

# Research Progress of Buyang Huanwu Decoction in the Treatment of Diabetic Peripheral Neuropathy

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**Abstract:** Diabetic peripheral neuropathy (DPN) is a chronic complication of diabetes, which is common in diabetic patients. Its incidence is increasing year by year, and it has a certain disability rate. Western medicine treatment of DPN is mainly to control the primary disease, supplemented by nutritional nerve and other drug support on the basis of maintaining blood glucose stability. Although this method alleviates the symptoms to a certain extent, the recurrence of the disease and poor clinical results are still urgent problems to be solved. Related studies have shown that traditional Chinese medicine and its compound are effective in the treatment of chronic complications of diabetes. Buyang Huanwu Decoction of Yi Lin Gai Cuo has the effects of tonifying qi, activating blood and dredging collaterals. Modern studies have shown that this prescription has the effects of anti-oxidative stress, repairing damaged nerves, inhibiting inflammatory response and regulating glycolipid metabolism, and can effectively treat various clinical symptoms caused by DPN. The purpose of this study is to read, integrate and explore the clinical research and related mechanism of Buyang Huanwu Decoction in the treatment of DPN in recent years, in order to provide more reference for the follow-up treatment of DPN.

**Keywords:** diabetic peripheral neuropathy; Buyang Huanwu decoction; Traditional Chinese Medicine; clinical research; mechanism of action

## 1. Introduction

As a metabolic disease, diabetes mellitus (DM) is closely related to the dysfunction of islet cells, which is rooted in the disorder of insulin secretion and / or utilization<sup>[1]</sup>. In recent years, due to the influence of living conditions, diet structure, work and rest habits and other factors, the incidence of DM is increasing. Statistics show that more than 10.8 % of adults worldwide suffer from DM<sup>[2]</sup>, while the prevalence rate of adults over 20 years old in China is as high as 9.7 %<sup>[3]</sup>. The various complications caused by DM are also increasing in the process of clinical diagnosis and treatment. Diabetic peripheral neuropathy (DPN) is one of the chronic complications of DM, accounting for 10%-15% of DM patients in clinical diagnosis<sup>[4]</sup>. Experimental data have confirmed that the incidence of DPN is closely related to the course of diabetes<sup>[5]</sup>. Under the condition of long-term high glucose, the body leads to metabolic dysfunction. DPN patients often have sensory abnormalities in many parts of the body, especially in the limbs. They consciously have needle-like and electric shock-like pain, or accompanied by numbness, ant line, burning sensation or itching. With the progress of the disease, it will induce diabetic foot and even cause amputation<sup>[6]</sup>. Therefore, early diagnosis and treatment is an important means of effective prevention and treatment of DPN. Although modern medicine has a certain effect on the treatment of DM and DPN, there are still some shortcomings in clinical practice, such as unsatisfactory treatment effect and prolonged healing of the disease. Traditional Chinese medicine and its compound have the advantages of multi-effect, multi-target and multi-system, which can effectively make up for the above shortcomings and play an irreplaceable role in clinical practice. A large number of studies have shown that Buyang Huanwu Decoction has a significant clinical effect in the treatment of DPN. It can not only alleviate clinical symptoms and improve the quality of life of patients, but also reduce blood glucose, accelerate the damaged nerve conduction rate, and reduce the degree of oxidative stress<sup>[7,8]</sup>. Based on the etiology and pathogenesis of DPN, this article summarizes and expounds the clinical research and related mechanism of Buyang Huanwu Decoction in the treatment of diabetic peripheral neuropathy in recent years, in order to provide more clinical choices for the treatment of DPN in traditional Chinese medicine.

