of urolithin production; Secondly, design delivery systems targeting the colon to improve the bioavailability of EA; Thirdly, conduct multi-center, large-sample long-term clinical studies to verify its practical application value. From a nutritional health perspective, EA relies on the regulatory path of the intestinal microbiota to avoid potential side effects of chemical drugs, and its interaction with microorganisms can assist in the intervention of metabolic diseases. In the future, further exploration of the association mechanism between EA and urolithin is needed, combined with precision nutrition (such as personalized intervention based on microbiota typing) optimization strategies, to improve bioavailability and promote the clinical transformation of natural polyphenols in the field of metabolic health.

References

[1] Amor, A. J., Gomez-Guerrero, C., & Ortega, E. (2020). Ellagic acid as a tool to limit the diabetes burden: Updated evidence. *Antioxidants, 9*(12), Article 1226.

[2] Konczak, I., Maillot, F., & Dalar, A. (2014). Phytochemical divergence in 45 accessions of Terminalia ferdinandiana (Kakadu plum). *Food Chemistry, 151*, 248–256.

[3] Ceci, C., Claudia, C., & Grazia, G. (2020). Strategies to improve ellagic acid bioavailability: From natural or semisynthetic derivatives to nanotechnological approaches based on innovative carriers. *Nanotechnology, 31*(38), Article 382001. https: //doi.org/10.1088/1361-6528/ab912c

[4] Brate, S. R., Vibeke, V., & Kristine, S. B. (2020). Ellagic acid and urolithin A modulate the immune response in LPS-stimulated U937 monocytic cells and THP-1 differentiated macrophages. *Food & Function*. Advance online publication. https: //doi.org/10.1039/c9fo03008e

[5] Gonzalez-Barrio, R., Edwards, C. A., & Crozier, A. (2011). Colonic catabolism of ellagitannins, ellagic acid, and raspberry anthocyanins: In vivo and in vitro studies. *Drug Metabolism and Disposition, 39*(9), 1680–1688.

[6] Piwowarski, J. P., Granica, S., & Zwierzyńska, M. (2014). Role of human gut microbiota metabolism in the anti-inflammatory effect of traditionally used ellagitannin-rich plant materials. *Journal of Ethnopharmacology, 155*(1), 801–809.

[7] Giménez-Bastida, J. A., González-Sarrías, A., & Larrosa, M. (2012). Ellagitannin metabolites, urolithin A glucuronide and its aglycone urolithin A, ameliorate TNF-α-induced inflammation and associated molecular markers in human aortic endothelial cells. *Molecular Nutrition & Food Research, 56*(5), 784–796.

[8] Singh, R., Chandrashekharappa, S., & Bodduluri, S. R. (2019). Enhancement of the gut barrier integrity by a microbial metabolite through the Nrf2 pathway. *Nature Communications, 10*(1), Article 89.

[9] Xu, Q., Shen, M., & Han, Y. (2021). Effects of ellagic acid supplementation on jejunal morphology, digestive enzyme activities, antioxidant capacity, and microbiota in mice. *Frontiers in Microbiology, 12*, Article 793576.

[10] Kawabata, K., Yoshioka, Y., & Terao, J. (2019). Role of intestinal microbiota in the bioavailability and physiological functions of dietary polyphenols. *Molecules, 24*(2), Article 370. https: //doi.org/10.3390/molecules24020370

[11] Xian, W., Deng, Y., Yang, Y., Tan, Z., Chen, C., Li, W., & Yang, R. (2023). Ameliorative Effect of Ellagic Acid on Aging in Rats with the Potential Mechanism Relying on the Gut Microbiota and Urolithin A-Producing Ability. *Journal of agricultural and food chemistry, 71*(19), 7396–7407. https://doi.org/10.1021/acs.jafc.3c00960

[12] Garcia-Mantrana, I., Calatayud, M., & Romo-Vaquero, M. (2019). Urolithin metabotypes can determine the modulation of gut microbiota in healthy individuals by tracking walnuts consumption over three days. *Nutrients, 11*(10), Article 2483. https: //doi.org/10.3390/nu11102483

[13] Yu, X., Li, M., & Li, H. (2025). The role of gut dysbiosis and mitochondrial dysfunction in type 2 diabetes: Insights on pathogenesis, intervention and future perspective. *Biomedicine & Pharmacotherapy, 193*, Article 118846. https: //doi.org/10.1016/j.biopha.2025.118846

[14] Montandon, A. S., & Jornayvaz, F. R. (2017). Effects of antidiabetic drugs on gut microbiota composition. *Genes, 8*(10), Article 250. https: //doi.org/10.3390/genes8100250

[15] Junjie, S., Fang, L., & Bing, Z. (2021). Liraglutide-induced structural modulation of the gut microbiota in patients with type 2 diabetes mellitus. *PeerJ, 9*, e11128. https: //doi.org/10.7717/peerj.11128

[16] Zhou, Y. D., Liang, F. X., & Tian, H. R. (2023). Mechanisms of gut microbiota-immune-host interaction on glucose regulation in type 2 diabetes. *Frontiers in Microbiology, 14*, Article 1121695.

