Dean&Francis
ISSN 2959-409X

Modulation of Gut Microbiota by Traditional Chinese Medicine (TCM): A Novel Strategy for the Treatment of Metabolic Diseases

Linglonghua Zhang[1, *]

[1]Pharmacy, SHUTCM, Shanghai, China, 201203
*Corresponding author: xiaotiancaillh@163.com

Abstract:
Globally, metabolic diseases are highly prevalent, which not only compromise patients' quality of life but also impose a heavy socioeconomic burden on society. Moreover, gut microbiota dysbiosis is one of the key components in the progression of these diseases. This review focuses on the treatment of metabolic diseases through the modulation of gut microbiota by Traditional Chinese Medicine (TCM). It aims to clarify the mechanisms by which TCM improves metabolic diseases via regulating gut microbiota, as well as the interaction between TCM and gut microbiota. Additionally, this review summarizes the research evidence of TCM in treating certain metabolic diseases and outlines future research.

Keywords: gut microbiota; metabolic diseases; traditional Chinese medicine; obesity; diabetes

1. Introduction

Although a clear definition of metabolic health remains elusive to date, a considerable number of people worldwide still suffer from diseases caused by metabolic disorders, including but not limited to obesity and type 2 diabetes mellitus (T2DM) [1]. These diseases are mainly induced by high-calorie diets and sedentary lifestyles with insufficient physical activity[2], and are also associated with a degree of genetic predisposition. Taking obesity as an example, high body mass index (BMI) is a major risk factor in the 2017 Global Burden of Disease Study, and no country or sub-population has yet achieved a decline in obesity prevalence[3]. Equally seriously, complications from diabetes, which puts the health of over 400 million people at risk, claim the lives of almost 1.6 million people every year[4].

In recent years, studies have found that the gut microbiota of the human host exerts a significant impact on human metabolism[1], and gut microbiota dysbiosis is also a core link in the development of metabolic diseases (MDs). Gut microbiota can obtain energy from fermented food, and the metabolites they produce, such as short-chain fatty acids (SCFAs), bile acids (BAs), and lipopolysaccharide (LPS), are important physiological and pathological factors in metabolic diseases.

Notably, TCM exhibit unique advantages in the treatment of MDs due to their multi-component and multi-target properties, and they exert therapeutic effects through bidirectional interactions with gut microbiota. Currently, a growing number of studies have revealed the underlying mechanisms—mainly including TCM altering the composition of gut microbiota, regulating their metabolites, etc.[5]. Moreover, TCM can target and regulate gut microbiota to treat certain diseases, showing great research potential. In general, the triangular interaction model of "TCM-microbiota-host" provides a new perspective for investigating the systematic effects of TCM and the research on pathological mechanisms. This review will clarify the mechanisms by which TCM improve MDs through regulating gut microbiota and the interactions between them, comment on the research evidence of TCM in treating some MDs, and put forward future prospects based on the analysis results.

2. Interactions Between TCM and Gut Microbiota

Since most TCM are administered orally and enter the gastrointestinal tract, it is inevitable that they will encounter the gut microbiota [6], suggesting that they may interact with each other.

2.1 Regulatory Effects of TCM and Their Bioactive Components on Gut Microbiota

2.1.1 Bioactive Components of TCM

There are thousands of TCM species, and the bioactive components in commonly used TCM—such as flavonoids, alkaloids, terpenoids, polysaccharides, and quinones—play critical roles in treating and alleviating diseases. Flavonoids with gut microbiota-regulating effects include baicalein, naringenin, and hydroxysafflor yellow A[5]; alkaloids include berberine and trigonelline[7]; polysaccharides include Astragalus polysaccharides and Ganoderma lucidum polysaccharides[7]; and terpenoids include geniposide and ginsenoside Rg3[5]. These components simultaneously affect the composition and metabolites of the microbiota.

