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# Research Advances in Traditional Chinese Medicine Treatment for Diabetic Retinopathy

**Xinmiao Liu[1], Jing'an Tong[2,*]**

[1]First Clinical Medical College, Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China
*Correspondence Author*

**Abstract:** ***Diabetic retinopathy (DR), as the primary microvascular complication of diabetes, is a major cause of blindness in adults. Traditional Chinese Medicine (TCM) classifies it under categories such as "night blindness," "internal cataract," and "sudden blindness," attributing its pathogenesis to factors including congenital deficiency, dietary and emotional imbalances, improper medication, and prolonged consumption of excessive sweets, liquids, and fats. In recent years, TCM has demonstrated unique advantages in DR prevention and treatment through stage- and pattern-specific therapies, including compound formulas, proprietary Chinese medicines, single herbs, and acupuncture. This systematic review summarizes recent advances in TCM understanding of DR pathogenesis and pattern-differentiated treatment approaches.***

**Keywords:** Diabetes, Traditional Chinese medicine, Retinopathy, Fundus**.**

## 1. Introduction

The pathogenesis of diabetic retinopathy (DR) [1-3] is relatively complex. As a complication of diabetes mellitus (DM), DR develops on the basis of underlying DM. Therefore, the causes of DM onset and progression also constitute the etiology of DR. "Diabetes Retinopathy Diagnosis and Treatment Guidelines: Integrating Syndrome and Disease" [4]: Outline the fundamental pathogenesis progression; Zhang Zihe, "On Filial Duty · The Three Forms of Extinction" [5]: Those afflicted with thirst often develop deafness, blindness, sores, eczema, and acne. This emphasizes that excessive dry heat causes stagnation and obstruction in the triple energizer, intestines, stomach, and skin pores. Fluids cannot permeate outward to nourish the body's structures, leading to malnourishment of the eye orifices and resulting blindness; "Filial Duty to Parents · Nine Types of Qi-Induced Illnesses and Mutual Treatment": It proposes that "where anger resides... eating causes qi to reverse and fail to descend, manifesting as dyspnea, thirst, restlessness, wasting syndrome, obesity, and sudden blindness, " emphasizing that emotional stagnation can transform into fire and injure yin, leading to diabetes and eye disorders. It posits that emotional imbalance disrupts the qi movement of zang-fu organs, causing stagnation or transformation into fire, which consumes yin and blood, resulting in diabetes and even sudden blindness. Li Zhiying [6] proposes dual deficiency of qi and yin. Liver-kidney yin deficiency constitutes the fundamental pathogenesis of diabetic retinopathy (DR); blood stasis and phlegm accumulation obstructing ocular collaterals represent key mechanisms in DR development. Tang Youzhi posited that DR pathogenesis involves qi-yin deficiency intermingled with stasis, aligning with modern medical concepts of capillary occlusion and microcirculatory dysfunction. Insufficient qi and yin cause blood vessel stagnation, blood stasis obstructing the collaterals, and loss of nourishment to the eyes. Spleen deficiency is also a fundamental pathogenesis of DR: qi deficiency impairs blood circulation, causing sluggish blood flow and stasis; impaired spleen function allows accumulation of dampness and phlegm, which intertwine with blood stasis to obstruct ocular collaterals, forming a vicious cycle. Professor Liu Huaidong proposed that the "Xuanfu" (mysterious orifices) represent the pivotal pathogenesis of DR. These orifices serve as pathways for the ascending and descending movements of qi, as well as the exchange of qi, blood, and body fluids. Prolonged diabetes induces an interplay between "deficiency" (liver-kidney yin deficiency, spleen qi deficiency, or combined kidney yin-yang deficiency) and "stagnation" (blood stasis, phlegm-dampness, stagnant heat, qi stagnation), leading to obstruction of the Xuanfu and impaired vision. The Diabetes Branch of the Chinese Medical Association posits a pathogenesis progressing from "dual deficiency of qi and yin" to "liver-kidney yin deficiency," ultimately resulting in "dual deficiency of yin and yang." Pathological factors including phlegm, stasis, and stagnation are present throughout this process. Xu Yunsheng's research group posits that DR pathogenesis involves a transformative process of deficiency, stasis, and phlegm. Early-stage DR is dominated by "deficiency": spleen deficiency impairs qi and blood generation, while liver-kidney yin deficiency deprives the eyes of nourishment. "Stasis" characterises moderate-to-severe non-proliferative DR, where yin deficiency generates internal heat; dry heat consumes qi and injures yin, obstructing blood flow and forming stasis. At this stage, blood stasis obstructs the collaterals, increasing retinal microaneurysms and haemorrhagic spots. "Phlegm" characterises the proliferative phase of DR, where blood stasis and phlegm-turbidity mutually reinforce each other, forming phlegm-stasis mutual entanglement that obstructs ocular collaterals. This leads to retinal neovascularisation, fibrous proliferation, and even retinal detachment.