## 2. The etiology and pathogenesis of DPN

DPN belongs to the syndrome of "diabetes" in traditional Chinese medicine. According to its symptom characteristics, it belongs to the category of "Bi syndrome", "flaccidity syndrome" and "pain syndrome" in traditional Chinese medicine. Professor TONG Xiaolin believes that the basic pathogenesis of diabetes arthralgia is qi deficiency and blood stasis<sup>[9]</sup>. Diabetes for a long time, deficiency of qi and blood, poor blood flow, coupled with emotional and other factors, leading to qi stagnation and blood stasis, blood stasis impedes the context, and ultimately into the image of qi deficiency and blood stasis. This disease is based on qi and blood weakness, qi stagnation and blood stasis as the standard, intermingled deficiency and excess, the disease is located in the collaterals, occurs in the limbs, often manifested as numbness, pain, cold limbs, for a long time, flaccid weakness, limbs do not use<sup>[10]</sup>. Professor Guo Baorong advocates that spleen and kidney deficiency is the root cause of DPN, and phlegm-dampness and blood stasis are the symptoms of DPN<sup>[11]</sup>. Professor Xu Jianqin blames the pathogenesis of DPN on the dysfunction of spleen and stomach and triple energizer, which eventually leads to deficiency of qi and yin. In addition, pathological products such as phlegm, blood stasis and toxin are blocked in collaterals, forming the syndrome of deficiency in origin and excess in superficiality for a long time<sup>[12]</sup>. Professor Feng Jianhua believes that the main pathogenesis of DPN is qi deficiency and blood stasis, phlegm and blood stasis. Qi deficiency leads to blood weakness, and long-term blood stasis obstructs the collaterals, and collateral obstruction further affects the operation of qi and blood and aggravates the disease<sup>[13]</sup>.

To sum up, although the doctors' understanding of the etiology and pathogenesis of DPN is slightly different, it is no more than two aspects of "qi deficiency" and "blood stasis". Yi Lin Gai Cuo said: "vitality is virtual, will not reach the blood vessels, blood vessels without gas, will stay and stasis". Qi deficiency is mental fatigue, less gas lazy words, blood stasis is limb tingling, DPN patients with symptoms are also more common in the above performance. As Tang Rongchuan's Xun Zheng Lun said: "Where there is blood stasis, it is possible to block the airway and block the qi machine". If the blood stasis obstructs the vein for a long time, it will damage the healthy qi, and the qi deficiency and blood obstruction will lead to yin deficiency and yang failure. In severe cases, the five internal organs and six internal organs will be damaged, and finally the yin and yang will be deficient, and the yin will be withered and the yang will be exhausted. In general, "qi deficiency" and "blood stasis" can affect each other and work together. Therefore, in clinical dialectics, it is mainly based on tonifying qi and replenishing qi, and promoting blood circulation and promoting blood circulation.

## 3. The historical origin and application of Buyang Huanwu decoction

Buyang Huanwu decoction is derived from the famous doctor Wang Qingren's Yi Lin Gai Cuo in the Qing Dynasty. It can supplement qi, promote blood circulation and dredge collaterals, and can effectively alleviate many diseases caused by qi deficiency and blood stasis. It is recorded in the book: "Those who are effective in treating all diseases can make the qi of the whole body pass through without stagnation, the blood is alive without stasis, and the qi passes through the blood." The original recipe consists of Astragalus, Angelica Sinensis tail, Paeoniae Radix Rubra, Earthworm, Chuanxiong Rhizoma, Carthami Flos and Persicae Semen. In the prescription, Astragalus membranaceus is used as the main medicine to supplement the vital qi and help the blood flow; Angelica Sinensis tail is the main medicine for tonifying blood circulation, removing blood stasis and clearing the meridians; Paeoniae Radix Rubra, Chuanxiong Rhizoma, Persicae Semen and Carthami Flos are adjuvant drugs to assist Angelica Sinensis tail in promoting blood circulation, removing blood stasis and dredging collaterals; Earthworm is good at dredging collaterals and can walk the whole body to improve the efficacy of medicine. Modern pharmacological research points out that there are 30 chemical components of Buyang Huanwu decoction entering the blood, and its therapeutic effect may be exerted through the comprehensive action of multiple components and multiple pathways; and by participating in anti-oxidative stress, inhibiting inflammatory response and other ways to prevent and treat DPN, thereby delaying and improving the occurrence and further development of DPN<sup>[14,15]</sup>. The main chemical components of Astragalus membranaceus can effectively improve hemodynamics, inhibit inflammatory response and promote microcirculation. At the same time, it can protect vascular endothelial cells by anti-oxidative stress<sup>[16]</sup>. The active ingredients of Angelica tail can be anti-inflammatory, anti-oxidation, anti-platelet aggregation and anti-thrombosis<sup>[17]</sup>. Total glucosides of paeony can protect vascular endothelial cells, improve blood viscosity, inhibit platelet adhesion, and prevent thrombosis<sup>[18]</sup>. At the same time, experimental results have shown that ethanol extract of Red peony root has a variety of hypoglycemic effects<sup>[19]</sup>. The active components of Chuanxiong can prevent

