

**Mechanistic Study of Zuogui Jiangtang Shuluo Formula in  
Regulating Lipid Metabolism and Inhibiting Ferroptosis for  
the Prevention and Treatment of Diabetic Peripheral  
Neuropathy**

**Research program**

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## 1 Background

As the global prevalence of diabetes continues to rise, the prevention and management of diabetic complications have become a major public health challenge. Diabetic peripheral neuropathy (DPN), a common chronic complication of type 2 diabetes mellitus (T2DM), can affect 35%–50% of patients with diabetes<sup>[1]</sup>. The onset and progression of neuropathy in patients with T2DM are closely associated with factors such as disease duration, glycemic control, obesity, insulin resistance, and chronic low-grade inflammation; patients with a disease duration exceeding 10 years are more likely to develop significant neuropathic symptoms, such as limb pain, numbness, or sensory abnormalities. Among these, diabetic distal symmetric polyneuropathy (DSPN) is the most representative form, characterized primarily by distal symmetric polyneuropathy, manifesting mainly as abnormal symptoms including distal limb pain, numbness, and reduced sensation; in severe cases, ulceration, gangrene, or even amputation may occur, imposing substantial economic and psychological burdens on affected patients<sup>[2]</sup>.

The pathogenesis of DSPN remains incompletely elucidated; current prevailing hypotheses suggest that it arises from metabolic disturbances induced by hyperglycemia, dyslipidemia, and insulin resistance, specifically, through the activation of the polyol pathway, accumulation of advanced glycation end products (AGEs), aberrant neural lipid signaling, and oxidative stress and inflammation triggered by lipid peroxidation, all of which ultimately lead to irreversible damage in neurons, glial cells, vascular endothelial cells, and other tissues<sup>[3-5]</sup>. In recent years, rapid advancements in multi-omics research technologies have provided researchers with novel approaches and methodologies for investigating the underlying mechanisms of DSPN at the molecular level<sup>[6,7]</sup>. Previous studies have confirmed significant alterations in serum metabolites and lipid profiles among patients with clinical DSPN<sup>[8]</sup>. For instance, differential metabolites such as  $\beta$ -alanine and hexanoic acid exhibit marked variations across mild, moderate, and severe DSPN patients, while lipid metabolites, including triglycerides, phosphatidylcholine, sphingomyelin, and ceramide, may also serve as potential biomarkers for DSPN<sup>[9,10]</sup>.

Currently, the treatment of DSPN in modern medicine primarily focuses on neurotrophic therapy, antioxidant stress mitigation, and microcirculation improvement; surgical intervention is considered only when necessary. The therapeutic approaches and pharmacological regimens employed are relatively limited, with drug side effects, potential dependence, and surgical risks exacerbating the psychological burden on

patients<sup>[11]</sup>. In contrast, Traditional Chinese Medicine (TCM) offers not only superior safety profiles and minimal adverse effects but also provides a broader spectrum of internal and external therapeutic modalities, thereby expanding treatment options for patients.

DSPN falls within the categories of "consumptive thirst complicated with vessel impediment" (Xiaoke Maibi), "sinew impediment" (Jinbi), "arthralgia syndrome" (Bizheng), and "flaccidity syndrome" (Weizheng) in TCM, and is considered a collateral disorder secondary to consumptive thirst (Xiaoke) disease. Based on long-term clinical observation and literature review, combined with the TCM pattern characteristics of DSPN, the principal investigator proposes that the core pathogenesis is Qi-Yin deficiency with blood stasis obstructing the collaterals. Prolonged consumptive thirst disease leads to Yin deficiency with internal heat, which consumes body fluids and transforms them into blood stasis. Blood stasis then obstructs the collaterals, blocking the vessels of the limbs, resulting in "pain due to obstruction" (Butong Ze Tong). Furthermore, the prolonged course of consumptive thirst consumes the body's vital Qi, and Qi deficiency fails to generate blood and nourish Yin, resulting in malnourishment of the muscles, sinews, and vessels, leading to "pain due to lack of nourishment" (Butong Ze Tong). This manifests clinically as limb numbness, pain, and paresthesia.

