The Unique Value and Application Exploration of TCM Collateral Disease Theory in the Prevention and Treatment of Diabetic Retinopathy

Gao Mohan

College of Traditional Chinese Medicine, Changchun University of Chinese Medicine, Changchun, China

1418071684@qq.com

Keywords: Collateral Disease Theory; diabetic retinopathy; pathogenesis reconstruction; stratified treatment; integrated traditional Chinese and Western medicine; prevention and treatment system

Abstract: This study systematically explores the unique value of Traditional Chinese Medicine (TCM) Collateral Disease Theory in the prevention and treatment of diabetic retinopathy (DR). By combing the three-dimensional network structure of "jing-luo-sun" (meridian-collateral-venule) and the therapeutic principle of "collaterals thriving on unobstructed flow", this study constructs a "Collateral Disease Pathogenesis Model" for DR, establishing a correspondence between DR's pathological process of "metabolic disorder-vascular injury-neurodegeneration" and the collateral disease evolution of "qi-yin deficiency, collateral blood stasis, and phlegm-blood stasis interblocking". The proposed preventive and therapeutic system features "stratified treatment and combined tonification-dredging therapy", including: Internal therapy with syndrome-specific formulas , combined with proprietary medicines like Tongluo Mingmu Capsule; External therapy integrating acupuncture and iontophoresis of Danshen (Salvia miltiorrhiza) and Huangqi (Astragalus membranaceus); Integrated therapy combining laser photocoagulation/anti-VEGF therapy with TCM intervention to form a multi-dimensional model. This research provides an innovative approach integrating TCM's holistic regulation with modern medicine's targeted therapy for DR, holding promise for promoting the modernization of TCM theory in major disease prevention and treatment.

1. Introduction

1.1. Disease Burden of Diabetic Retinopathy and Challenges in Modern Medicine

As one of the most severe microvascular complications of diabetes, diabetic retinopathy (DR) has become a leading cause of blindness among working-age populations worldwide. Data from the International Diabetes Federation shows that 20%-40% of the global 370 million diabetic patients develop DR, with 5%-10% progressing to blindness. The pathological process of DR involves microvascular leakage, neovascularization, and retinal detachment. Although modern medicine has developed interventions such as laser photocoagulation and anti-vascular endothelial growth factor (VEGF) injections, these face significant limitations: laser therapy is destructive and may cause visual field defects; anti-VEGF therapy requires repeated intravitreal injections, carrying risks of infection and high costs; surgical outcomes for advanced DR with fibrous proliferation or retinal detachment remain limited. These challenges highlight the urgency of exploring safe, effective, and systematic prevention strategies.

1.2. Scientific Connotations and Innovative Value of TCM Collateral Disease Theory

After over two millennia of evolution, Traditional Chinese Medicine (TCM) Collateral Disease Theory has formed a three-dimensional network structure of "jing-luo-sun" (meridian-collateral-venule) and the therapeutic principle of "collaterals thriving on unobstructed flow". This theory views the human body as a complex system of interacting "blood collaterals - qi collaterals", showing unique correspondence with DR pathology in explaining microvascular diseases: DR's "vascular endothelial injury and basement membrane thickening" highly aligns with the collateral disease pathogenesis of "collateral blood stasis"; the pathological chain of "ischemia-hypoxia-neovascularization" corresponds to the transmission law of "long-term disease invading collaterals and stagnation turning

  DOI: 10.25236/icetmr.2025.017

into heat". Compared with modern medicine's local targeted therapy, Collateral Disease Theory emphasizes the coordination of holistic regulation and micro-collateral dredging, demonstrating multi-target intervention advantages in improving microcirculation, inhibiting inflammation, and protecting nerve cells, thus providing an innovative theoretical framework for DR's full-course management.

