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# Observation on Clinical Efficacy of External Treatment of Traditional Chinese Medicine Combined with Qiju Dihuang Pill in the Treatment of Diabetic Retinopathy

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**Abstract**

**Objective**: This study observed the clinical effect of external treatment of traditional Chinese medicine (TCM) combined with Qiju Dihuang pill on the treatment of diabetic retinopathy. **Methods**: 62 patients with diabetic retinopathy, who were treated with Qiju Dihuang pill combined with TCM external treatment from January 2021 to May 2023 in our hospital, were included as the combination group, and 60 patients treated with Qiju Dihuang pill were set as the control group. The clinical efficacy in the two groups was compared. The best corrected visual acuity, macular central retinal thickness, retinal hemodynamic indexes, oxidative stress indexes, and angiogenesis-related factors of the two groups were collected. The occurrence of adverse reactions in the two groups during treatment was statistically sorted out. **Results**: The total effective rate was higher in the combination group than the control group ($p < 0.05$). After treatment, optimal corrected visual acuity, peak systolic velocity of central retinal artery, end-diastolic velocity of blood flow, average blood flow velocity, glutathione peroxidase, total antioxidant capacity, and pigment epithelium-derived factor levels were increased ($p < 0.05$), while the levels of macular central retinal thickness, central retinal vein return velocity, blood flow resistance index, pulse index, advanced oxidized protein products and vascular endothelial growth factor were decreased ($p < 0.05$) in both groups. Notably, the changes of these indexes were more evident in the combination group than the control group ($p < 0.05$). **Conclusion**: Qiju Dihuang pill combined with TCM for external treatment has good clinical efficacy on diabetic retinopathy, which can effectively improve visual acuity and retinal hemorheology, reduce the macular central retinal thickness, and inhibit oxidative stress and angiogenesis, indicating its certain clinical application value.

## 1 Introduction

Diabetic retinopathy (DR) is one of the common complications of diabetes, with the ocular fundus characteristics of different microvascular diseases such as microangioma, venous beading, etc., which may affect the vision of patients, and even worse, cause complications including retinal detachment, glaucoma, and reduce the quality of life of patients [1-2]. Hence, improving the microcirculation of the ocular fundus and protecting the optic nerve are the key to treating DR. More than 100 million people worldwide are living with DR, the leading cause of blindness and visual impairment, and the global prevalence of DR is expected to increase significantly, from approximately 103 million in 2020 to 130 million in 2030 [3]. Therefore, it is very important to find a better treatment method for the clinical treatment of DR.

Clinically, intravitreal injection of anti-vascular endothelial growth factor drugs is commonly used to treat DR patients through suppressing the expressions of endothelial cells and retinal vascular endothelial growth factors and decreasing vascular permeability [4]. However, some patients may experience adverse reactions such as retinal detachment and uveitis after treatment [5]. In recent years, integrated traditional Chinese medicine (TCM) and Western medicine (WM) have been gradually applied for clinical treatment of DR. In TCM, DR belongs to "obscured vision", the underlying pathogenesis which has been confirmed as the deficiency of central qi that makes it difficult for qi to reach the eyes and causes failure of blood pattern control and blood stasis of meridian. Therefore, the treatment should focus on tonifying qi and nourishing yin, circulating blood and draining water retention [6]. Qiju Dihuang pill, a classic prescription for ophthalmic diseases, is composed of *Rehmanniae Radix Praeparata*, Dioscoreae Rhizoma, *Corni Fructus*, etc., with the functions of tonifying kidney and strengthening essence, nourishing the liver, and improving visual acuity [7]. To further improve the clinical efficacy of DR, on the basis of the internal treatment of TCM, external treatments of TCM can be performed including ion-introduction therapy of TCM drugs and acupoint injection that are simple, convenient, inexpensive, effective [8]. Besides, Danshen injection can repress platelet aggregation, reduce blood viscosity, improve microcirculation, activate blood circulation, remove blood stasis, invigorate qi and nourish yin [9]. This study adopted Qiju Dihuang pill combined with external treatment of TCM including ocular ion-introduction of Danshen injection, acupoint injection of Danshen, and acupoint massage to treat DR and explored the clinical efficacy.