thrombosis, relax blood vessels, inhibit cell excitability, and also have anti-inflammatory, anti-oxidation and anti-glycosylation effects<sup>[20, 21]</sup>. Peach kernel can be anticoagulant, antithrombotic, and inhibit platelet aggregation. Its chemical component, peach kernel oil, also has lipid-regulating effect<sup>[22]</sup>. Safflower yellow pigment, as an effective component of safflower, has the effects of anti-inflammation, anti-oxidation, improving microcirculation and anti-platelet focusing<sup>[22,23]</sup>. Earthworms contains proteins, polypeptides, a variety of lumbricokinases, plasmin and lumbricoides. Among them, Lumbricus peptides can enhance the immune function of the body. Lumbricokinase can anticoagulant blood and prevent the formation of thrombosis<sup>[24]</sup>. All the drugs were combined, and the emperor, the subjects and the adjuvant drugs were combined to improve the symptoms and characteristics of DPN patients such as shortness of breath, weakness, limb numbness, pain, pale or dark complexion, pale or dark tongue or ecchymosis, heavy and thin pulse.

#### **4. Clinical study of Buyang Huanwu decoction in the treatment of DPN**

##### **4.1. Buyang Huanwu decoction and its modified decoction for DPN**

On the basis of Buyang Huanwu decoction, Professor Zhou Guoying added and subtracted drugs according to the different symptoms of DPN patients. In the case mentioned above, Radix FiciHirtae, Eucommia ulmoides, Curcumae Radix, Polygonatum sibiricum and other medicinal herbs were added to this recipe, which effectively improved the symptoms of pain and numbness of both lower limbs, difficult stool, fatigue, dry mouth and polydipsia, and achieved significant curative effect<sup>[25]</sup>. Gao Ting et al.<sup>[26]</sup> observed the effect of Buyang Huanwu decoction in the treatment of DPN through randomized controlled trials, and a total of 80 patients were selected for clinical research. The final results showed that compared with the control group, the treatment group had an improvement in body pain score, and a reduction in fasting blood glucose and 2-hour postprandial blood glucose. Therefore, the combination of Buyang Huanwu decoction can regulate the blood glucose level, improve the progress of the patient's disease, and significantly improve the quality of life. Niu Zhanhai et al.<sup>[27]</sup> selected Buyang Huanwu decoction and Zengye decoction in the treatment of DPN, compared with the simple treatment of western medicine, and found that the total effective rate and nerve conduction velocity of the treatment group were significantly higher than those of the control group. The observation results obtained by Li Renliang<sup>[28]</sup> in his study were consistent with Niu Zhanhai. Buyang Huanwu decoction combined with Zengye decoction can significantly improve the therapeutic effect of DPN patients, improve their symptoms and regulate nerve function.

Therefore, whether it is a single Buyang Huanwu decoction, modified Buyang Huanwu decoction, or the combination of Buyang Huanwu decoction and other prescriptions, can greatly improve the clinical efficacy of patients with DPN, improve symptoms, and the effect is satisfactory.

##### **4.2. Buyang Huanwu decoction combined with conventional western medicine in the treatment of DPN**

Li Ming<sup>[29]</sup> divided 80 patients with DPN into two groups. Both groups were treated with conventional hypoglycemic therapy combined with mecobalamin, and the observation group was additionally treated with Buyang Huanwu decoction. The results showed that the Toronto clinical scoring system (TCSS) score of the observation group was lower than that of the control group, and the nerve conduction velocity was significantly faster than that of the control group. At the same time, there were no adverse reactions in the two groups after treatment. Sun Miaona et al.<sup>[30]</sup> selected 50 patients with DPN of qi stagnation and blood stasis type according to the treatment methods. The control group was treated with intravenous  $\alpha$ -lipoic acid, and the treatment group was treated with Buyang Huanwu decoction. The study showed that the conduction velocity of median and common peroneal nerve in the combined treatment group was significantly improved, and the clinical symptoms were effectively relieved. The overall effective rate of the combined treatment group was 90.00%, which was significantly better than 68.00% of the control group. Ke Wenjin<sup>[31]</sup> conducted a 1:1 grouping study on the included 110 patients according to the random number method. The control group was treated with conventional western medicine (intramuscular injection of mecobalamin, oral vitamin B1 tablets, etc.), and the observation group was treated with Buyang Huanwu decoction on the basis of the control group. The results showed that the quality of life score, treatment efficiency, sensory and motor nerve conduction velocity of the observation group were higher than those of the control group. The TCM symptom score, platelet aggregation rate, plasma viscosity, fasting and postprandial 2h blood glucose, glycosylated hemoglobin levels were significantly lower than those of the control