## 2. Traditional Chinese Medicine Therapies

### 2.1 Yin-Yang Treatment Approach

Diabetic retinopathy (DR), a common severe microvascular complication of diabetes, exhibits complex pathogenesis and dynamic progression. Although fundamentally rooted in deficiency of the spleen, liver, and kidney organs, alongside qi and yin-yang depletion, it manifests distinct pathological characteristics across different disease stages. Given this dynamic nature, clinical treatment must precisely target each

stage's specific focus to achieve individualised, precise therapy. Patients frequently present in the Yin-deficiency with dry-heat phase. Yin deficiency constitutes the root, while dry-heat represents the manifest symptom; treatment should thus focus on nourishing Yin and clearing heat. Where Yin-deficiency symptoms predominate, clinical selection may include Lycium and Chrysanthemum Rehmannia Pill, which nourishes the Kidney and Liver to improve vision; Two-to Pill can tonify the Liver and Kidney, nourish Yin and arrest bleeding; Vision-Clarifying Decoction [8-9] (derived from a modification of Baihehuang Decoction combined with Erzhi Pill) also demonstrates excellent efficacy in nourishing yin, clearing heat, improving vision, and reducing opacities. Modified Yunuo Decoction can clear stomach heat and nourish kidney yin, being suitable for patterns of stomach heat with yin deficiency. As the condition progresses, patients are prone to manifesting signs of both qi and yin deficiency. With deficiency of the body's vital energy and insufficiency of yin fluids, treatment should focus on tonifying qi, nourishing yin, and supporting the body's inherent vitality. The Mimenghua Formula can clear liver heat and improve vision while tonifying qi and nourishing yin; the Shengmai Powder benefits qi, generates fluids, consolidates yin, and stops sweating; the Shenqi Dihuang Decoction [10-12] can tonify qi and nourish yin, nourish the liver and kidneys, and are all suitable for DR patients with both qi and yin deficiency. When the condition progresses further, leading to yin depletion and yang deficiency, treatment must focus on tonifying yang. However, when tonifying yang, one must strictly adhere to the pathogenesis and fully consider the interdependent relationship between yin and yang. As Zhang Jingyue [13] stated: The adept practitioner of yang tonification must seek yang within yin." This signifies that while fortifying yang, one should appropriately incorporate yin-nourishing agents to enable yang to thrive through yin's support, thereby sustaining its transformative vitality. The formula Youguiwan, renowned for warming and tonifying kidney yang while replenishing essence and arresting leakage, embodies precisely this therapeutic principle. Clinical studies reveal that Youguiwan with appropriate modifications effectively ameliorates fundus lesions in non-proliferative DR patients, further validating its efficacy during this stage. Addressing the distinct pathomechanisms of DR across its various stages, clinicians should flexibly employ therapeutic approaches such as nourishing yin and clearing heat, tonifying qi and nourishing yin to fortify the constitution, and supplementing yang. Precise selection of corresponding formulas with appropriate modifications is essential. This not only embodies the essence of TCM pattern differentiation and treatment but also provides robust theoretical foundations and practical guidance for enhancing the clinical efficacy of DR management.