## 2 Methods and Materials

### 2.1 General information

62 patients with diabetic retinopathy, who were treated with Qiju Dihuang pill combined with TCM external treatment from January 2021 to May 2023 in our hospital, were included as the combination group, and 60 patients treated with Qiju Dihuang pill were set as the control group. The comparability of the general information between the two groups was confirmed, as evidenced by their subtle differences regarding information ($p > 0.05$, Table 1). This study was authorized by the Ethics Committee of our hospital and obtained the signed written informed consent from all patients. This study was conducted in accordance with the Declaration of Helsinki.

**Table 1** Comparison of general information between the two groups.

| Group | | Control group (n = 60) | Combination group (n = 62) | $\chi^2/t$ | $p$ |
|---|---|---|---|---|---|
| Sex (case) | Male | 27 | 36 | 2.084 | 0.149 |
| | Female | 33 | 26 | | |
| Age (years old) | | 54.36 ± 7.20 | 55.18 ± 6.92 | -0.641 | 0.522 |
| Body mass index (kg/m$^2$) | | 24.65 ± 1.84 | 24.34 ± 2.09 | 0.868 | 0.387 |
| Duration of diabetes (year) | | 7.48 ± 1.25 | 7.19 ± 1.46 | 1.177 | 0.242 |
| Duration of retinopathy (year) | | 2.87 ± 0.92 | 2.73 ± 1.15 | 0.741 | 0.460 |
| Affected side of eyes | Left | 41 | 38 | 0.663 | 0.416 |
| | Right | 19 | 24 | | |

### 2.2 Inclusion criteria

(1) Meet the DR diagnostic criteria in *the Guidelines for Clinical Diagnosis and Treatment of diabetes retinopathy in China* (2014) [8]; (2) Fasting blood glucose < 16.7 mmol/L, and blood pressure < 160/100 mmHg.

### 2.3 Exclusion criteria

(1) Other types of eye diseases such as cataracts and glaucoma; (2) Acute and severe diabetes in the last month including hyperosmolar hyperglycemic state, and ketoacidosis; (3) Vascular complications such as lower limb vascular disease, cerebrovascular accidents, and coronary heart disease; (4) Allergy to medication used in this study; (5) Severe dysfunction of important organs such as the heart, liver, and kidney; (6) Diseases of the blood and immune systems; (7) Lung infection, urinary system infection and other infectious diseases in recent times; (8) Pregnant or lactating women.

### 2.4 Treatment methods

Both groups received diabetes education, diabetes diet and blood glucose control. Patients in the control group took Qiju Dihuang pill (8 pills/time, 3 times/day, 200 pills/bag; National Medicine Permission Number (NMPN): Z42021299; Hubei Ruihua Pharmaceutical Co., Ltd.), on the basis of routine treatment. Both groups of patients were treated for two courses (2 weeks as 1 course of treatment) with a 2-day interval between each course. Patients in the combination group underwent TCM external treatment based on the treatment in the control group. To be specific, (1) ocular ion-introduction of Danshen injection: 2 mL of Danshen Injection (2 mL * 10 injections; NMPN: Z35020384; Fujian Gutian Pharmaceutical Co., Ltd.) was sprayed evenly onto two layers of disinfectant gauze (5 cm × 6 cm) which was then applied to the affected eye. For patients with monocular involvement, the unaffected eye should be covered with dry gauze for isolation. DY multifunctional oculopathy treatment instrument (Xi'an Huaya Electronics Co., Ltd.) was used under the mode of "ion conduction" and the current of 0.3-0.8 mA which was regulated according to the patient's tolerance. 15 min later, the "pulse" mode was selected for 5 min within patient's tolerance. The treatment was repeated 4 times for a total of 20 min, once/day. (2) acupoint injection: Danshen injection was injected into Zusanli acupoint (1 mL/acupoint) once every other day. (3) acupoint massage: standard eye acupoint massage was performed through eye exercises, with local skin slightly red to meet the requirements of massage, 2 times /day, in the morning and afternoon, respectively. The treatment lasted for 2 consecutive courses (2 weeks as 1 course of treatment).