group. Yang Yongqing et al.<sup>[32]</sup> adopted experimental methods consistent with those listed above and drew similar conclusions: After treatment, the levels of fasting and postprandial 2h blood glucose, glycosylated hemoglobin and serum ferritin in the Buyang Huanwu decoction group were significantly lower than those in the mecobalamin group. The levels of superoxide dismutase, reduced glutathione and TSS score in the Buyang Huanwu decoction group were higher than those in the mecobalamin group. The results indicate that conventional western medicine combined with Buyang Huanwu decoction is more effective and safer than single western medicine in the treatment of DPN.

In conclusion, on the premise of conventional western medicine treatment for patients with DPN, Buyang Huanwu decoction can not only regulate blood glucose level, but also improve clinical symptoms by accelerating nerve conduction velocity and reducing oxidative stress, without other adverse reactions such as damage to liver and kidney function, which further indicates that the application of Buyang Huanwu decoction in the treatment of DPN has important clinical significance.

#### ***4.3. Buyang Huanwu decoction combined with traditional Chinese medicine characteristic therapy in the treatment of DPN***

Wang Yue et al.<sup>[7]</sup> used the two-color ball method to divide the patients into the control group and the observation group, with 50 cases in each group. The control group was treated with oral mecobalamin tablets and intravenous infusion of lipoic acid injection at the same time, and the study group was treated with Buyang Huanwu decoction combined with acupuncture at Yanglingquan(GB34), Yinlingquan(SP9), Fenglong(ST40), etc. After 4 weeks of treatment, it was found that the total clinical effective rate of the study group was higher than that of the control group, and the study group could significantly improve the hematocrit, fibrinogen and other indicators compared with the control group. The results indicate that Buyang Huanwu decoction and acupuncture have a synergistic effect to correct hemorheology and accelerate nerve conduction velocity in patients with DPN. Wang Cheng et al.<sup>[33]</sup> randomly selected 75 cases of DPN patients for clinical trial, 37 cases in the control group were treated with shock wave therapy along meridian acupoints, 38 cases in the treatment group were treated with Buyang Huanwu decoction on the premise of the above therapy. The results showed that the total effective rate of the treatment group was higher than that of the control group, and the improvement of TCSS sensory examination score, nerve reflex score and nerve velocity were better than those of the control group. The results indicate that Buyang Huanwu decoction combined with shock wave therapy can significantly improve the clinical efficacy of DPN. Han Mingzhu et al.<sup>[34]</sup> first conducted a 2-week run-in period or washout period for 86 patients with DPN, and then they were treated with mecobalamin tablets (control group) and Buyang Huanwu decoction combined with mecobalamin tablets (treatment group) for 4 weeks. It was found after treatment that the TCM symptom score, TCSS score, TCM symptom efficacy and nerve conduction velocity of the treatment group were significantly improved than those of the control group, and the safety was higher. Zeng Xiaomin et al.<sup>[35]</sup> included 50 patients with DPN in the study. The control group was treated with mecobalamin tablets and epalastat tablets, and the observation group was treated with Buyang Huanwu decoction and Jixueteng Duhuo mutg decoction diet therapy and acupoint injection of vitamin B1 at Zusanli(ST36). The results showed that the curative effect of clinical symptoms and nerve reflex in the observation group was more significant, which could better improve the patient's left and right biceps brachii, left and right knee tendon and other nerve reflex, relieve limb pain and numbness.

From above, Buyang Huanwu decoction combined with traditional Chinese medicine characteristic therapy has a good clinical effect and high safety in the treatment of DPN. However, there are few clinical studies on the treatment of DPN with TCM characteristics, so we look forward to exploring more TCM characteristics therapies in the future to prevent and treat DPN with minimum risk and maximum efficacy.