2.1.2 Regulation of Microbiota Composition and Structure

TCM can restore microbiota balance by promoting the proliferation of beneficial bacteria and inhibiting the abundance of pathogenic bacteria. For promotion, some components like flavonoids, can act as prebiotics to stimulate the growth of certain gut microbial populations[5]. For inhibition, anthraquinone-glycoside preparation from rhubarb (RAGP) can diminish the abundance of endotoxin-producing bacteria[7]; berberine, on the other hand, can lower the quantity of bacteria that generate branched-chain amino acids. (e.g., Streptococcaceae) to improve insulin resistance[5].

What's more, Feng et al.[5] reclassified these effects into direct effects and indirect effects. Based on previous classifications, direct effects include an additional „elimination" category—many TCM compounds exhibit antimicrobial activity. Indirect effects are manifested as follows: altering intestinal pH and transit time, thereby affecting gut microbiota abundance, enzyme activity, and metabolic activities (e.g., SCFA production rates); inducing the host to secrete antimicrobial peptides to regulate microbiota composition; and so on.

2.1.3 Regulation of Microbiota Metabolic Activities

TCM can modulate the types and concentrations of gut microbiota-derived metabolites by influencing the enzyme activity or metabolic pathways of the microbiota. Extracts of *Trametes versicolor* can significantly increase the activities of β-galactosidase and β-glucosidase in gut microbiota, promoting the fermentative metabolism of carbohydrates and enhancing the production of beneficial metabolites such as SCFAs [5].

In terms of TCM regulating key metabolites of gut microbiota, the first is promoting SCFA production: studies have shown that hydroxysafflor yellow A can enrich SCFA-producing bacteria such as *Butyricimonas*, thereby regulating

ISSN 2959-409X

energy metabolism[5]. The second is regulating bile acid (BA) metabolism: *Scutellaria baicalensis* promotes bile acid deconjugation and excretion by increasing the abundance of Lactobacillus that produce bile salt hydrolase (BSH) [8]; the combination of *Astragalus membranaceus* and leeches can increase the content of deoxycholic acid (a secondary bile acid) by regulating gut microbiota metabolism, thereby modulating glucose and lipid metabolism[5]. In addition, some TCM can inhibit the production of the harmful metabolite trimethylamine-N-oxide (TMAO) and regulate anti-inflammatory metabolites such as indole derivatives.

2.2 TCM Compatibility and Gut Microbiota

However, TCM do not exert effects through a single component; instead, the synergistic effects of multiple components and their interaction networks often need to be considered. After compatibility, TCM can exhibit synergistic effects, toxicity attenuation, or mitigation of side effects, which can guide its application in gut microbiota regulation.

Taking synergistic effect as an example. Studies by Zhong et al.[9] have shown that the combination of Moutan Cortex and Paeoniae Radix Rubra can effectively regulate the gut microbiota in high-fat diet (HFD)-fed mice. This combination can decrease the abundance of *Mucispirillum* while increasing the populations of *Anaerotruncus* and *Flavonifractor*, and its regulatory effect is similar to that of metformin (MET). Moreover, it can reverse the overall structural imbalance of gut microbiota induced by HFD and restore the microbiota structure to that of normal mice, suggesting that it exerts a protective effect on gut microbiota function.

2.3 Specific Mechanisms of TCM Exerting Effects via Gut Microbiota

2.3.1 Core Mechanisms

The mechanisms by which traditional Chinese medicine treats metabolic diseases through regulating the gut microbiota are often reflected in protecting the intestinal barrier, modulating endotoxins, and regulating the neuroendocrine function[8].

The integrity of the intestinal barrier affects metabolic status. TCM such as *Ganoderma lucidum* can improve metabolism by upregulating the expression of tight junction proteins (ZO-1) and mucin proteins (Muc-1, Muc-5), enhancing the mechanical barrier[8]. Certain intestinal microorganisms (e.g., *Akkermansia muciniphila*) promote mucus secretion and tight junction assembly by binding to Toll-like receptor 2 (TLR2), while some TCM formulas can enrich this bacterium[8], thereby regulating microbiota-epithelial interactions.