### 2.5 Observation indicators

#### 2.5.1 Clinical efficacy

According to the therapeutic efficacy evaluation

criteria set forth in the Guiding Principles for Clinical Research of New Traditional Chinese Medicine [10]. Significant improvement: after treatment, the patient's visual acuity is improved by ⩾ 4 lines, or ⩾ 1.0; retinal microvascular tumors, ocular fundus hemorrhage, and exudate are decreased from (+++) to (++), or from (++) to (+), or from (+) to disappearance; 2 or more indicators of microvascular tumors, hemorrhage, and exudate changes meet the requirements; the average circulation time of the retina is significantly shortened, the degree of macular edema is evidently reduced, the non-perfusion area of retinal capillaries is narrowed, and vascular leakage is apparently decreased. Effectiveness: after treatment, the patient's visual acuity is improved by ⩾ 2 lines; retinal microvascular tumors, fundus hemorrhage, and exudate are decreased from (+++) to (++), or from (++) to (+), or from (+) to disappearance; 1 or more indicators of microvascular tumors, hemorrhage, and exudate changes meet the requirements; the average circulation time of the retina is shortened, the degree of macular edema is reduced, the non-perfusion area of retinal capillaries is narrowed, and vascular leakage is apparently decreased. Ineffectiveness: all indicators do not meet the above effective standards. Total effective rate = (significant improvement + effectiveness)/total number of cases × 100%.

### 2.5.2 The best corrected visual acuity and macular central retinal thickness

The best corrected visual acuity was determined using an international visual acuity standard, and the macular central retinal thickness was measured with a three-dimensional optical coherence tomography (Toncan, 2D0CT2000, Japan). The test was performed by the same experienced senior professional doctor, and repeated three times. The average value was taken as the experimental result.

### 2.5.3 Retinal hemodynamic indexes

The GELOGIQP3 color Doppler ultrasound machine (America) was used to detect the central retinal vein return velocity (CRV), peak systolic velocity of central retinal artery (PSVCRA), end-diastolic velocity of blood flow (EDVBF), blood flow resistance index (BFRI), pulse index (PI) and mean blood flow velocity (Vm) in two groups of patients.

### 2.5.4 Oxidative stress indicators

6 mL of fasting elbow vein blood was extracted from two groups of patients, and centrifuged at a rate of 3000 r/min for 15 min at 4 ℃, with a centrifugation radius of 10 cm to separate the serum. The level of glutathione peroxidase (GSH-Px) was measured using colorimetric method. The levels of advanced oxidative protein products (AOPP) and total antioxidant capacity (TAOC) were quantified by enzyme-linked immunosorbent assay (ELISA).

### 2.5.5 Levels of angiogenesis-related factors

6 mL of fasting elbow vein blood was harvested from two groups of patients, and centrifuged (3000 r/min, 15 min, 4 ℃, a centrifugation radius of 10 cm) to separate the serum. The ELISA was performed to detect levels of vascular endothelial growth factor (VEGF) and pigment epithelial cell-derived factor (PEDF).

### 2.5.6 Statistical analysis

Statistical analyses were conducted using SPSS 26.0. The count data were described by case (%) and compared by $\chi^2$ tests. The mean ± standard deviation was employed to represent measurement data. The continuity variables were analyzed for normality using the Kruskal-Wallis method. Measurement data conforming to a normal distribution were expressed in the form of mean ± standard deviation. Independent samples $t$-tests were used for comparison between the two groups, and paired samples $t$-tests were for comparison before and after treatment in the same group. The difference of $p$

< 0.05 was considered to be statistically significant.