### **5. The related mechanism of Buyang Huanwu Decoction in the treatment of DPN**

#### ***5.1. Anti-oxidative stress***

Oxidative stress is a key factor in the occurrence of DPN and diabetic complications<sup>[36]</sup>. Glutathione (GSH) and malondialdehyde (MDA) can effectively reflect the oxidative stress level of the body. GSH is an important antioxidant in the body, which can remove free radicals in the body, regulate redox state, and play an antioxidant role. However, the body's high glucose state will consume GSH through polyols and other pathways, and promote the occurrence of oxidative stress<sup>[37]</sup>. MDA is a commonly used index

of membrane lipid peroxidation, which is often used to monitor the degree of peroxidation damage in the body<sup>[38]</sup>.

Zhang Tianya et al.<sup>[39]</sup> used Buyang Huanwu decoction to treat DPN rats and found that the expression of GSH in DPN rats was significantly increased, and the expression of MDA was decreased. And the activities of respiratory chain complexes I, II, III, IV and mitochondrial membrane potential were significantly increased, and the expression of phosphorylated adenosine monophosphate-activated protein kinase, phosphorylated nuclear factor erythroid 2-related factor 2, heme oxygenase-1, and quinone NADH dehydrogenase 1 was significantly increased. These results suggest that Buyang Huanwu Decoction may treat DPN by regulating AMPK/Nrf2 signaling pathway to inhibit oxidative stress response. Benying et al.<sup>[40]</sup> used Buyang Huanwu decoction of different doses of astragalus to treat DPN rats and found that this decoction could down-regulate MDA by promoting the expression of superoxide dismutase, catalase and GSH-Px, improve oxidative stress and increase sciatic nerve conduction velocity in DPN rats, and the effect of high-dose astragalus was better. Jiang Bin<sup>[8]</sup> used Buyang Huanwu decoction combined with lipoic acid to treat DPN, and the results showed that: Compared with the zinc sulfate group, the SOD and total antioxidant levels of DPN patients in the combined treatment group were increased, and the sensory and motor nerve conduction velocities were accelerated, indicating that Buyang Huanwu decoction can inhibit oxidative stress, promote the body's nerve conduction, and relieve clinical symptoms. Zu Lihua et al.<sup>[36]</sup> also reached the same conclusion by using Buyang Huanwu decoction combined with lipoic acid in the treatment of DPN. These results suggest that Buyang Huanwu decoction may improve the ability of anti-oxidative stress and nerve conduction function by regulating AMPK/Nrf2 signaling pathway and down-regulating GSH and MDA levels.

### 5.2. Regulating neurotrophic factors

Nerve growth factor deficiency is one of the most important factors in DPN. Nerve tissue growth factor (NGF) and insulin-like growth factor 1 (IGF-1) are key neurotrophic factors *in vivo*, which can protect and repair neurons and accelerate the growth and differentiation of neurons<sup>[41, 42]</sup>.

Ning Ruizhao et al.<sup>[43]</sup> used Buyang Huanwu Decoction combined with methylcobalamide to treat DPN. Compared with the control group, IGF-1 expression was significantly increased in the treatment group, and Michigan diabetic peripheral neuropathy (MDNS) score was significantly decreased, indicating that Buyang Huanwu decoction could improve the neurological function of DPN patients by regulating IGF-1 level. Pei Qiang et al.<sup>[44]</sup> used modified Buyang Huanwu Decoction to treat DPN patients, and found that this prescription could promote the expression of IGF-1 and serum anterior nerve antihypertensive-peptide, and improve the conduction rate of common peroneal nerve, posterior median nerve and median nerve. Benying et al.<sup>[45]</sup> used Buyang Huanwu Decoction to treat DPN rats and found that the expression of NGF, sensation and motor conduction of sciatic nerve in rats were significantly improved. These studies all indicate that Buyang Huanwu decoction can regulate neurotrophic factors, thereby improving the neurological function of DPN patients