The therapeutic principle is to nourish Yin, supplement Qi, activate blood circulation, and unblock the collaterals, with Zuogui Jiangtang Shuluo Formula (ZGJTSLF) as the primary prescription. This formula was modified and developed from the Jiangtang Shuluo Formula originally established by Professor Chen Dashun at Hunan University of Traditional Chinese Medicine<sup>[12]</sup>. It is composed of ten Chinese medicinal herbs: *Astragalus membranaceus* (Huangqi), *Rehmannia glutinosa* (Shengdihuang), *Coptis chinensis* (Huanglian), *Dioscorea opposita* (Shanyao), *Pueraria lobata* (Gegen), *Cornus officinalis* (Shanzhuyu), *Spatholobus suberectus* (Jixueteng), *Pheretima* (Dilong), *Smilax china* (Baqia), and *Tribulus terrestris* (Cijili). The formula addresses both the root and the branch: it nourishes Yin, supplements Qi, and replenishes the source of Qi and blood to treat the root, while activating blood circulation, resolving stasis, extinguishing wind, and unblocking collaterals to treat the branch. Previous clinical studies have shown that Jiangtang Shuluo Formula can effectively improve TCSS scores and nerve conduction velocity in DSPN patients compared with mecobalamin, and ZGJTSLF has demonstrated significant clinical efficacy in treating DSPN. However, high-level evidence-based medical evidence is still lacking.

## **2. Method**

### **2.1 Trial overview, ethical consideration, and patient recruitment**

This study is a single-center, randomized, parallel-controlled clinical trial. The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Hunan University of Chinese Medicine (Approval No. HN-LL-YJSLW-2026-06) in accordance with the Declaration of Helsinki and relevant ethical standards. Written informed consent will be obtained from all participants prior to enrollment.

The study is currently being conducted at the First Affiliated Hospital of Hunan University of Chinese Medicine and involves three groups of participants: a healthy control group, a diabetic distal symmetric polyneuropathy (DSPN) treatment group receiving Zuogui Jiangtang Shuluo Formula, and a DSPN control group receiving mecobalamin. Subjects will be recruited from inpatients and outpatients of the Department of Endocrinology at the First Affiliated Hospital of Hunan University of Chinese Medicine. Additionally, healthy subjects will be recruited from the general public through advertisements and invitations. The total number of individuals proposed to be recruited is approximately 100, with 37 DSPN patients in each of the two DSPN groups (treatment and control).

### **2.2 Study outcomes**

#### **Primary outcome:**

To evaluate the clinical efficacy and safety of Zuogui Jiangtang Shuluo Formula in the treatment of diabetic peripheral neuropathy, as measured by changes in Traditional Chinese Medicine (TCM) syndrome scores, Toronto Clinical Neuropathy Score (TCSS), and nerve conduction velocity from baseline to post-treatment (Week 4).

#### **Secondary outcome:**

To assess changes in painful diabetic sensorimotor polyneuropathy (DSPN) using the Douleur Neuropathique 4 (DN4) questionnaire and Visual Analogue Scale (VAS); to evaluate alterations in the ankle-brachial index (ABI); and to examine changes in glucolipid metabolic markers including fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).

#### **Exploratory outcome:**

To explore the metabolomic and lipidomic profiles associated with DSPN and the therapeutic response to Zuogui Jiangtang Shuluo Formula. In accordance with the omics results, integrated bioinformatic analyses of differential metabolites and lipid species will be conducted to elucidate the potential pathways through which Zuogui Jiangtang Shuluo Formula regulates lipid metabolism and inhibits Schwann cell ferroptosis, thereby providing mechanistic insights into its protective effects against DSPN.

### **2.3 Study population**

This study primarily recruits healthy individuals and patients with type 2 diabetic peripheral neuropathy.

#### **2.3.1 Inclusion criteria**

##### **DSPN patient inclusion criteria**

Subjects who meet all of the following criteria are eligible for enrollment in the DSPN groups:

- (1) Meet the diagnostic criteria for type 2 diabetes mellitus with distal symmetric polyneuropathy (DSPN) according to Western medicine standards.
- (2) Meet the TCM syndrome differentiation criteria for consumptive thirst complicated with arthromyodynia of the pattern of Qi-Yin deficiency with blood stasis.
- (3) Glycated hemoglobin (HbA1c) between 6.5% and 9.0% (inclusive).
- (4) Aged 35 to 75 years (inclusive) at the time of screening, regardless of gender.
- (5) Have not participated in any other clinical trial within 2 weeks prior to the start of treatment, and have not taken lipid-lowering agents, antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, immunosuppressants, or other traditional Chinese medicines that may affect metabolomic and lipidomic profiles.
- (6) Willing to voluntarily participate in the trial and adhere to the 4-week traditional Chinese medicine treatment regimen.
- (7) Right-handed.
- (8) Provide written informed consent and are able to understand and comply with the study protocol requirements, including dietary and exercise recommendations and blood glucose monitoring.