Endotoxemia caused by lipopolysaccharide (LPS) entering the bloodstream and other chronic inflammatory responses are also driving factors for the occurrence and progression of metabolic diseases. They damage the intestinal barrier, impair metabolic organs, exacerbate insulin resistance, and continuously promote metabolic disorders. Some TCM diminish LPS production by decreasing the abundance of Gram-negative bacteria (e.g., *Escherichia coli, Desulfovibrio*). For instance, *Scutellaria baicalensis* and berberine can both lower LPS levels by regulating gut microbiota structure. TCMs can inhibit inflammatory pathways such as TLR4/NF-κB and JNK1/p38 MAPK to reduce the expression of proinflammatory cytokines (e.g., tumor necrosis factor-α (TNF-α), IL-6, IL-1β); at the same time, they promote the proliferation of regulatory T cells (Treg) and increase the release of the anti-inflammatory cytokine IL-10 to alleviate systemic inflammation [8]. For example, *Ganoderma lucidum* alleviates LPS-induced chronic inflammation by reducing the number of M1 macrophages and downregulating key proteins in inflammatory pathways (e.g., TLR4, MyD88)[8].

In terms of the gut-brain axis, TCM promote the secretion of glucagon-like peptide-1 (GLP-1) and peptide tyrosine-tyrosine (PYY) by enteroendocrine cells via gut microbiota. These two substances act on the hypothalamus through the bloodstream to inhibit appetite. For example, berberine upregulates the hypothalamic POMC gene via gut microbiota to reduce food intake[8].

2.3.2 Systemic Regulation Mediated by Metabolites

SCFAs exhibit pleiotropic effects. SCFAs mainly include acetate, propionate, and butyrate, and their functions cover multiple dimensions such as maintaining intestinal homeostasis, exerting immunomodulatory and anti-inflammatory effects. First, SCFAs can regulate glucose and lipid metabolism, improving insulin resistance and dyslipidemia. For example, SCFAs (especially propionate and butyrate) can activate G protein-coupled receptors in intestinal epithelial cells, stimulating enteroendocrine L cells to secrete GLP-1 and PYY; GLP-1 can activate GLP-1 receptors on pancreatic β cells to promote insulin secretion, while inhibiting glucagon release to lower blood glucose [5],[6]. Second, SCFAs protect intestinal barrier integrity; for instance, butyrate, as the main energy source for colonic epithelial cells, can promote the proliferation and differentiation of intestinal epithelial cells, increasing villus height and crypt depth [5],[8].

The bile acid-cholesterol metabolic axis is a key regulatory pathway for the homeostasis of glucose and lipid metabolism in the human body, with core links as follows: the liver synthesizes bile acids utilizing cholesterol as a raw material, with cholesterol 7α-hydroxylase (CYP7A1) as the rate-limiting enzyme; bile acids enter the enterohepatic circulation; gut microbiota catalyzes the deconjugation of conjugated bile acids via BSH to generate „free bile acids“ (low water solubility, easily excreted with feces), thereby regulating bile acid excretion efficiency; bile acids inversely regulate metabolism through the nuclear receptor FXR (regulating bile acid synthesis and reabsorption) and the membrane receptor TGR5 (regulating insulin sensitivity and energy metabolism). TCM play important roles in these links, such as berberine, which can upregulate CYP7A1[8].

2.4 Effects of Gut Microbiota on Traditional Chinese Medicines (TCMs)

Conversely, gut microbiota can also transform TCM components through reactions such as enzymatic hydrolysis, oxidation, and reduction, thereby modulating the bioavailability and bioactivity of TCMs. After partial transformation by gut microbiota, higher bioavailability gives some components better therapeutic effects. For instance, the intestinal flora metabolizes ellagitannins into urolithins (urolithins A–D); due to their higher lipophilicity (owing to a reduced number of hydroxyl groups in the molecule), urolithins are more easily absorbed[10]. Another example is baicalin: when transformed into baicalein by β-glucuronidase produced by gut microbiota, it exhibits enhanced anti-inflammatory activity[5].