### 5.3. Inhibit inflammation

Chronic inflammation is one of the important pathways for the occurrence and development of DPN. Long-term high expression of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin-1 (IL-1), interleukin6 (IL-6) and other pro-inflammatory factors will aggravate nerve damage in DPN patients and cause neuropathic pain<sup>[46, 47]</sup>. Huang Yin-luan et al.<sup>[48]</sup> treated DPN patients with Buyang Huanwu decoction plus epalrestat. After treatment, it was found that the expression levels of serum C-reactive protein, 8-isoprostaglandin F<sub>2</sub> $\alpha$ , TNF- $\alpha$  and IL-6 in DPN patients were decreased, the motor conduction velocity of median nerve and tibial nerve was increased, and the sensory conduction velocity of common peroneal nerve, median nerve and sural nerve was increased. The patient's clinical symptoms were significantly relieved. Bao Peng et al.<sup>[49]</sup> used animal experiments to prove that Buyang Huanwu Decoction can treat DPN by inhibiting inflammatory response, and its mechanism of action may be related to the inhibition of TNF- $\alpha$ , IL-6 and IL-1 $\beta$  expression by this formula. At the same time, the expression of toll-like receptor 4, p38 MAPK, phosphorylated P38, nuclear factor  $\kappa$ B inhibited protein  $\alpha$ , P65, phosphorylated I $\kappa$ B- $\alpha$ , and phosphorylated P65 could be decreased, thereby improving the level of inflammation in mice. These results indicate that Buyang Huanwu decoction can inhibit the activation of TLR4 /MAPK/NF- $\kappa$ B signaling axis pathway, relieve inflammatory response, protect peripheral nerves, and have the effect of treating DPN.

#### 5.4. Regulation of glycolipid metabolism

The disorder of glucose and lipid metabolism is the basis of diabetic peripheral neuropathy. Wang Yue et al.<sup>[7]</sup> used Buyang Huanwu Decoction combined with acupuncture to treat DPN, and the results showed that compared with the control group, the levels of FPG, 2hPG, glycated hemoglobin, erythrocyte ratio, fibrinogen, whole blood viscosity (high cut) and whole blood viscosity (low cut) in the treatment group were improved. The sensory conduction velocity and motor conduction velocity of common peroneal nerve and median nerve were significantly improved, indicating that Buyang Huanwu Decoction combined with acupuncture can regulate the level of glucose and lipid metabolism in DPN patients, and fundamentally delay the occurrence of the disease.

#### 5.5. Inhibit the polyol pathway

The initiation of polyol pathway is an important mechanism to induce DPN. The polyol pathway is activated in the state of high glucose, converting glucose into sorbitol, affecting cell osmotic pressure, causing cell swelling and rupture, and inducing oxidative stress in the body<sup>[50,51]</sup>. Benying et al.<sup>[52]</sup> used Buyang Huanwu Decoction of Astragalus without dosage to treat DPN rats, and the results showed that Buyang Huanwu decoction could inhibit the activity of aldose reductase in DPN rats, reduce the content of sorbitol and fructose, increase the content of inositol, improve the expression level of Na<sup>+</sup>-K<sup>+</sup>-ATPase, and play a role in nerve repair, and the effect of high-dose Astragalus group was more obvious. These results suggest that the mechanism of Buyang Huanwu Decoction in repairing damaged nerves may be related to the effective reduction of the activity of aldose reductase in the body. The inhibition of the activity of aldose reductase in the body leads to the enhancement of the activity of Na<sup>+</sup>-K<sup>+</sup>-ATPase, and the inhibition of the polyol pathway thus plays a role in protecting nerves.

### 6. Conclusions

DPN is one of the common chronic complications in the middle and late stage of diabetes. Long-term hyperglycemia, abnormal glucose and lipid metabolism, and autoimmune factors are all risk factors aggravating DPN. The risk and disability of DPN are increasing day by day, which seriously damages the quality of life of patients. Current studies have shown that Buyang Huanwu Decoction and Buyang Huanwu Decoction combined therapy have significant clinical efficacy in the treatment of DPN, which can inhibit oxidative stress, regulate neurotrophic factors, inhibit inflammation, regulate glucose and lipid metabolism, and inhibit polyol pathway, thereby increasing blood circulation, playing an anticoagulant role, repairing damaged nerves, and effectively alleviating clinical symptoms of DPN. Promote patients from illness to recovery. However, the existing clinical studies have the defect of small sample size and lack of large sample randomized controlled experiments. The systematic review and meta-analysis of Buyang Huanwu decoction for DPN also need to be further studied. Secondly, there are few basic experimental studies on the treatment of DPN by Buyang Huanwu Decoction. Although experiments have proved that Buyang Huanwu Decoction can play anti-inflammatory, antioxidant, nutritional neurofactors and other functions, the molecular signaling pathway and specific targets of its effects still need to be further studied. Therefore, the follow-up studies on the treatment of DPN by Buyang Huanwu Decoction should be based on randomized controlled trials with large samples and molecular signaling pathways, so as to clarify the specific mechanism of action of Buyang Huanwu Decoction in the treatment of DPN, and provide a solid basis for the clinical treatment of DPN by Buyang Huanwu Decoction.

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