1.3. Research Status and Gaps in Integrated TCM-Western Medicine for DR

Current studies on integrated TCM-Western medicine for DR have made preliminary progress, such as TCM compound formulas showing potential in improving retinal microcirculation and reducing laser therapy side effects. However, the following gaps remain: Lack of systematic mechanism analysis based on Collateral Disease Theory, making it difficult to establish scientific correspondence between TCM syndrome types and DR pathological stages; Clinical research is mostly limited to empirical formula observation, lacking standardized diagnosis-treatment protocols based on "collateral syndrome differentiation"; Insufficient cross-research on TCM action targets and modern medical pathways restricts theoretical innovation and technological transformation. Therefore, constructing a DR prevention system based on Collateral Disease Theory is not only an important practice of TCM theory modernization but also a key path to breaking through DR prevention bottlenecks.

2. The Formation and Evolution of Collateral Disease Theory

The origin of Collateral Disease Theory can be traced back to the Huangdi Neijing (Inner Canon of Huangdi) during the Spring and Autumn and Warring States periods, a foundational TCM classic that first established the conceptual system of "collaterals". The Ling Shu · Mai Du (Pulse Measurement in Ling Shu) constructs a three-tier framework of collaterals—"meridians as the interior, horizontal branches as collaterals, and subdivided collateral branches as minute collaterals"—through its assertion. Physiologically, the Neijing emphasizes the perfusion function of collaterals in "transporting qi and blood to nourish yin and yang, moistening muscles and bones, and facilitating joint mobility", regarding them as a key network maintaining the interconnection of zang-fu organs. Pathologically, it proposes the transmission pathway of "pathogens invading the skin and fur, then lodging in minute collaterals", laying the pathogenetic foundation of "collateral obstruction" and providing philosophical and methodological support for the theory's subsequent development [1].

In the Eastern Han Dynasty, Zhang Zhongjing first introduced the concept of "blood collaterals" in the Shang Han Za Bing Lun (Treatise on Cold Damage and Miscellaneous Diseases), establishing the clinical paradigm for collateral disease treatment. For collateral-related disorders such as liver stagnation and consumptive dry blood, he created classic formulas: Xuanfu Hua Tang (Inula Flower Decoction) for warming and dredging collaterals to resolve stagnation, Dahuang Zhechong Wan (Rhubarb and Eupolyphaga Pill) for activating blood circulation with insect drugs, and Biejia Jian Wan (Soft-Shelled Turtle Shell Decoction Pill) for comprehensive phlegm-resolving and stasis-dispersing. These formulas translated collateral theory into clinical practice through strategies like "warming-collateral with pungent-warm herbs" and "dredging-collateral with insect drugs", whose formulating principles remain the core of collateral-dredging therapy.

In the Qing Dynasty, Ye Tianshi proposed the pathogenetic theories of "prolonged disease invading collaterals" and "persistent pain involving collaterals" in Lin Zheng Zhi Nan Yi An (Medical Cases from the Clinical Guidance), expanding collateral disease research from exogenous to endogenous disorders. He argued that prolonged diseases caused collateral obstruction, establishing a stratified treatment system: mild syndromes were treated with pungent-warm herbs like Inula flower and Xin Jiang (cinnabar stem), while severe cases used insect drugs such as shui zhi (leech) and meng chong (gadfly) for dredging. This theoretical breakthrough developed collateral diseases from simple qi-blood obstruction into an independent system encompassing diverse pathogeneses such as collateral stasis, spasm, and deficiency, providing a three-dimensional framework of "location-course-syndrome" for collateral syndrome differentiation.

In the late 1970s, Academician Wu Yiling's team systematically constructed the Collateral Disease Theory by integrating original TCM theories with interdisciplinary concepts. The proposed "three-dimensional network system" explain the basic pathogeneses of collateral diseases—"collateral stasis, collateral spasm, and collateral deficiency and malnutrition"—from three dimensions: structure (collateral anatomy), function (qi-blood circulation), and pathology (collateral lesions), establishing the therapeutic principle of "collaterals thrive on unobstructed flow". The publication of Luo Bing Xue (Collateral Disease Theory) in 2004 marked the formal establishment of the "collateral disease diagnosis-treatment" system, further refined by subsequent monographs Mai Luo Lun (Theory of Blood Collaterals) and Qi Luo Lun (Theory of Qi Collaterals) [2]:

Mai Luo Lun proposes the concept of "minute collaterals-microvessels", linking collateral lesions with modern diseases like cardiovascular and chronic heart failure, serving as a theoretical bridge for integrative research on microvascular diseases.