## 3 Results

### 3.1 Comparison of clinical efficacy of patients between the two groups after treatment

The combination group had a higher total effective rate relative to the control group after treatment ($p$ < 0.05, Table 2)

**Table 2** Comparison of clinical efficacy of patients between the two groups after treatment [case (%)].

| Group | Case | Significant improvement | Effectiveness | Ineffectiveness | Total effective rate |
|---|---|---|---|---|---|
| Control group | 60 | 19 (31.67) | 24 (40.00) | 17 (28.33) | 43 (71.67) |
| Combination group | 62 | 37 (59.68) | 20 (32.26) | 5 (8.06) | 57 (91.94) |
| $\chi^2$ | | | | | 8.475 |
| $p$ | | | | | 0.000 |

### 3.2 Comparison of the best corrected visual acuity and macular central retinal thickness before and after treatment

Prior to treatment, the best corrected visual acuity and macular central retinal thickness had no statistically significant difference in both groups ($p$ > 0.05). After treatment, the best corrected visual acuity was elevated and the macular central retinal thickness was diminished ($p$ < 0.05), and the changes were more apparent in the combination group than the control group ($p$ < 0.05, Table 3).

**Table 3** Comparison of the best corrected visual acuity and macular central retinal thickness in both groups before and after treatment.

| Group | Case | Best corrected visual acuity | | Macular central retinal thickness (cm) | |
|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment |
| Combination group | 62 | 0.13 ± 0.04 | 0.45 ± 0.15 * | 347.82 ± 86.37 | 228.94 ± 52.16 * |
| Control group | 60 | 0.12 ± 0.05 | 0.22 ± 0.10 * | 354.68 ± 92.40 | 273.41 ± 63.87 * |
| $t$ | | 1.222 | 9.931 | -0.424 | -4.218 |
| $p$ | | 0.224 | 0.000 | 0.672 | 0.000 |

Note: compared to before treatment: *$p$ < 0.05.

### 3.3 Comparison of Retinal hemodynamic indexes in both groups before and after treatment

Before treatment, there was no statistically significant difference in the levels of CRV, PSVCRA, EDVBF, BFRI, PI and Vm ($p$ > 0.05). Through treatment, the CRV, BFRI and PI levels were decreased ($p$ < 0.05) and the PSVCRA, EDVBF and Vm levels were increased ($p$ < 0.05) in both groups; however, the changing trends were more notable in the combination group than the control group ($p$ < 0.05, Table 4).

### 3.4 Comparison of oxidative stress indicators in both groups before and after treatment

In both groups, GSH-Px, AOPP and TAOC levels had no statistically significant difference before treatment ($p$ > 0.05). After treatment, GSH-Px and TAOC levels were elevated, while AOPP level was lessened in both groups ($p$ < 0.05). Also, the changes were more significant in the combination group than the control group ($p$ < 0.05, Table 5).

**Table 4** Comparison of Retinal hemodynamic indexes in both groups before and after treatment.

| Observation indicators | | Combination group (n = 62) | Control group (n = 60) | *t* | *p* |
|---|---|---|---|---|---|
| CRV (cm/s) | Before treatment | 5.36 ± 0.28 | 5.41 ± 0.32 | -0.919 | 0.360 |
| | After treatment | 3.74 ± 0.46 * | 4.12 ± 0.58 * | -4.016 | 0.000 |
| PSVCRA (cm/s) | Before treatment | 8.21 ± 1.13 | 8.16 ± 0.74 | 0.288 | 0.774 |
| | After treatment | 12.34 ± 0.72 * | 9.64 ± 1.29 * | 14.335 | 0.000 |
| EDVBF (cm/s) | Before treatment | 2.46 ± 0.35 | 2.53 ± 0.46 | -0.948 | 0.345 |
| | After treatment | 4.97 ± 1.04 * | 3.72 ± 0.94 * | 6.957 | 0.000 |
| BFRI | Before treatment | 0.89 ± 0.15 | 0.91 ± 0.27 | -0.508 | 0.612 |
| | After treatment | 0.48 ± 0.07 * | 0.62 ± 0.10 * | -8.982 | 0.000 |
| PI | Before treatment | 1.65 ± 0.22 | 1.70 ± 0.34 | -0.967 | 0.335 |
| | After treatment | 1.12 ± 0.43 * | 1.38 ± 0.32 * | -3.779 | 0.000 |
| Vm (cm/s) | Before treatment | 5.32 ± 0.95 | 5.28 ± 1.14 | 0.211 | 0.833 |
| | After treatment | 7.91 ± 1.37 * | 6.54 ± 0.92 * | 6.463 | 0.000 |

Note: compared to before treatment:*$p < 0.05$.