**Healthy population inclusion criteria**

Subjects who meet all of the following criteria are eligible for enrollment in the healthy control group:

- (1) Aged 18 to 55 years (inclusive) at the time of screening, regardless of gender.
- (2) Body mass index (BMI) within the range of 19.0 to 26.0 kg/m<sup>2</sup> (inclusive).
- (3) No severe diseases of the heart, liver, kidney, cerebrovascular system, or malignant tumors; routine laboratory tests, electrocardiogram, and chest X-ray are essentially within normal limits.
- (4) Have not participated in any other clinical trial within 2 weeks prior to the start of treatment, and have not taken lipid-lowering agents, antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, immunosuppressants, or other traditional Chinese medicines that may affect metabolomic and lipidomic profiles.
- (5) Voluntarily sign the informed consent form and are willing and able to cooperate with the investigators to complete the clinical study.

**2.3.2 Exclusion criteria****DSPN exclusion criteria**

subjects meeting any of the following criteria will be excluded:

- (1) Patients with type 1 diabetes mellitus or other specific types of diabetes mellitus.
- (2) Women who are pregnant, breastfeeding, planning pregnancy, or taking oral contraceptives long-term.
- (3) Neuropathies caused by other conditions, including but not limited to multiple sclerosis, Parkinson's disease, Guillain-Barré syndrome, epilepsy, spinal cord injury, cervical or lumbar spine lesions (nerve root compression, spinal stenosis, cervical or lumbar degenerative diseases), neuromuscular diseases, severe arterial or venous vascular diseases (venous thrombosis, lymphangitis, etc.), sequelae of cerebrovascular disease, or post-surgical status of lower extremity vasculature.
- (4) History of stroke, transient ischemic attack, unstable angina, or myocardial infarction within 3 months prior to study enrollment.
- (5) History of acute diabetic complications (diabetic ketoacidosis, lactic acidosis, or hyperosmolar hyperglycemic state) within 3 months prior to study enrollment.

(6) Concomitant severe complications of diabetes, such as end-stage diabetic kidney disease, or proliferative diabetic retinopathy.

(7) Concomitant severe diseases of the heart, liver, kidney, cerebrovascular system, or malignant tumors, defined as serum creatinine  $>200 \mu\text{mol/L}$ , blood urea nitrogen  $>1.5$  times the upper limit of normal, or alanine aminotransferase or aspartate aminotransferase  $>3$  times the upper limit of normal.

(8) Any infection that, in the investigator's opinion, makes the patient unsuitable for participation prior to study enrollment, including but not limited to urinary tract infection, respiratory infection, or diabetic foot with infection requiring further treatment.

(9) Patients with psychiatric disorders, cognitive impairment, or inability to cooperate with the study procedures; or individuals with a history of alcohol abuse or drug addiction.

### **Healthy subject exclusion criteria**

subjects meeting any of the following criteria will be excluded:

(1) Women who are planning pregnancy, pregnant, or lactating, and female patients on long-term oral contraceptives.

(2) Individuals with mental illness or cognitive impairment who are unable to cooperate.

(3) Individuals with a history of alcohol abuse or drug addiction.

### **2.3.3 Withdrawal criteria**

Subjects may withdraw from the study at any time without prejudice to their medical care. The investigator may also withdraw a subject if continued participation is deemed to pose a risk to the subject's health, if the subject develops significant protocol deviations, or if the subject's compliance is  $< 80\%$  or  $> 120\%$  (calculated as  $\text{actual dose taken} / \text{prescribed dose} \times 100\%$ ). All withdrawals will be documented with the reason. For subjects who withdraw due to adverse events, follow-up will be continued until the event resolves or stabilizes.

### **2.3.4 Termination criteria**

The trial may be terminated prematurely if serious safety concerns arise, if significant flaws in the study design are identified that preclude meaningful evaluation of the

intervention, or if major deviations in protocol implementation occur that would compromise data integrity.