Qi Luo Lun focuses on neuro-endocrine-immune diseases, constructing a cross-research model of "qi collaterals-neuroendocrine-immune network" by associating qi collateral disorders with insomnia and autoimmune diseases.

After over two millennia of evolution, Collateral Disease Theory has formed an anatomical system of "meridians-collaterals-minute collaterals", a pathogenetic cognition of "prolonged disease invading collaterals", a therapeutic principle of "stratified collateral dredging", and a modern framework of "three-dimensional network". It not only inherits TCM's holistic view and syndrome differentiation but also provides innovative approaches for major disease prevention through interdisciplinary integration with modern medicine, becoming a paradigm of TCM theory modernization.

3. Basic Concepts and Theoretical Connotations of Collateral Diseases

3.1. Anatomical Structure and Physiological Functions of Collaterals

Collaterals form the branching network of the meridian system, with the Ling Shu · Mai Du (Pulse Measurement in Ling Shu) defining their hierarchical structure as three levels—bie luo (branch collaterals), fu luo (superficial collaterals), and sun luo (minute collaterals)—through the assertion: "Meridians serve as the interior, horizontal branches are collaterals, and subdivided collateral branches are minute collaterals".

Bie luo (Branch collaterals): Larger collaterals characterized by "one meridian diverging to another", mostly branching below the elbow and knee joints to connect interior-exterior meridians. For example, the branch collateral of the Hand-Taiyin Lung Meridian diverges to the Hand-Yangming Large Intestine Meridian, strengthening superficial connections.

Fu luo (Superficial collaterals): Collaterals running superficially ("visibly floating"), responsible for connecting meridians and dredging the muscle surface, as recorded in Ling Shu · Jing Mai (Meridians in Ling Shu): "Observing superficial collaterals, their colors correspond to specific body regions".

Sun luo (Minute collaterals): The smallest collateral branches ("subdivided collateral branches"), distributed throughout the body, functioning to "drain abnormal pathogens and circulate ying-wei qi", cooperating with wei qi to resist pathogens.

The physiological function of collaterals centers on "perfusion of qi and blood". As stated in Ling Shu · Ben Zang (Fundamentals of the Body in Ling Shu), collaterals "transport qi and blood to nourish yin and yang, moisten muscles and bones, and facilitate joints". Through their crisscrossing network, collaterals connect internal zang-fu organs with external limbs, maintaining the circulation of ying-wei qi, blood, and body fluids, thus forming the material basis of physiological homeostasis.

3.2. Etiology and Pathogenesis System of Collateral Diseases

Collateral diseases originate from disorders of collateral physiological functions, with their etiology and pathogenesis summarized into three categories:

Wai xie qin xi (Exogenous pathogen invasion): Wind, cold, dampness, heat, etc., invade collaterals through the body surface. For instance, dampness combined with wind-cold blocking joint collaterals causes "shi bing (dampness disease)", while wind-dampness flowing into collaterals induces joint pain in "li jie bing (arthralgia syndrome)".

Qing zhi shi diao (Emotional disorders): Rage impairs liver qi, causing qi dysfunction; depression damages the spleen, leading to qi-blood deficiency. As described in Lin Zheng Zhi Nan Yi An (Medical Cases from Clinical Guidance), "Emotional frustration generates internal fire, scorching collaterals".

Zheng xu xie cou (Vacuity of righteous qi with pathogen invasion): Improper diet, excessive fatigue, aging, etc., lead to righteous qi deficiency and collateral vacuity. As stated in Jin Kui Yao Lue (Synopsis of the Golden Chamber), "When collaterals are vacuous, pathogens cannot be relieved", predisposing to exogenous invasion or internal phlegm-blood stasis.

3.3. Core Pathological Changes of Collateral Diseases

Luo mai yu zu (Collateral stasis): The most common pathology, resulting from qi-blood dyscirculation and blood stasis. For example, gan zhuo bing (liver stagnation) arises from "liver invasion, failure of qi regulation, and liver collateral stagnation", while xu lao gan xue (consumptive dry blood) is caused by "collateral qi-blood obstruction and blood stasis".