### 2.2 Pattern Differentiation and Treatment

In treating DR, TCM employs pattern differentiation and treatment, selecting appropriate methods based on distinct syndromes. Yin Deficiency with Dry Heat Damaging the Ocular Vessels: This represents the most prevalent pattern in early-stage DR. Its essence lies in the "thirst and wasting" (xiāo kě) pathogenesis of diabetes, fundamentally rooted in yin deficiency with dry heat manifesting as a secondary symptom. Deficient fire ascends to scorch the ocular vessels, causing vascular fragility and leakage. Systemic manifestations include dry mouth and throat, irritability with excessive thirst and polyuria, weight loss, red tongue with scant coating, and a fine, rapid pulse. Qi and Yin deficiency with stasis in the collaterals: This represents the most central and prevalent pattern in DR. Prolonged disease progression damages Yin, which in turn impairs Qi, resulting in dual deficiency of Qi and Yin. Qi governs blood; qi deficiency fails to propel blood circulation. Yin deficiency thickens blood, and both jointly generate internal "blood stasis" obstructing ocular vessels. General symptoms include fatigue, shortness of breath, reluctance to speak, dry mouth without excessive thirst, spontaneous or night sweats, heat in palms and soles, pale-red or dark-red tongue with tooth marks or ecchymoses on edges, sparse coating, and a fine, weak pulse. Spleen-Kidney Deficiency with Water-Damp Retention Pattern: In later stages, the spleen and kidney become involved. Spleen deficiency impairs water-damp transformation, while kidney deficiency fails to govern fluid metabolism, causing water-damp retention within the eye and inducing macular oedema. Systemic manifestations include sallow or pallid complexion, poor appetite with loose stools, soreness in the lower back and knees, oedema in the limbs, aversion to cold, pale and swollen tongue with white slippery coating, and deep, weak pulse. Blood stasis obstructing collaterals: "Prolonged illness invades the collaterals," and "blood departing from the vessels becomes stasis." Blood stasis underlies the entire DR disease process, particularly prominent during the proliferative phase. Blood stasis obstructs ocular collaterals, impeding blood circulation and depriving the eyes of nourishment, potentially leading to neovascularisation (which may be regarded as "malignant blood" or "blood deviating from the meridians"). Systemic manifestations include a sallow complexion, dry and rough skin, numbness and prickling pain in the limbs, a dark purple tongue with ecchymoses, and pulse. Phlegm-stasis mutual entanglement pattern: With prolonged disease course, blood stasis obstructs qi movement, disrupting fluid distribution and causing dampness to accumulate as phlegm. Conversely, phlegm-damp obstruction further exacerbates blood stasis. These two pathological products intertwine within the eye, forming complex pathological changes. Systemic symptoms include heaviness in the head as if shrouded, chest oppression and epigastric fullness, heaviness and numbness in the limbs, dark purple tongue with white greasy or yellow greasy coating, slippery or pulse. Liver Yang Rising with Disturbance of the Eye Collaterals: Some patients present with concomitant hypertension. Liver and kidney yin deficiency fails to restrain liver yang, leading to its excessive rise that disturbs ocular vessels and forces blood to flow erratically. Systemic symptoms include dizziness, tinnitus, flushed face and red eyes, irritability, soreness in the lower back and knees, red tongue, and wiry-thready rapid pulse.

### 2.3 Staged Treatment

Clinical management of DR emphasises a combined approach of staging and pattern differentiation. DR is categorised into NPDR, PDR, and NPDR with DME. In NPDR, with microaneurysms, punctate/cotton-wool spots, and minimal hard exudates, vision remains relatively preserved. Treatment aims to tonify qi and nourish yin, cool the blood and activate blood circulation to stabilise vessels, reduce leakage, and

promote absorption of minor haemorrhages and exudates. Representative formulas include modified Yuquan Pill, modified Shengmai Powder, and modified Liuwei Dihuang Pill. In early proliferative stage (PDR) with increased haemorrhage, cotton-wool spots, venous beading, and potential neovascularisation, treatment focuses on vigorously improving ischaemia and hypoxia by tonifying qi and nourishing yin, invigorating blood and resolving stasis, and unblocking collaterals to disperse nodules. This aims to dissolve stasis and inhibit neovascularisation. Representative formula: Bu Yang Huan Wu Tang with modifications. During the PDR with DEM phase, characterised by substantial vitreous haemorrhage, fibrotic proliferative membranes, traction retinal detachment, and severe macular oedema, treatment focuses on dual Yin-Yang tonification, phlegm resolution, and stasis clearance. combined with laser or surgical intervention to manage refractory oedema and proliferative lesions. Representative formulas include Wuling San combined with Siwu Tang with modifications for oedema predominance, and Wendan Tang combined with Xuefu Zhuyu Tang with modifications for proliferative predominance.

**2.4 Treatment with Chinese Herbal Extracts**

(1) Ginkgo Biloba Leaf Extract Research indicates it possesses significant effects in promoting blood circulation, resolving stasis, clearing oxygen free radicals, antagonising platelet-activating factor, improving blood rheology and retinal microcirculation, and inhibiting retinal ganglion cell apoptosis.