## **2.4 Study procedures**

### **2.4.1 Questionnaire to collect information**

The following information will be collected from all subjects (healthy controls and DPN patients) upon enrollment:

- (1) Demographic data: sex, age, height, weight, body mass index (BMI), and waist circumference.
- (2) General clinical data (DPN group only): duration of diabetes, duration of diabetic neuropathy, other diabetic complications (diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy), concomitant diseases (hypertension, coronary artery disease, hyperlipidemia, cerebrovascular disease, hyperuricemia), past medical history, history of smoking and alcohol consumption, family history, and medication history.
- (3) TCM symptoms, tongue and pulse assessment (DPN group only).
- (4) Education level, labor intensity, and dietary preferences.

### **2.4.2 Outcome measures**

#### **Safety indicators:**

Physical examination (including general condition, blood pressure, heart rate, heart rhythm, body temperature, and respiratory rate) will be performed prior to sample collection to assess the basic condition of all subjects. Additionally, blood routine, liver function, renal function, and electrocardiogram (ECG) will be assessed in DPN patients. Any adverse events will be documented in detail, including clinical manifestations, severity, abnormal laboratory findings, management measures, and time course, to provide a basis for objective safety evaluation.

#### **Primary outcome measures:**

**(1) TCM syndrome score:** Based on the Guiding Principles for Clinical Research of New Chinese Medicine Drugs and the Clinical Diagnosis and Treatment Guidelines for Diabetic Peripheral Neuropathy in Traditional Chinese Medicine (2016 edition), a TCM syndrome scoring scale has been developed. For all DPN patients, the primary symptoms (limb weakness, limb pain, and/or numbness) are graded as absent, mild, moderate, or severe and assigned scores of 0, 2, 4, and 6, respectively. The secondary symptoms (fatigue, shortness of breath, spontaneous sweating, night sweating, vexing

heat in the chest, palms and soles, soreness of the lower back and knees, localized stabbing pain with nocturnal exacerbation, squamous and dry skin, and dark purple lips) are graded as absent, mild, moderate, or severe and assigned scores of 0, 1, 2, and 3, respectively. The cumulative maximum score is 30, with higher scores indicating more severe symptoms. Scores will be assessed at baseline, Week 2, and Week 4 (post-treatment).

**(2) Toronto Clinical Neuropathy Score (TCSS):** The TCSS will be used to assess neuropathic symptoms, sensory function, and reflex function in all DPN patients at baseline, Week 2, and Week 4. Neuropathic symptoms are scored as 1 point for each abnormal symptom and 0 for normal. For reflex assessment, each side is scored as 0 for normal, 1 for reduced, and 2 for absent reflexes. Sensory function is scored as 1 point for each abnormal finding and 0 for normal. The total TCSS score is 19, with higher scores indicating more severe neurological impairment.

The sensory examination methods include: (A) Pinprick sensation test using a neurotip applied to the dorsal skin of the great toe; (B) Temperature sensation test using a thermal sensory analyzer with metal (cold) and polyester (warm) ends; (C) Vibration perception test using a 128 Hz tuning fork applied to the bony prominence of the dorsal aspect of the great toe bilaterally; (D) Pressure sensation test using a 10-gauge monofilament at the great toe, medial forefoot, and anterior forefoot plantar surface on each foot; (E) Ankle reflex test; and (F) Knee reflex test.

**(3) Nerve conduction velocity:** Bilateral upper and lower limb electromyography results will be collected at baseline and Week 4, including motor nerve conduction velocity of the median nerve and ulnar nerve in the upper limbs, and the tibial nerve and common peroneal nerve in the lower limbs, as well as sensory nerve conduction velocity of the median nerve in the upper limbs and the sural nerve in the lower limbs.

### **Secondary outcome measures:**

**(1) Painful DSPN assessment:** The Douleur Neuropathique 4 (DN4) questionnaire and Visual Analogue Scale (VAS) will be used to screen for neuropathic pain in DPN patients. The DN4 questionnaire includes 7 self-reported items and 3 clinical examination items; each positive item scores 1 point, and a total score  $\geq 4$  indicates the presence of diabetic peripheral neuropathic pain (DPNP). The VAS ranges from 0 (no pain) to 10 (worst pain imaginable), and pain severity can be assessed according to the VAS score.