Luo mai chu ji (Collateral spasm): Collateral contraction due to cold stagnation or emotional stimulation. Chest bi pain (chest obstruction pain) stems from "cold congealing heart collaterals, blocking qi-blood flow", while stomach pain is triggered by "emotional distress causing collateral spasm".

Luo xu bu rong (Collateral deficiency and malnutrition): Collateral qi-blood insufficiency leading to nourishment failure. As described in Zhong Feng Li Jie Bing (Wind-Stroke and Arthralgia Syndrome), "When the cun kou pulse is floating and tight... floating indicates blood vacuity and collateral vacuity", where ying-wei deficiency allows wind-cold invasion, causing limb numbness.

3.4. Clinical Manifestations and Syndrome Differentiation Key Points of Collateral Diseases

Ji fu bu ren (Skin numbness): Pathogens blocking collaterals, leading to qi-blood failure in nourishment. As stated in Zhong Feng Li Jie Bing, "When pathogens reside in collaterals, the skin becomes numb", similar to the "body numbness like wind-bi syndrome" in xue bi bing (blood obstruction disease).

Ju bu bao kuai (Local mass): Phlegm and blood stasis cementing in collaterals over time, such as nüe ji (malaria mass) from "malaria pathogens and stasis blocking hypochondriac collaterals, forming a tangible mass".

Chu xue zheng hou (Bleeding syndromes): Collateral injury causing blood extravasation. The Jin Kui Yao Lue records "hematemesis, hematochezia, and epistaxis", resulting from damp-heat or deficiency-cold injuring yang luo (superficial collaterals) or yin luo (internal collaterals).

Jiu tong bu yu (Persistent pain): Collateral obstruction leading to "no free flow, no ease from pain". For example, chest bi (chest obstruction) with "chest and back pain" is due to phlegm-stasis blocking heart collaterals, while dampness disease pain arises from "dampness combined with wind-cold blocking superficial collaterals".

4. Pathogenesis and Clinical Progression of Diabetic Retinopathy

4.1. Multidimensional Pathogenesis: Hyperglycemia-Driven Cascade Injury

The pathological basis of diabetic retinopathy (DR) originates from metabolic disorders and vascular damage induced by long-term hyperglycemia, with its core mechanisms involving four abnormal pathways [3]:

Polyol pathway activation: Under hyperglycemia, glucose is converted to sorbitol by aldose reductase, leading to intracellular sorbitol accumulation that causes osmotic imbalance, resulting in retinal cell swelling and rupture. Concurrently, this process consumes nicotinamide adenine

dinucleotide phosphate (NADPH), weakening antioxidant capacity and exacerbating oxidative stress injury. Animal studies have confirmed that inhibiting aldose reductase reduces sorbitol production and alleviates retinal cell damage.

Protein kinase C (PKC) pathway hyperactivity: Hyperglycemia promotes diacylglycerol (DAG) synthesis, which activates PKC, leading to phosphorylation of vascular endothelial tight junction proteins. This disrupts the blood-retinal barrier, increases vascular permeability, and induces vascular endothelial growth factor (VEGF) expression to stimulate neovascularization. Clinically, PKC activity in the intraocular fluid of DR patients correlates positively with disease severity.

Accumulation of advanced glycation end products (AGEs): Non-enzymatic glycosylation of glucose with biomacromolecules generates AGEs, which bind to receptor for AGEs (RAGE) to activate the nuclear factor-κB (NF-κB) pathway. This promotes the release of inflammatory cytokines like tumor necrosis factor-α (TNF-α), inducing retinal inflammation, while causing vascular basement membrane thickening to exacerbate ischemia-hypoxia. AGEs content in DR retinal tissue is significantly elevated.

Oxidative stress imbalance: Hyperglycemia disrupts mitochondrial electron transport chains, generating excessive reactive oxygen species (ROS) that exceed the body's antioxidant capacity. ROS damage retinal vascular endothelial cells, pericytes, and neurons through oxidative modification, activating mitogen-activated protein kinase (MAPK) pathways to further aggravate inflammation and cell injury. DR patients exhibit elevated malondialdehyde (MDA) levels and reduced superoxide dismutase (SOD) activity.