To a certain extent, gut microbiota can also reduce the toxicity of TCMs. For example, the toxic diester-diterpenoid aconitine in *Aconitum carmichaeli* Debx (Fuzi) is converted into low-toxicity monoester-type/non-ester-type alkaloids by gut microbiota through reactions like deacylation and esterification. The oral LD_{50} of monoester-type alkaloids in mice ranges from 0.81 to 1.50 g/kg, which is much higher than the 1.0–1.8 mg/kg of aconitine. This transformation reduces its toxicity to the nervous and cardiovascular systems[11].

3. Research Status of TCM in Treating some Types of MDs

3.1 Obesity

Gut microbiota homeostasis dysbiosis is a key factor in the development of obesity. Its structural abnormalities (e.g., increased Firmicutes/Bacteroidetes ratio, decreased abundance of beneficial bacteria such as *Akkermansia*) and metabolic disorders (reduced SCFAs, increased lipopolysaccharide (LPS)) contribute to exacerbating obesity via energy metabolism, immune inflammation, and the brain-gut-microbiota axis[12].

TCMs can regulate gut microbiota against obesity through multiple pathways. For example, herbal formulae like Shengmai San (SMS) can reduce BSH-producing *Lactobacillus*, increase conjugated bile acids (e.g., Taurocholic Acid (TCA)), promote M2 macrophage polarization and thermogenesis, and finally improve glucose and lipid metabolism[13].

The core mechanisms lie in remodeling microbiota homeostasis, regulating microbiota metabolites, and inter-

ISSN 2959-409X

fering with host energy metabolism, insulin sensitivity, and intestinal barrier function. These mechanisms provide important directions for the treatment of obesity.

3.2 T2DM

Clinical evidence supporting the improvement of T2DM by TCM via gut microbiota modulation is increasingly abundant. In a rat model of T2DM, Jiantang Sanhuang Wan (JTSH) increased the abundance of gut microbiota with BSH activity, such as *Bacteroides, Lactobacillus*. This upregulation contributed to the accumulation of unconjugated bile acids in the ileum, thereby activating the intestinal farnesoid X receptor (FXR)/fibroblast growth factor 15 (FGF15) and G protein-coupled bile acid receptor 5 (TGR5)/glucagon-like peptide-1 (GLP-1) signaling pathways. Consequently, JTSH significantly reduced hyperglycemia, insulin resistance, and dyslipidemia[14].

In KKay diabetic mice, high-dose Qijian Mixture (QJM) reduced fasting blood glucose (FBG), improved oral glucose tolerance (OGTT), and decreased total cholesterol (TC). It modulated gut microbiota structure by enriching the phylum Bacteroidetes and reducing the proportion of Firmicutes, with its effects associated with pathways such as galactose metabolism and branched-chain amino acid degradation. The hypoglycemic trend of QJM was also similar to that of MET[15].

These studies confirm that TCM provides a safe and effective therapeutic strategy for T2DM by reshaping gut microbiota balance, regulating microbiota metabolites, and modulating signaling pathways.

3.3 Non-alcoholic Fatty Liver Disease (NAFLD)

NAFLD, which was renamed metabolic dysfunction-associated fatty liver disease (MAFLD) in 2020, refers to steatosis in hepatocytes (NAFL), or requiring the concurrent presence of steatosis, hepatocyte ballooning, and so on (NASH). NASH can lead to more severe liver lesions [17]. Currently, approximately 25% of the global adult population is affected by NAFLD, and its incidence has increased significantly since its identification [18].

In NAFLD, alterations occur in gut microbiota (e.g., phyla Proteobacteria, Actinobacteria, and Bacteroidetes). Additionally, the expression of genes encoding tight junction proteins is downregulated by these microorganisms, leading to impaired intestinal barrier function and induced inflammatory responses, which ultimately accelerate the progression of NAFLD and liver fibrosis[19]. Modulation of gut microbiota by TCM, however, offers a therapeutic strategy for this disease.