**Table 5** Comparison of oxidative stress indicators in both groups before and after treatment.

| Group | Case | GSH-Px (U/mL) | | AOPP (μmol/L) | | TAOC (IU/mL) | |
|---|---|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Combination group | 62 | 128.37 ± 21.89 | 169.58 ± 34.83 * | 28.36 ± 5.42 | 14.21 ± 2.48* | 13.25 ± 2.46 | 24.50 ± 3.62* |
| Control group | 60 | 130.25 ± 23.14 | 150.26 ± 24.56 * | 27.90 ± 4.65 | 19.35 ± 2.17 * | 12.93 ± 2.88 | 18.49 ± 2.76 * |
| *t* | | -0.461 | 3.532 | 0.502 | -12.167 | 0.661 | 10.287 |
| *p* | | 0.646 | 0.001 | 0.616 | 0.000 | 0.510 | 0.00 |

Note: compared to before treatment:*$p < 0.05$.

### 3.5 Comparison of angiogenesis-related factors in both groups before and after treatment

There was no statistically significant difference in VEGF and PEDF levels before treatment ($p > 0.05$). The treatment signally diminished VEGF level and augmented PEDF level ($p < 0.05$), and the changes were more remarkable in the combination group than the control group ($p < 0.05$, Table 6).

**Table 6** Comparison of angiogenesis-related factors in both groups before and after treatment.

| Group | Case | VEGF (pg/mL) | | PEDF (μg/mL) | |
|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment |
| Combination group | 62 | 158.27 ± 20.89 | 122.94 ± 24.86 * | 342.16 ± 25.73 | 486.24 ± 31.08 * |
| Control group | 60 | 157.62 ± 21.43 | 143.18 ± 23.55 * | 340.78 ± 26.45 | 392.83 ± 26.44 * |
| *t* | | 0.170 | -4.614 | 0.292 | 17.853 |
| *p* | | 0.866 | 0.000 | 0.771 | 0.000 |

Note: compared to before treatment:*$p < 0.05$.