These mechanisms collectively lead to retinal microvascular lesions: endothelial injury causes vascular leakage, pericyte loss results in vascular deformation, basement membrane thickening impairs blood flow, ultimately triggering ischemia-hypoxia that stimulates neovascularization, forming the pathological basis of DR progression.

4.2. Clinical Staging: From Microvascular Lesions to Vision Loss

The international staging criteria classify DR into six stages, exhibiting progressive pathological features:

Stage I (Early): Retinal microaneurysms (red spots, 10-100μm in diameter) and petechiae appear due to capillary endothelial bulging and vessel wall injury. Patients show no obvious symptoms, with normal vision.

Stage II: Hard exudates emerge as yellow-white spots from plasma lipid-protein exudation, mostly located in the posterior pole. Some patients experience mild visual acuity decline or blurring.

Stage III: Cotton-wool spots (gray-white lesions from ischemic necrosis of nerve fiber layers) and hemorrhages increase, with significant vision loss, accompanied by blurred vision and floaters.

Stage IV: Retinal neovascularization forms with fragile walls, prone to rupture and vitreous hemorrhage. Patients suffer abrupt vision loss, with large shadow obstructions in the visual field.

Stage V: Fibrovascular membranes develop around neovascularization, tractionally distorting and displacing the retina, leading to severe vision impairment (light perception or minimal vision).

Stage VI (End-stage): Sustained traction from fibrovascular membranes causes tractional retinal detachment, separating the neurosensory retina from the retinal pigment epithelium, resulting in near-total vision loss or blindness.

DR progression follows the pathological chain of "microvascular injury-ischemia-hypoxia-neovascularization-fibrous proliferation-retinal detachment". Early intervention can significantly delay disease progression, while advanced stages often lead to irreversible vision loss.

5. Mechanistic Analysis and Therapeutic Insights of DR from the Perspective of Collateral Disease Theory

5.1. Homologous Mechanisms between Collaterals and Retinal Microvasculature

Structurally, the three-tier branching structure of TCM collaterals ("jing mai - luo mai - sun luo" [meridians - collaterals - minute collaterals]) is highly congruent with the dendritic network of retinal

microvasculature (arteries - arterioles - capillaries) [4]. The Ling Shu · Mai Du defines sun luo (minute collaterals) as "subdivided collateral branches", whose fine characteristics correspond to the material exchange function of retinal capillaries (diameter 5-10μm). This micro-network structure determines their core role in qi-blood/blood perfusion—collaterals maintain organ nourishment through "transporting qi and blood to nourish yin and yang", while retinal microvasculature supplies oxygen and nutrients to the neuroepithelium via microcirculation. The pericyte-endothelial cell structure shows modern medical analogy to the regulatory function of collaterals in "ying-wei qi and blood" [5].

Functionally, the pathogenesis of "collateral obstruction" in Collateral Disease Theory corresponds to DR microvascular lesions. Mechanisms like hyperglycemia-induced polyol pathway activation and PKC pathway hyperactivity can be analogized as "pathogens invading sun luo, blocking qi and blood": sorbitol accumulation causing cellular edema resembles "disordered fluid metabolism in collaterals"; AGEs-induced basement membrane thickening corresponds to the pathological process of "collateral stasis". Clinically observed DR lesions such as increased retinal vascular permeability and pericyte loss validate cross-theoretical correspondence with collateral disease pathogenesis—vascular endothelial injury leading to leakage belongs to "collateral instability"; ischemia-hypoxia-induced neovascularization belongs to "stasis transforming into heat, forming new collaterals".

5.2. Pathogenetic Reconstruction of DR Based on Collateral Disease Theory

Based on the "three-dimensional network system" theory, DR pathogenesis can be summarized as "benxu biaoshi (deficiency in root and excess in branch)": qi-yin deficiency as the root, blood stasis blocking collaterals as the branch [6]. Prolonged disease consumes qi and yin, leading to "collateral vacuity", as stated in Zhong Feng Li Jie Bing: "floating pulse indicates blood vacuity and collateral vacuity", consistent with the pathological basis of insulin resistance and oxidative stress injury in DR. Hyperglycemia-driven metabolic disorders can be viewed as "phlegm-blood stasis interblocking in collaterals"—advanced glycation end products (AGEs) resemble "phlegm turbidity", while blood stasis corresponds to "collateral obstruction", collectively disrupting the retinal "blood-nerve barrier" and causing stage I-II manifestations like microaneurysms and hard exudates.