**(2) Ankle-brachial index (ABI):** ABI measurements will be collected from DPN patients at baseline and Week 4.

**(3) Glucolipid metabolic markers:** Fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) will be collected from both healthy controls and DPN patients at baseline and Week 4.

**(4) Non-targeted metabolomics:** Plasma samples will be collected from DPN patients at baseline and Week 4. Non-targeted metabolomic analysis will be performed using liquid chromatography-mass spectrometry (LC-MS).

**(5) Quantitative lipidomics:** Plasma samples will be collected from DPN patients at baseline and Week 4. Lipid species will be identified using LipidBlast and quantified using MultiQuant software (SCIEX, Concord, Canada). Missing values will be imputed using the k-nearest neighbors (KNN) algorithm, and data will be normalized using internal standards. Lipids identified in both positive and negative ion modes will be merged as mean values.

### **Study flow:**

The DPN clinical trial is divided into screening, run-in, treatment, and follow-up periods. Screening: within 3 days before entering the run-in period. Run-in period: 4 weeks. Subjects who meet the criteria for basic treatment may directly enter the treatment period. For subjects who do not meet the basic treatment requirements or have used prohibited medications, a 4-week run-in period will be implemented during which they will receive basic diabetes treatment according to the Chinese Guidelines for the Prevention and Treatment of Diabetes Mellitus (2024 edition), including blood glucose control, health education, dietary management, exercise therapy, smoking cessation, alcohol abstinence, and weight control. Appropriate administration of oral hypoglycemic agents or insulin will be based on individual patient conditions to maintain blood glucose within a reasonable range and prevent the occurrence of diabetic ketoacidosis and hypoglycemia. Prohibited medications must be discontinued for at least 2 weeks. At the end of the run-in period, baseline data are collected. Treatment period: 4 weeks, divided into pre-treatment and post-treatment. Eligible DPN patients will be randomized using a randomization table generated by SPSS software by an independent third-party statistician, and allocated in a 1:1 ratio to either the control group (basic treatment + mecobalamin tablets, 0.5 mg, three times daily, oral administration) or the treatment group (basic treatment + Zuogui Jiangtang

Shuluo Formula decoction). The Zuogui Jiangtang Shuluo Formula consists of: *Astragalus membranaceus* (Huangqi) 20 g, *Rehmannia glutinosa* (Shengdihuang) 15 g, *Coptis chinensis* (Huanglian) 5 g, *Dioscorea opposita* (Shanyao) 10 g, *Cornus officinalis* (Shanzhuyu) 10 g, *Spatholobus suberectus* (Jixueteng) 15 g, *Pheretima aspergillum* (Dilong) 5 g, *Smilax china* (Baqia) 15 g, *Pueraria lobata* (Gegen) 15 g, and *Tribulus terrestris* (Cijili) 10 g. The herbs will be decocted with 1000 mL water and concentrated to 400 mL, packaged into vacuum-sealed bags (200 mL/bag) by the Pharmacy Center of the First Affiliated Hospital of Hunan University of Chinese Medicine. The decoction will be taken twice daily (morning and evening), with each course lasting 2 weeks. Two courses (4 weeks total) will be observed. Follow-up period: at Week 2, TCM syndrome scores, TCSS, vital signs, and adverse events will be assessed.

### **Concomitant medications:**

Subjects with concomitant hypertension, coronary artery disease, hyperuricemia, or other conditions may continue their pre-existing treatment regimens. However, lipid-lowering agents, antibiotics, NSAIDs, antidepressants, and immunosuppressants must be discontinued for at least 2 weeks prior to and throughout the treatment period. During the observation period, symptomatic treatment for other concomitant diseases may be administered provided that it does not affect the evaluation of efficacy and safety of the study drug. All concomitant medications must be recorded in the case report form with the generic name, dosage, indication, and duration of use.

### **2.5 Data analysis**

SPSS 26.0 will be applied for statistical analysis of clinical indicators. Data that exhibit a normal distribution will be expressed as the mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ), and an independent samples t-test will be employed for comparison between two groups. Data that do not conform to a normal distribution will be expressed as the median and interquartile range [M (IQR)], and the Mann-Whitney U test will be used for comparison between two groups. For count data, these will be expressed as frequencies or percentages. For unordered categorical count data, comparisons between two groups will be performed using either the chi-squared ( $\chi^2$ ) test for fourfold tables or contingency tables. Fisher's exact probability method will be employed in accordance with the sample size and the size of the theoretical frequency. For ordered categorical count data, comparisons between two groups will be performed using the Mann-Whitney U test. A two-sided test will be employed for the

normality test and variance homogeneity test, with an alpha level of 0.1. For other significance tests, an alpha level of 0.05 will be used, with  $P < 0.05$  considered statistically significant.