(2) Puerarin Puerarin, a flavonoid glycoside extracted from the roots of Pueraria lobata (L.) DC., possesses spasmolytic and meridian-unblocking properties while improving microcirculation. It is frequently employed clinically for conditions including coronary atherosclerotic heart disease, angina pectoris, myocardial infarction, and venous obstruction.

(3) Chuanxiongzine Powder An alkaloid extract from the plant Ligusticum chuanxiong, possessing potent blood-activating properties and the ability to regulate qi and unblock meridians. Widely employed in clinical treatment.

(4) Astragalus Injection An extract from the leguminous plants Astragalus mongholicus or Astragalus membranaceus. It fortifies qi and nourishes vital substances, bolsters the body's defences against pathogens, enhances immunity, protects vascular endothelial cells, and reduces vascular permeability. This action minimises disruption to the blood-retinal barrier and vascular leakage.

(5) Ginseng-Ophiopogon Injection An extract derived from red ginseng and ophiopogon. It fortifies qi to prevent collapse, nourishes yin to generate fluids, and possesses antioxidant, anti-apoptotic, and metabolic-enhancing properties. It protects retinal neurons and blood vessels at the cellular level.

**2.5 Acupuncture Therapy**

Acupuncture is widely employed in diabetic retinopathy (DR) treatment, exhibiting unique efficacy for retinal lesions. Its mechanisms include: (1) Improving microcirculation: Needling modulates autonomic nervous function and vasoactive substances, dilating ocular vessels and reducing blood viscosity to enhance retinal blood and oxygen supply. (2) Protecting the blood-retinal barrier: Through anti-inflammatory and antioxidant effects, it mitigates high glucose-induced damage to vascular endothelial cells, reducing vascular leakage. (3) Neuroprotection: Stimulation of periorbital acupoints may promote the release of neurotrophic factors, exerting a protective effect on retinal ganglion cells. Holistic Regulation: By modulating endocrine systems such as the hypothalamic-pituitary-adrenal axis, it assists in stabilising blood glucose and blood pressure, thereby reducing damage to the fundus at its root.

**2.6 Integrated Traditional Chinese and Western Medicine Treatment**

Western medicine focuses on "targeted intervention", while Chinese medicine emphasises "holistic regulation". Western medicine employs highly direct and potent methods (laser therapy, anti-VEGF drugs, surgery) to address specific DR lesions (e.g., neovascularisation, macular oedema). It rapidly eliminates critical lesions to preserve vision, with clear staging criteria and treatment guidelines. TCM approaches treatment through systemic regulation, addressing the fundamental pathogenesis of qi and yin deficiency alongside blood stasis obstructing the collaterals in diabetic patients. Through methods such as tonifying qi and nourishing yin, promoting blood circulation and resolving stasis, it comprehensively improves microcirculation, protects vascular endothelium, and reduces oxidative stress. Individualised treatment enhances patients' overall symptoms and quality of life. The advantages of integrated Chinese and Western medicine lie in employing Western medicine's "spear" for rapid targeted intervention (addressing symptoms) while using traditional Chinese medicine's "shield" to consolidate the foundation (treating root causes). This approach delays disease progression, reduces Western medication dosage and side effects, enhances therapeutic efficacy, and improves patient quality of life. This integrated approach embodies modern medicine's shift from disease-centred to patient-centred care. It harnesses both the precision and efficiency of contemporary medicine alongside traditional medicine's holistic regulatory strengths, offering diabetic retinopathy patients a more comprehensive and humanised therapeutic option.

## 3. Reflections on TCM Treatment for DR

(1) Treatment of diabetic retinopathy (DR) should not be confined to the stage where retinal lesions become apparent. For diabetic patients, the preventive intervention philosophy of Traditional Chinese Medicine holds significant value, with the timing of intervention shifted to the "pre-disease" or "pre-pathogenic" stage. This philosophy emphasises taking action before disease formation or at its earliest signs to prevent its onset or halt its progression. Diabetic patients should undergo comprehensive risk assessment in the early stages to predict their likelihood of developing DR. Drawing upon TCM's holistic perspective and principles of pattern differentiation and treatment, personalised preventive intervention plans should be formulated based on factors such