## 4 Discussion

It has been reported that the incidence of DR is 33% in diabetes patients, and the incidence of retinopathy is as high as 90% in patients with diabetes more than 10 years. The rate of blindness caused by DR is 16.4%, which seriously affects people's life quality and social activities [11-12]. Accordingly, this study intervened in DR patients using TCM external treatment combined with Qiju Dihuang pill and explored its clinical efficacy. Persistent hyperglycemia can damage the blood-retinal barrier, cause hypoxic endothelial cells, and activate hypoxia inducible factor-1 α (HIF-1 α) which can mediate the secretion of vascular factors such as VEGF by endothelial cells, and VEGF can participate in angiogenesis by binding to specific receptors, leading to DR and affecting retinal hemodynamics [13]. This study indicated that TCM external treatment combined with Qiju Dihuang pill had better clinical efficacy on DR patients through improving visual acuity and retinal hemorheology, reducing the macular central retinal thickness and inhibiting angiogenesis, and had certain clinical promotion and application value. Qiju Dihuang pill is mainly composed of *Corni Fructus*, *Rehmanniae Radix Praeparata*, *Moutan Cortex*, *Dioscoreae Rhizoma*, *Alismatis Rhizoma, Poria*, *Chrysanthemi Flos*, *Lycii Fructus*, and *Astragali Radix*. Of them, *Corni Fructus* can promote astriction and stem desertion and prevent qi exhaustion, *Rehmanniae Radix Praeparata* can tonify essence and supplement marrow, *Moutan Cortex* can circulate blood and remove stasis, *Dioscoreae Rhizoma* can tonify kidneys and benefit essence, *Alismatis Rhizoma* has the function of transforming turbidity and reducing lipid, *Poria* can promote urination and drain dampness, *Chrysanthemi Flos* can disperse wind and remove heat, *Lyii Fructus* can moisten the lung and improve eyesight, and *Astragali Radix* can promote bowel movement. These medicinal materials together can benefit qi, tonify yin, nourish liver and kidney, circulate blood and remove stasis [2]. The modern pharmacology indicated that Astragalus polysaccharides in *Astragali Radix* mainly promote pancreatic islets β cell proliferation and inhibit cell apoptosis to enhance the sensitivity to insulin and alleviate the high glucose [14]. It has been reported that Qiju Dihuang Pills has better effect on reducing glycated hemoglobin of DR patients [15]. Qiju Dihuang pill can effectively reduce the blood sugar level of patients with DR [16]. Meanwhile, astragaloside A extracted from *Astragali Radix* can repress retinal cell apoptosis, effectively protecting ganglion cells and improving vision in DR patients [17]. *Lycii Fructus* can block the advanced glycation end products (AGEs) and the receptor for AGEs signaling pathway, effectively alleviate retinal vascular occlusion caused by the accumulation of AGEs, improve endothelial cell hypoxia, reduce the secretion of vascular factors such as VEGF, repress angiogenesis and formation, and prevent and treat DR [18]. Danshen injection can promote microvessel relaxation, reduce blood viscosity, accelerate microcirculation, further improve hemodynamic level and prognosis of DR [19]. Compound Danshen Dripping Pills prevents early DR through vascular and neuroprotection, it improved cellular disarrangement, and reduced vascular permeability and the expression levels of inflammatory factors in both the retina and serum; moreover, Compound Danshen Dripping Pills resisted vascular leakage, and inhibited oxidative stress to provided protective effects in DR [20]. In addition, ocular ion-introduction of Danshen injection refers to make the effective ion components and charged colloidal particles pass through the eyelid skin, conjunctiva, and cornea to enter the eye, greatly prolonging the action time of the drug in the patient's body and improving the absorption rate [21]. Danshen Injection is injected into bilateral Zusanli aupoint, and electroacupuncture of Zusanli mainly regulates the activity of glycogen synthase kinase (GSK-3 β) signaling molecules in pancreas and hippocampus,

reduces the expression level of phosphorylated TAU protein in hippocampus, mediates blood glucose to a certain extent, and prevents or improves the condition of DR [22]. Collectively, TCM external treatment combined with Qiju Dihuang pill had better clinical efficacy on DR patients through improving visual acuity and retinal hemorheology, effectively reducing the macular central retinal thickness and inhibiting angiogenesis, which thus had better therapeutic effects than the single use of Qiju Dihuang pill.

Oxidative stress is one of the vital mechanisms of DR, the occurrence and progression of which are generally accompanied by the continuous accumulation of free radical toxins that may disrupt the oxidative-antioxidant balance [23]. The results of this study unveiled that the combination of TCM external treatment and Qiju Dihuang pill can effectively alleviate oxidative stress in DR patients. The modern pharmacology showed that the total iridoid glycosides of *Corni Fructus* in Qiju Dihuang pill can dampen the activity of xanthine oxidase, rapidly increase the content of GSH-Px, thus reduce the accumulation of hydrogen peroxide and effectively alleviate oxidative stress damage induced by DR [24]. Danshen injection can inhibit inward flow of calcium ions in DR patients, diminish intracellular calcium ion overload, counteract lipid peroxidation, and further reduce inflammatory response [25]. At the same time, the salvianolic acid component in Danshen injection has the effect of clearing superoxide anions and inhibiting lipid peroxidation, which can reduce the levels of lipid peroxides and attenuate oxidative stress [26]. Zusanli acupoint is one of the main acupoints in the stomach meridian of foot-Yangming, and has the effects of tonifying qi of the spleen and stomach, unblocking meridians and collaterals, dispersing wind and dampness, and reinforcing healthy qi to eliminate pathogenic factors, which is mainly used to treat symptoms of deficiency and consumption that is in line with the pathogenesis of deficiency-caused blood stasis in DR [27]. Based on this, the combination of TCM external treatment and Qiju Dihuang pill can effectively alleviate oxidative stress in DR patients.