For metabolomic and lipidomic data analyses, multivariate statistical methods including principal component analysis (PCA), partial least squares discriminant analysis (PLS-DA), and orthogonal partial least squares discriminant analysis (OPLS-DA) will be employed to identify differential metabolites and lipid species between groups. Metabolites and lipids meeting the criteria of variable importance in projection (VIP)  $> 1.0$  and  $P < 0.05$  will be considered significantly altered. Pathway enrichment analysis will be performed using the Kyoto Encyclopedia of Genes and Genomes (KEGG) and MetaboAnalyst databases. An integrated correlation analysis will be performed using a variety of analytical techniques, including Spearman's correlation analysis, network analysis, and random forest analysis to investigate the relationships between differential metabolites, lipid species, and clinical indicators, as well as their associations with the regulation of Schwann cell ferroptosis.

## Reference:

- [1] Pan Q, Li Q, Deng W, et al. Prevalence of and Risk Factors for Peripheral Neuropathy in Chinese Patients With Diabetes: A Multicenter Cross-Sectional Study[J]. *Frontiers in Endocrinology*, 2018, 9: 617.
- [2] Galiero R, Caturano A, Vetrano E, et al. Peripheral Neuropathy in Diabetes Mellitus: Pathogenetic Mechanisms and Diagnostic Options[J]. *International Journal of Molecular Sciences*, 2023, 24(4): 3554.
- [3] Callaghan B C, Gao L, Li Y, et al. Diabetes and obesity are the main metabolic drivers of peripheral neuropathy[J]. *Annals of Clinical and Translational Neurology*, 2018, 5(4): 397-405.
- [4] Callaghan B C, Xia R, Banerjee M, et al. Metabolic Syndrome Components Are Associated With Symptomatic Polyneuropathy Independent of Glycemic Status[J]. *Diabetes Care*, 2016, 39(5): 801-807.
- [5] Christensen D H, Knudsen S T, Gylfadottir S S, et al. Metabolic Factors, Lifestyle Habits, and Possible Polyneuropathy in Early Type 2 Diabetes: A Nationwide Study of 5,249 Patients in the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) Cohort[J]. *Diabetes Care*, 2020, 43(6): 1266-1275.

- [6] Hur J, Sullivan K A, Pande M, et al. The identification of gene expression profiles associated with progression of human diabetic neuropathy[J]. *Brain*, 2011, 134(11): 3222-3235.
- [7] Pande M, Hur J, Hong Y, et al. Transcriptional Profiling of Diabetic Neuropathy in the BKS db/db Mouse[J]. *Diabetes*, 2011, 60(7): 1981-1989.
- [8] Leal-Julià M, Vilches J J, Onieva A, et al. Proteomic quantitative study of dorsal root ganglia and sciatic nerve in type 2 diabetic mice[J]. *Molecular Metabolism*, 2021, 55: 101408.
- [9] Afshinnia F, Reynolds E L, Rajendiran T M, et al. Serum lipidomic determinants of human diabetic neuropathy in type 2 diabetes[J]. *Annals of Clinical and Translational Neurology*, 2022, 9(9): 1392-1404.
- [10] Rumora A E, Guo K, Alakwaa F M, et al. Plasma lipid metabolites associate with diabetic polyneuropathy in a cohort with type 2 diabetes[J]. *Annals of Clinical and Translational Neurology*, 2021, 8(6): 1292-1307.
- [11] Zhu J, Hu Z, Luo Y, et al. Diabetic peripheral neuropathy: pathogenetic mechanisms and treatment[J]. *Frontiers in Endocrinology*, 2024, 14: 1265372.
- [12] Ji Juliang, Chen Dashun. Effects of the nourishing yin, boosting qi, activating blood, extinguishing wind, and channeling method on intracellular sugar alcohol content and nerve conduction speed in red blood cells in DPN patients [J]. *Chinese Journal of Traditional Chinese Medicine*, 2007(06): 1197-1199