as the patient's constitutional characteristics, disease severity, and living environment. Early intervention aids in regulating the body's internal environment and enhancing resistance, thereby preventing the onset of DR. It is noteworthy that non-proliferative DR and proliferative DR exhibit significant differences in treatment strategies and prognosis. Non-proliferative DR presents with relatively milder symptoms; when treated promptly and appropriately, its prognosis markedly improves compared to proliferative DR. Actively controlling the progression of non-proliferative DR to prevent its advancement to the proliferative stage constitutes a critical component of clinical management. Clinically, TCM treatment options for non-proliferative DR are not lacking, encompassing oral and topical herbal medications alongside non-pharmacological therapies such as acupuncture and massage. Most treatment approaches lack definitive evidence regarding long-term efficacy, specifically whether they can effectively halt or delay progression to proliferative DR. Further clinical validation and research are required. To address this gap, high-quality, large-scale clinical studies are needed to establish long-term efficacy data for TCM in treating non-proliferative DR. Concurrently, in-depth research into the mechanisms of TCM action should be intensified to elucidate how it exerts its preventive and therapeutic effects on DR through multi-pathway, multi-target mechanisms, such as regulating metabolism, improving microcirculation, and protecting retinal cells. In summary, for diabetic patients, TCM intervention should be initiated at the disease's early stages through timely risk assessment and prompt intervention to prevent DR development. Emphasis should be placed on actively controlling non-proliferative DR, with enhanced research into the long-term efficacy of TCM treatment methods to provide more scientifically sound and effective therapeutic strategies for clinical practice.

(2) When weighing the merits and drawbacks of DR treatment options to select the most suitable approach, we must comprehensively evaluate the current therapeutic landscape and potential advantages of both Western and Chinese medicine in this field. Presently, Western medicine offers diverse DR treatment modalities, ranging from fundamental oral hypoglycaemic agents and/or insulin injections to more specialised interventions such as retinal laser photocoagulation, intravitreal drug injections, and vitrectomy. These interventions play a crucial role in controlling blood glucose levels, slowing disease progression, and improving visual acuity. However, Western medical treatments are not universally applicable; certain patient groups cannot undergo specific therapies due to relative contraindications. For instance, intravitreal anti-VEGF injections demand stringent cardiovascular physiological prerequisites, while glucocorticoid medications pose significant challenges to blood glucose control. Against this backdrop, the integration of Traditional Chinese Medicine offers novel therapeutic options for such specialised patient populations. TCM possesses a distinctive theoretical framework and therapeutic approaches for managing DM and its complications, including DR. The condition's characteristic "metabolic memory" of elevated glucose levels [14] implies that the risk of complications persists even after glycaemic control is achieved. Leveraging its multi-target pharmacological properties, TCM demonstrates distinct advantages in addressing damage caused by "metabolic memory". It regulates bodily functions holistically, improves the internal environment, and provides more comprehensive therapeutic support for DR patients. There remains insufficient research evidence regarding the relationship between pharmaceutical interventions and the progression of DR prognosis in improving "metabolic memory." Clarifying this relationship and delving into the mechanisms of TCM through big data computer simulation analysis and mechanism validation undoubtedly constitutes a vast and complex undertaking. This necessitates the allocation of greater research resources to conduct multicentre, large-scale clinical studies, thereby obtaining more accurate and reliable data support. Consequently, in the treatment of DR, we should adhere to the principle of weighing benefits against risks and selecting the most appropriate approach. Based on the patient's specific condition, we should rationally choose either Western or traditional Chinese medical treatment methods, or adopt an integrated treatment model combining both, with the aim of providing patients with more personalised and effective therapeutic solutions.

## 4. Conclusion

Current therapeutic strategies for diabetic retinopathy (DR) primarily focus on disease prevention and intervention against progression. Traditional Chinese Medicine (TCM), with its unique holistic approach of syndrome differentiation and treatment, has demonstrated significant efficacy in preventing and delaying DR progression. Nevertheless, this field still faces numerous challenges and shortcomings. There remains no widely accepted consensus on methods and strategies for identifying early-stage DR lesions, which to some extent limits early intervention and effective disease management. Secondly, the "metabolic memory" effect present in diabetes mellitus (DM) patients significantly impacts the prevention and treatment of DR. While TCM holds potential advantages in metabolic regulation, specific TCM solutions targeting this effect are rarely reported, necessitating further in-depth research. Moreover, diagnostic criteria for TCM pattern differentiation in DR treatment remain inconsistent and lack objective evidence-based support, undermining the standardisation and efficacy of TCM interventions. Consequently, TCM practitioners bear significant responsibility. While leveraging the therapeutic strengths of TCM, they must conduct in-depth research and improvements to address these shortcomings, thereby advancing TCM's role in DR prevention and treatment.

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