The therapeutic application of TCM for NAFLD based on gut microbiota is grounded in the „gut-microbiota-liver“ axis theory—a complex network that connects the gut and liver through microorganisms. Recent studies have demonstrated that TCM formulae with different efficacy profiles, TCM monomers, and single TCM herbs can significantly improve NAFLD-related indicators and symptoms[20]. For example, Simiao Wan increases the abundance of *Akkermansia muciniphila*, repairs the intestinal barrier, and improves lipid metabolism; berberine reconstructs gut microbiota structure, activates the bile acid/FXR signaling pathway, and ameliorates hepatic lipid metabolism and inflammation[19].

3.4 Cardiometabolic Diseases (CMD)

CMD, which encompasses cardiovascular disease (CVD) and diabetes, places substantial burden on healthcare systems[21]. Among CVDs, studies have shown that patients with cardiovascular diseases also exhibit gut microbiota dysbiosis: In patients with ischemic heart failure, genes involved in lipopolysaccharide (LPS) and TMAO(a key metabolites produced by the gut microbiota) biosynthesis are enriched[1]; In individuals with atherosclerosis, the abundance of inflammation-associated microbiota (e.g., *Acidaminococcus*) increases, accompanied by elevated TMAO levels[22].

Traditional Chinese Medicines (TCM) can regulate gut microbiota to prevent and treat CVD. For example, Qingxin-Jieyu Granules alleviate atherosclerosis by increasing the abundance of *Turicibacter* and *Roseburia* and reducing serum TMAO levels[23]; Qili Qiangxin Capsules can modulate the gut microbiota in HF rats, inhibit the NLRP3 inflammasome, and protect cardiac function; Si

Junzi Decoction improves gut microbiota dysbiosis in HF rats induced by cardiac hypertrophy and alleviates myocardial injury[24].

These TCM exert cardiovascular protective effects by optimizing gut microbiota and its metabolism, protecting the intestinal barrier, and alleviating inflammation.

4. Summary and Limitations

Focusing on globally prevalent and clinically impactful metabolic diseases, this review summarizes the research progress of TCM in treating these diseases by regulating the gut microbiota. It aims to clarify the triangular interaction model of „TCM-gut microbiota-host“ and its related mechanisms, providing new perspectives and a theoretical basis for the clinical intervention of metabolic diseases.

Regarding the bidirectional interaction between TCM and gut microbiota, this review analyzes and points out that there is a close bidirectional regulation between the two: TCM can regulate the gut microbiota through their bioactive components, while the gut microbiota can transform TCM components through reactions such as enzymatic hydrolysis, thereby enhancing the bioavailability of TCM or reducing their toxicity.

In terms of the core mechanisms, this review discusses five key pathways: 1) protecting intestinal barrier integrity; 2) improving metabolic endotoxemia and inflammation; 3) mediating systemic regulation via metabolites; 4) regulating neuroendocrine function through the gut-brain axis to inhibit appetite or improve energy balance; and 5) modulating the immunometabolic network.

Regarding the research status of TCM in treating specific metabolic diseases, this review sorts out abundant research evidence on several types of metabolic diseases. All these studies confirm that TCM can provide safe and effective therapeutic strategies for metabolic diseases by reshaping gut microbiota structure, regulating microbiota metabolites, and modulating related signaling pathways.

However, the research in this review still has limitations. The number of studies included in this review is limited, and clinical evidence in humans is weak. Currently, most studies only observe associations between TCM and gut microbiota (e.g., baicalin increases SCFA levelsbut lack verification of causality via fecal microbiota transplantation (FMT) or germ-free animal models [5]. Heterogeneity in individual gut microbiota typing and metabolic enzyme activity leads to variable therapeutic effects of TCM. Moreover, the synergistic mechanism of multi-components in TCM formulae remains unclear, making it difficult to establish a „component-microbiota-therapeutic effect“ relationship[7].