## 5 Conclusion

Collectively, TCM external treatment combined with Qiju Dihuang pill has a good clinical efficacy in treating DR patients, which can improve vision and retinal hemorheological indicators, reduce the macular central retinal thickness and inhibit oxidative stress and angiogenesis, and has certain clinical promotion and application value. For the treatment of patients with DR, this study provides more data support for the combination therapy approach and provides more treatment options for patients. However, there is also room for improvement in our research, such as short research cycles, insufficient sample size, a certain risk of bias in the results. Hence, the future research should further prolong research cycles, expand sample size, and refine animal experiments to probe into the efficacy and mechanism of the combined therapy on DR and provide theoretical basis for clinical application.

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## Conflicts of Interest

The author(s) declare(s) no conflicts of interest.

## Author Contributions

Substantial contributions to conception and design: X.W. Data acquisition, data analysis and interpretation: Y.X. Drafting the article or critically revising it for important intellectual content: Y.X. Final approval of the version to be published: All authors. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved:

All authors.

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## Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

## References

[1] VUJ0SEVII S, ALDINGTON S J, SILVA P, et al. Screening for diabetic retinopathy: new perspectives and challenges. *Lancet Diabetes Endocrinol* 2020; 8(4): 337-347.

[2] Li HM, Yao PY, Li XH. Clinical study on Qiju Dihuang Pills combined with extract of ginkgo biloba leaves in treatment of nonproliferative diabetic retinopathy. *Drugs & Clinic* 2020; 35(6): 1176-1180.

[3] Tan TE, Wong TY. Diabetic retinopathy: Looking forward to 2030. *Frontiers in endocrinology* 2023; 13: 1077669.

[4] Chong DD, Das N, Singh RP. Diabetic retinopathy: Screening, prevention, and treatment. *Cleveland Clinic Journal of Medicine* 2024; 91(8): 503-510.

[5] Liu HY, Ji QX, Peng MZ, et al. Study on the Mechanism and Effects of Astragali Radix in Treating Diabetic Retinopathy. *Chinese Journal of Information on Traditional Chinese Medicine* 2023; 30(4): 58-64.

[6] Liao TT, Huang Q, Zhang CT, et al. Experience of Professor XIE Chunguang in Treating Nonproliferative Diabetic Retinopathy from "Deficiency" and "Blood Stasis" *Journal of Sichuan of Traditional Chinese Medicine* 2019; 37(2): 1-3.

[7] Sabiiti W, consortium T. Beyond the Numbers: Interpreting WHO ' s Global Tuberculosis Report 2016 to Inform TB Policy and Practice in the East African Community. *The East African health research journal* 2017; 1(1): 2-7.

[8] Sun Y, Cai TY, Chen J, et al. An evidence map of clinical practice guideline recommendations and quality on diabetic retinopathy. *Eye (London, England)* 2020; 34(11): 1989-2000.

[9] SOLA-ADELL C, BOGDANOV P, HERNANDEZ C, et al. Calcium dobesilate prevents neurodegeneration and vascular leakage in experimental diabetes. *Current eye research* 2017; 42(9): 1273-1286.

[10] Lin WX, Yu QY, Qin YS, et al. To explore the clinical efficacy of Traditional Chinese Medicine bath in the treatment of psoriasis vulgaris with blood-heat syndrome and its effect on related cytokines based on different temperature and different concentration. *Medicine (Baltimore)* 2020; 99(19): e20172.

[11] Tian X, Wang Z, Yang WH, et al. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. *Journal of Nurses Training* 2019; 34(12): 1100-1103.