During stage III-IV progression, cotton-wool spots and neovascularization conform to the transmission law of "prolonged pain involving collaterals" and "stasis transforming into heat". Retinal ischemia-hypoxia stimulating VEGF expression is analogous to "collateral heat forcing blood to flow abnormally", echoing Ye Tianshi's theory of "prolonged disease invading collaterals, qi-blood stagnation". Stage V-VI fibrous proliferation and retinal detachment belong to "collateral fibrosis" and "collateral injury with blood extravasation", representing the terminal stage of extreme stasis and collateral structure disintegration.

5.3. Innovative Therapeutic Paradigm of "Collaterals Thriving on Unobstructed Flow"

The therapeutic principles of "invigorating qi and nourishing yin, activating blood circulation and dredging collaterals" established by Collateral Disease Theory provide multi-level intervention strategies for DR [7]:

Invigorating qi and nourishing yin to strengthen the root: Astragalus polysaccharides regulate immunity and improve insulin resistance, with astragaloside IV reducing oxidative stress by activating the AMPK pathway, corresponding to "qi-tonifying and collateral-dredging"; yin-nourishing drugs like Rehmannia and Ophiopogon inhibit aldose reductase activity to alleviate sorbitol accumulation, embodying "yin-nourishing and collateral-moistening".

Activating blood circulation to dredge collaterals: Tanshinone IIA inhibits the PKC pathway to reduce vascular permeability and promote hemorrhage absorption; ligustrazine suppresses the NF-κB pathway to mitigate AGEs-RAGE-mediated inflammation, aligning with "blood-activating and collateral-dredging". Clinical studies show that TCM compound formulas based on these principles can effectively reduce whole blood viscosity and accelerate retinal microcirculation, outperforming pure western medicine in visual acuity improvement.

This cross-theoretical mapping of "structure-function-syndrome" not only provides a "collateral

syndrome differentiation" diagnostic framework for DR but also achieves synergistic innovation between TCM theory and modern medicine through "combined tonification and dredging" strategies, opening a new path for preventing diabetic microvascular complications.

6. Exploration of Preventive and Therapeutic System for DR Based on Collateral Disease Theory

6.1. Internal Therapy: Syndrome Differentiation and Proprietary Formula Innovation

6.1.1. Syndrome-Typed Treatment

Based on the therapeutic principle of "collaterals thriving on unobstructed flow", DR is differentiated into three syndromes:

Qi-yin deficiency with blood stasis blocking collaterals: Manifested as blurred vision and fatigue, treated with Shengmai San (Ginseng-M Decoction) combined with Xuefu Zhuyu Tang (Blood Mansion Decoction). Ginseng and Ophiopogon invigorate qi and nourish yin, while peach kernel and safflower activate blood circulation. Clinical studies show this formula promotes effective absorption of fundus hemorrhage in stage III DR patients.

Liver-kidney yin deficiency with collateral stasis: Characterized by visual distortion and soreness in waist-knees, treated with Liuwei Dihuang Wan (Six-Ingredient Rehmannia Pill) combined with Taohong Siwu Tang (Peach-Safflower Four Substances Decoction). Rehmannia and Cornus nourish liver-kidney yin, while peach kernel and Chuanxiong dredge collaterals. After 4 months of treatment, retinal exudates in stage IV patients are effectively absorbed [8].

Yin-yang deficiency with blood stasis and water retention: In advanced stages, sudden vision loss, cold limbs, and edema are treated with Jinkui Shenqi Wan (Golden Chamber Kidney Qi Pill) combined with Zhenwu Tang (True Warrior Decoction). Aconite and cinnamon warm yang and activate qi, while Poria and Atractylodes remove water and stasis. Retinal edema in stage VI patients significantly resolves after six-month treatment.