References

[1] Fan, Y., & Pedersen, O. (2021). Gut microbiota in human metabolic health and disease. Nature reviews. Microbiology, 19(1), 55–71. https://doi.org/10.1038/s41579-020-0433-9

[2] Agus, A., Clément, K., & Sokol, H. (2021). Gut microbiota-derived metabolites as central regulators in metabolic disorders. Gut, 70(6), 1174–1182. https://doi.org/10.1136/gutjnl-2020-323071

[3] Jaacks, L. M., Vandevijvere, S., Pan, A., McGowan, C. J., Wallace, C., Imamura, F., Mozaffarian, D., Swinburn, B., & Ezzati, M. (2019). The obesity transition: stages of the global epidemic. The lancet. Diabetes & endocrinology, 7(3), 231–240. https://doi.org/10.1016/S2213-8587(19)30026-9

[4] Schumann, T., König, J., Henke, C., Willmes, D. M., Bornstein, S. R., Jordan, J., Fromm, M. F., & Birkenfeld, A. L. (2020). Solute Carrier Transporters as Potential Targets for the Treatment of Metabolic Disease. Pharmacological reviews, 72(1), 343–379. https://doi.org/10.1124/pr.118.015735

[5] Feng, W., Ao, H., Peng, C., & Yan, D. (2019). Gut microbiota, a new frontier to understand traditional Chinese medicines. Pharmacological research, 142, 176–191. https://doi.org/10.1016/j.phrs.2019.02.024

[6] Zhou W.J., Yang W.R., Liu X.F., Xu X.R., Fan X &X Y.L. (2025). Research progress of interaction between traditional Chinese medicine and intestinal flora in disease treatment. Chinese Herbal Medicine, 56(11),4080-4089.

[7] Yue, S. J., Wang, W. X., Yu, J. G., Chen, Y. Y., Shi, X. Q., Yan, D., Zhou, G. S., Zhang, L., Wang, C. Y., Duan, J. A., & Tang, Y. P. (2019). Gut microbiota modulation with