[17] Shen, X., Ma, C., & Yang, Y. (2024). The role and mechanism of probiotics supplementation in blood glucose regulation: A review. *Foods, 13*(17), Article 2719. https: //doi.org/10.3390/foods13172719

[18] Zhou, X., Zheng, W., & Kong, W. (2025). Glucose parameters, inflammation markers, and gut microbiota changes of gut microbiome-targeted therapies in type 2 diabetes mellitus: A systematic review and

meta-analysis of randomized controlled trials. *The Journal of Clinical Endocrinology and Metabolism, 110*(10), 2980–3008. https: //doi.org/10.1210/clinem/dgaf340

[19] Mengyao, Y., Shuli, M., & Benyue, S. (2023). Gut-liver-brain axis in diseases: The implications for therapeutic interventions. *Signal Transduction and Targeted Therapy, 8*(1), Article 443. https: //doi.org/10.1038/s41392-023-01673-4

[20] Praveen, A. M., Parvathy, K. K., & Jayabalan, R. (2019). Dietary fiber from Indian edible seaweeds and its in vitro prebiotic effect on the gut microbiota. *Food Hydrocolloids, 96*, 343–353. https: //doi.org/10.1016/j.foodhyd.2019.05.031

[21] Sayin, S. I., Wahlström, A., & Felin, J. (2013). Gut microbiota regulates bile acid metabolism by reducing the levels of tauro-β-muricholic acid, a naturally occurring FXR antagonist. *Cell Metabolism, 17*(2), 225–235.

[22] Cani, P. D., Amar, J., & Iglesias, M. A. (2007). Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes, 56*(7), 1761–1772.

[23] Gddoa, T. S. S. A., J. W. K. A., & Abd, J. A. A. (2022). Effects of β-glucan extracted from Saccharomyces cerevisiae on the quality of bio-yoghurts: In vitro and in vivo evaluation. *Journal of Food Measurement and Characterization, 16*(5), 3607–3617. https: //doi.org/10.1007/s11694-022-01468-1

[24] Ren, X., Zhang, F. L., & Zhang, M. (2024). Fecal microbiota transplantation: Whole grain highland barley improves glucose metabolism by changing gut microbiota. *Food Science and Human Wellness, 13*(4), 2014–2024.

[25] Zhang, L. C., & Liu, Y. H. (2021). Preparation and oral bioavailability of ellagic acid phospholipids complex. *Chinese Traditional Patent Medicine, 43*(7), 1685–1690.

[26] Tremaroli, V., & Bäckhed, F. (2012). Functional interactions between the gut microbiota and host metabolism. *Nature, 489*(7415), 242–249.

[27] Elbandrawy, M. M., Sweef, O., & Elgamal, D. (2022). Ellagic acid regulates hyperglycemic state through modulation of pancreatic IL-6 and TNF-α immunoexpression. *Saudi Journal of Biological Sciences, 29*(5), 3871–3880.

[28] Tian, Y. L. (2020). *Effect and mechanism of ellagic acid and its metabolite on liver insulin resistance in diabetic mice* [Doctoral dissertation, Xinjiang Medical University].

[29] Yang, J., Guo, Y., Henning, S. M., Chan, B., Long, J., Zhong, J., Acin-Perez, R., Petcherski, A., Shirihai, O., Heber, D., & Li, Z. (2020). Ellagic Acid and Its Microbial Metabolite Urolithin A Alleviate Diet-Induced Insulin Resistance in Mice. *Molecular nutrition & food research, 64*(19), e2000091. https: //doi.org/10.1002/mnfr.202000091

[30] Bayle, M., Neasta, J., & Dall'Asta, M. (2019). The ellagitannin metabolite urolithin C is a glucose-dependent regulator of insulin secretion through activation of L-type calcium channels. *British Journal of Pharmacology, 176*(20), 4065–4078.

[31] Leng, P., Wang, Y., & Xie, M. (2025). Ellagic acid and gut microbiota: Interactions and implications for health. *Food Science & Nutrition, 13*(4), Article e70133.

[32] Abdel Moneim, A. M., & Al-Ghafari, A. B. (2017). Estimation of ellagic acid and/or repaglinide effects on insulin signaling, oxidative stress, and inflammatory mediators of liver, pancreas, adipose tissue, and brain in insulin resistant/type 2 diabetic rats. *Applied Physiology, Nutrition, and Metabolism, 42*(2), 181–192. https: //doi.org/10.1139/apnm-2016-0429

[33] Han, B., Shi, L., & Bao, M. Y. (2024). Dietary ellagic acid therapy for CNS autoimmunity: Targeting on Alloprevotella rava and propionate metabolism. *Microbiome, 12*(1), Article 114.

[34] Kang, I., Buckner, T., & Shay, N. F. (2016). Improvements in metabolic health with consumption of ellagic acid and subsequent conversion into urolithins: Evidence and mechanisms. *Advances in Nutrition, 7*(5), 961–972.

[35] Luo, C., Hou, C., & Yang, D. (2023). Urolithin C alleviates pancreatic β-cell dysfunction in type 1 diabetes by activating Nrf2 signaling. *Nutrition & Diabetes, 13*(1), Article 24.

[36] Chávez-Carbajal, A., Pizano-Zárate, M. L., & Hernández-Quiroz, F. (2021). Gut microbiota influence in type 2 diabetes mellitus (T2DM). *Gut Pathogens, 13*(1), Article 50. https: //doi.org/10.1186/s13099-021-00446-0

[37] Jin, L., Dang, H., Wu, J., Yuan, L., Chen, X., & Yao, J. (2022). Weizmannia coagulans BC2000 plus ellagic acid inhibits high-fat-induced insulin resistance by remodeling the gut microbiota and activating the hepatic autophagy pathway in mice. *Nutrients, 14*(19), Article 4206. https: //doi.org/10.3390/nu14194206

[38] Ghadimi, M., Foroughi, F., & Hashemipour, S. (2021). Decreased insulin resistance in diabetic patients by influencing sirtuin-1 and fetuin-A following supplementation with ellagic acid: A randomized controlled trial. *Diabetology & Metabolic Syndrome, 13*(1), Article 16.

[39] Wang, X., Zhou, X., & Zhang, X. (2024). Effects of ellagic acid on glucose and lipid metabolism: A systematic review and meta-analysis. *Journal of Nutrition and Metabolism, 2024*, Article 5558665.