6.1.2. Application of Proprietary Formulas and Drugs

Tongluo Mingmu Capsule: Composed of Red Peony Root, Astragalus, etc., it removes stasis and dredges collaterals, significantly improving eye dryness and fatigue.

Yangyin Mingmu Decoction: Astragalus combined with Danshen (Salvia miltiorrhiza) improves microcirculation, demonstrating better efficacy than calcium dobesilate in treating simple DR.

Danju Mingmu Decoction: Ginseng Radix and Notoginseng promote blood flow, reducing blood viscosity and enhancing retinal perfusion.

6.2. External Therapy: Local Intervention of Acupuncture and Iontophoresis

6.2.1. Acupuncture Therapy

Point selection strategy: Local points (Cuanzhu, BL2; Sizhukong, SJ23) regulate ocular qi-blood; distal points (Hegu, LI4; Zusanli, ST36) invigorate spleen-qi; syndrome-specific points (Pishu, BL20; Shenshu, BL23 for qi-yin deficiency; Xuehai, SP10; Geshu, BL17 for blood stasis) are added.

Manipulation key points: Even reinforcing-reducing method for ocular points; reinforcing-reducing based on deficiency-excess for limb points. Clinical observation shows acupuncture combined with western medicine improves vision in stage III DR patients.

6.2.2. Ocular Iontophoresis

Using direct current electric field to deliver ions of Danshen and Astragalus into the eye, avoiding systemic drug dilution. Studies show ligustrazine iontophoresis effectively improves fundus microcirculation and reduces blood viscosity in stage II DR.

6.3. Integrated TCM-Western Medicine: Complementary Comprehensive Intervention

6.3.1. Laser Combined with TCM

Laser photocoagulation destroys hypoxic retina to inhibit neovascularization, while Shengmai San-Xuefu Zhuyu Tang alleviates laser-induced injury. Clinical data shows this protocol promotes neovascular regression in stage IV DR, outperforming pure laser therapy [9].

6.3.2. Anti-VEGF Therapy Combined with TCM

Anti-vascular endothelial growth factor therapy rapidly resolves macular edema but requires repeated injections. TCM reduces injection frequency by regulating immunity, accelerating edema resolution and lowering complication rates.

7. Conclusions

7.1. Theoretical Innovation: Pathogenetic Reconstruction of DR by Collateral Disease Theory

This study, based on Traditional Chinese Medicine (TCM) Collateral Disease Theory, first constructs a "Collateral Disease Pathogenesis Model" for diabetic retinopathy (DR). The model takes "qi-yin deficiency" as the fundamental pathogenesis, "blood stasis blocking collaterals" as the core pathology, and "phlegm-blood stasis interblocking" as the secondary manifestation, forming a three-dimensional cognitive system of "deficiency in root, excess in branch, and collateral injury". It is found that pathological features of DR at different stages—including microaneurysm formation, vascular leakage, and neovascularization—significantly correspond to the pathogenetic evolution of "collateral spasm", "collateral obstruction", and "collateral injury with blood extravasation" in Collateral Disease Theory. This establishes a cross-theoretical mapping between TCM collateral theory and DR's pathological process of "metabolic disorder-vascular injury-neurodegeneration", providing an innovative interpretation for DR syndrome differentiation by integrating traditional theory and modern medicine.

7.2. Prevention and Treatment System: DR Intervention Strategies Guided by Collateral Disease Theory

Based on the core principle of "collaterals thriving on unobstructed flow", this study constructs a comprehensive DR prevention and treatment system of "stratified treatment and combined tonification-dredging":

Internal therapy: According to syndrome types of "qi-yin deficiency with blood stasis", "liver-kidney yin deficiency with collateral stasis", and "yin-yang deficiency with blood stasis and water retention", formulas such as Shengmai San combined with Xuefu Zhuyu Tang, Liuwei Dihuang Wan combined with Taohong Siwu Tang, and Jinkui Shenqi Wan combined with Zhenwu Tang are used, supplemented by proprietary formulas like Tongluo Mingmu Capsule, forming an internal medication system for different DR stages.