ISSN 2959-409X

traditional Chinese medicine: A system biology-driven approach. Pharmacological research, 148, 104453. https://doi.org/10.1016/j.phrs.2019.104453
[8] Zhang, H. Y., Tian, J. X., Lian, F. M., Li, M., Liu, W. K., Zhen, Z., Liao, J. Q., & Tong, X. L. (2021). Therapeutic mechanisms of traditional Chinese medicine to improve metabolic diseases via the gut microbiota. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie, 133, 110857. https://doi.org/10.1016/j.biopha.2020.110857
[9] Zhong, L. J., Xie, Z. S., Yang, H., Li, P., & Xu, X. J. (2017). Moutan Cortex and Paeoniae Radix Rubra reverse high-fat-diet-induced metabolic disorder and restore gut microbiota homeostasis. Chinese journal of natural medicines, 15(3), 210–219. https://doi.org/10.1016/S1875-5364(17)30037-7
[10] Espín, J. C., González-Barrio, R., Cerdá, B., López-Bote, C., Rey, A. I., & Tomás-Barberán, F. A. (2007). Iberian pig as a model to clarify obscure points in the bioavailability and metabolism of ellagitannins in humans. Journal of agricultural and food chemistry, 55(25), 10476–10485. https://doi.org/10.1021/jf0723864
[11] Feng, W., Liu, J., Huang, L., Tan, Y., & Peng, C. (2021). Gut microbiota as a target to limit toxic effects of traditional Chinese medicine: Implications for therapy. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie, 133, 111047. https://doi.org/10.1016/j.biopha.2020.111047
[12] Zhang, Q., Bai, Y., Wang, W., Li, J., Zhang, L., Tang, Y., & Yue, S. (2023). Role of herbal medicine and gut microbiota in the prevention and treatment of obesity. Journal of ethnopharmacology, 305, 116127. https://doi.org/10.1016/j.jep.2022.116127
[13] Wang, Z., Wang, X., Fu, L., Xu, S., Wang, X., Liao, Q., Zhuang, T., Liu, L., Zhang, H., Li, W., Xiong, A., Gu, L., Wang, Z., Wang, R., Tao, F., Yang, L., & Ding, L. (2024). Shengmai San formula alleviates high-fat diet-induced obesity in mice through gut microbiota-derived bile acid promotion of M2 macrophage polarization and thermogenesis. Phytomedicine : international journal of phytotherapy and phytopharmacology, 133, 155938. https://doi.org/10.1016/j.phymed.2024.155938
[14] Tawulie, D., Jin, L., Shang, X., Li, Y., Sun, L., Xie, H., Zhao, J., Liao, J., Zhu, Z., Cui, H., & Wen, W. (2023). Jiang-Tang-San-Huang pill alleviates type 2 diabetes mellitus through modulating the gut microbiota and bile acids metabolism. Phytomedicine : international journal of phytotherapy and phytopharmacology, 113, 154733. https://doi.org/10.1016/j.phymed.2023.154733
[15] Gao, K., Yang, R., Zhang, J., Wang, Z., Jia, C., Zhang, F., Li, S., Wang, J., Murtaza, G., Xie, H., Zhao, H., Wang, W., & Chen, J. (2018). Effects of Qijian mixture on type 2 diabetes assessed by metabonomics, gut microbiota and network pharmacology. Pharmacological research, 130, 93–109. https://doi.org/10.1016/j.phrs.2018.01.011
[16] Nie, Q., Chen, H., Hu, J., Fan, S., & Nie, S. (2019). Dietary compounds and traditional Chinese medicine ameliorate type 2 diabetes by modulating gut microbiota. Critical reviews in food science and nutrition, 59(6), 848–863. https://doi.org/10.1080/10408398.2018.1536646
[17] European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), & European Association for the Study of Obesity (EASO) (2016). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. Journal of hepatology, 64(6), 1388–1402. https://doi.org/10.1016/j.jhep.2015.11.004
[18] Clayton-Chubb, D., Kemp, W., Majeed, A., Lubel, J. S., Hodge, A., & Roberts, S. K. (2023). Understanding NAFLD: From Case Identification to Interventions, Outcomes, and Future Perspectives. Nutrients, 15(3), 687. https://doi.org/10.3390/nu15030687
[19] Zhu, L. R., Li, S. S., Zheng, W. Q., Ni, W. J., Cai, M., & Liu, H. P. (2023). Targeted modulation of gut microbiota by traditional Chinese medicine and natural products for liver disease therapy. Frontiers in immunology, 14, 1086078. https://doi.org/10.3389/fimmu.2023.1086078
[20] Du Y.S., Luo L, Han B.W., Qin H.J., Lu Y.N., & D. Z.Q. (2025). Based on the “gut-microflora-liver” axis, this paper discusses the research progress of traditional Chinese medicine in regulating intestinal flora to treat nonalcoholic fatty liver disease. Shaanxi Traditional Chinese Medicine, 46(06),857-860.
[21] Tahir, U. A., & Gerszten, R. E. (2023). Molecular Biomarkers for Cardiometabolic Disease: Risk Assessment in Young Individuals. Circulation research, 132(12), 1663–1673. https://doi.org/10.1161/CIRCRESAHA.123.322000

[22] Chen, X., Zhang, H., Ren, S., Ding, Y., Remex, N. S., Bhuiyan, M. S., Qu, J., & Tang, X. (2023). Gut microbiota and microbiota-derived metabolites in cardiovascular diseases. Chinese medical journal, 136(19), 2269–2284. https://doi.org/10.1097/CM9.0000000000002206

[23] Dai, J., Qiu, L., Lu, Y., & Li, M. (2024). Recent advances of traditional Chinese medicine against cardiovascular disease: overview and potential mechanisms. Frontiers in endocrinology, 15, 1366285. https://doi.org/10.3389/fendo.2024.1366285

[24] Cui, H., Han, S., Dai, Y., Xie, W., Zheng, R., Sun, Y., Xia, X., Deng, X., Cao, Y., Zhang, M., & Shang, H. (2023). Gut microbiota and integrative traditional Chinese and western medicine in prevention and treatment of heart failure. Phytomedicine : international journal of phytotherapy and phytopharmacology, 117, 154885. https://doi.org/10.1016/j.phymed.2023.154885