External therapy: Integrating acupuncture point selection and drug iontophoresis, local points (Cuanzhu, Sizhukong) and distal points (Hegu, Zusanli) are synergistically used, combined with ocular iontophoresis of Danshen and Huangqi, achieving local qi-blood regulation and targeted drug delivery.

Integrated TCM-Western medicine: Combining modern medical approaches such as laser photocoagulation and anti-VEGF therapy with TCM internal and external treatments forms a complementary intervention model, providing a new technical pathway for DR individualized therapy.

7.3. Clinical Value and Future Prospects

This study confirms that DR prevention and treatment strategies guided by Collateral Disease Theory have multi-dimensional advantages: balancing systemic qi-blood homeostasis and retinal microcirculation improvement through the coordination of "holistic regulation-local collateral dredging"; demonstrating comprehensive effects in regulating glucose-lipid metabolism, inhibiting inflammation, and protecting vascular endothelium based on "multi-target intervention"; and

providing feasible solutions for reducing western medicine dependence and treatment risks due to the safety and economy of TCM therapy. Future research can focus on: deepening the mechanism study of TCM based on the "sun luo-microvessel" theory, establishing quantitative correlation between DR TCM syndrome types and modern imaging examinations, and promoting the research and development of innovative TCM formulations with independent intellectual property rights. This integrated TCM-Western medicine approach is expected to provide a "Chinese solution" integrating traditional wisdom and modern technology for global DR prevention and treatment, promoting the modernization of TCM theory in major disease management.

References

[1] Lei Yan. (1998). Exploration of the Theory of Network Diseases. Journal of Beijing University of Chinese Medicine, (02),17-22+71.

[2] Li Yan, Zhao Yan, Huang Qifu, and Wang Yongyan. (2002). Modern Understanding of TCM Network Diseases. Journal of Beijing University of Chinese Medicine, (03),1-5.

[3] Duan Yingying, An Xuedong, Zhang Yuehong, Kang Xiaomin, and Lian Fengmei. (2023). Analysis of the Pathogenesis and Treatment Ideas of Diabetic Retinopathy Based on the Theory of Network Diseases from the Perspective of 'Qi Stagnation'. Journal of Jilin University of Traditional Chinese Medicine, 43(05),501-505.DOI:10.13463/j.cnki.jlzyy.2023.05.002.

[4] Chang Liping, Ma Jing, Ma Kun, Jia Zhenhua, and Wei Cong. (2025). Theoretical Exploration of Diabetic Retinopathy Guided by the Theory of Network Diseases. Chinese Journal of Experimental Formula, 31(01),253-258.DOI:10.13422/j.cnki.syfjx.20241266.

[5] Bu Xianghui, An Haiyan, Guo Xiaoyuan & Lu Kai (2022). A Study on the Correlation of Diabetes Nephropathy and Diabetic Retinopathy with Traditional Chinese Medicine. Journal of Hunan University of Chinese Medicine, 42(03),486-491.DOI:10.3969/j.issn.1674-070X.2022.03.025.

[6] Wu Yiling (2003). The Theory of Network Diseases in Traditional Chinese Medicine and a Three-Dimensional Stereoscopic Network System. Journal of Traditional Chinese Medicine, 06),407-409.doi:10.13288/j.11-2166/r.2003.06.002.

[7] Wang Jia, Li Qingwei, Yang Yingying, Gao Zezheng & Pang Bing (2017). Tong Xiaolin's Experience in Preventing and Treating Early Diabetic Retinopathy. Beijing Journal of Chinese Medicine, 36(06),512-515.doi:10.16025/j.1674-1307.2017.06.009.

[8] Pang Bing & Ni Qing (2024). From the Perspective of' Eye-Kidney Synergy' on the Prevention and Treatment of Diabetic Microvascular Lesions with Traditional Chinese Medicine. Journal of Basic Medical Sciences of China, 30(01),32-34.

[9] Song Yi, Lei He, Wang Yanjing, Liu Chuyu (2005). Research Progress on the Application of Traditional Chinese Medicine in Laser Treatment for Diabetic Retinopathy. Journal of Yunnan University of Chinese Medicine, (02),67-70.doi:10.19288/j.cnki.issn.1000-2723.2005.02.028.