[12] Yuan M, Jin W, Hao XL, et al. Research advances in the pathogenesis of neurovascular injury in diabetic retinopathy. *Recent Advances in Ophthalmology* 2020; 40(9): 885-888.

[13] Song SJ, Han K, Choi KS, et al. Trends in diabetic retinopathy and related medical practices among type 2 diabetes patients: Results from the National Insurance Service Survey 2006-2013. *Journal of Diabetes Investigation* 2018; 9(1): 173-178.

[14] Tang SM, Yang ZM, Chen WQ, et al. Astragalus polysaccharide improves type 2 diabetes mellitus in rats by protecting islet β cells. *Academic Journal of Second Military Medical University* 2017; 38(4): 482-487.

[15] Li HD, Li MX, Zhang WH, et al. Effectiveness and safety of traditional Chinese medicine for diabetic retinopathy: A systematic review and network meta-analysis of randomized clinical trials. *World Journal of Diabetes* 2023; 14(9): 1422-1449.

[16] Wu YF. Observation on the effect of Qiju Dihuang Pills in the adjuvant treatment of diabetic retinopathy. *Zhongguo Xiangcun Yiyao*. 2018; 25(19): 22-23.

[17] Wang YL, Fang ZH. Experience of FANG Zhaohui inTreating Early Diabetic Retinopathy with Ligustrum Fructus-Dogwood-Astragalus decoction. *Clinical Journal of Traditional Chinese Medicine* 2022; 34(8): 1431-1434.

[18] KATAGIRI M, SHOJI J, INADA N, et al.Evaluation of vitreous levels of advanced glycation end products and angiogenic factors as biomarkers for severity of diabetic retinopathy. *International ophthalmology* 2018; 38(2): 607-615.

[19] Liu J, Li L, Feng F, et al. Effect of Salvia Miltiorrhiza Injection in the treatment of type Ⅱ respiratory failure and its influence on respiratory function and hemodynamics. *China Medical Herald* 2019; 16(21): 147-150.

[20] Liu L, Li X, Cai W, et al. Coadministration of Compound Danshen dripping pills and bezafibrate has a protective effect against diabetic retinopathy. *Frontiers in Pharmacology* 2022;

13:1014991.

[21] Ke BH, Yuan Y, Peng SQ. Observation on the efficacy of external treatment of traditional Chinese medicine as an adjunct treatment for diabetic retinopathy. *International Medicine & Health Guidance News* 2021; 27(16): 4.

[22] Yuan F, Hong XP, Duan YJ, et al. Electroacupuncture at "Zusanli" (ST36) ameliorates tau hyperphosphorylation in pancreas and hippocampus of diabetic rats. *Acupuncture Research* 2021; 46(11): 901-906+947.

[23] Tangvarasittichai O, Tangvarasittichai S, Oxidative Stress. Ocular Disease and Diabetes Retinopathy. *Current Pharmaceutical Design* 2018; 24(40): 4726-4741.

[24] Pi WX, Cai BC, Xu HQ, et al. Protective Effects of Iridoid Glycoside from Corni Fructus on Type 2 Diabetes with Nonalcoholic Fatty Liver in Mice. *Traditional Chinese Drug Research and Clinical Pharmacology* 2003; (1): 23-24.

[25] Chen P, Liu Y. Effects of Somatostatin Combined with Salvia Miltiorrhiza Injection on In-flammatory Factor and Acute and Chronic Health Scores in Patients with Severe Acute Pancreatitis. *China & Foreign Medical Treatment* 2022; 41(35): 128-131.

[26] Feng YH, Li HY, Qin C. Clinical effect of astragalus injection combined with salvia miltiorrhiza injection in the treatment of chronic obstructive pulmonary disease and its effect on oxidative stress in patients. *Shaanxi Journal of Traditional Chinese Medicine* 2018; 39(08): 1048-1050.

[27] Wang J, Yu Y, Zhang HL, et al. Effects of Ginkgo Leaves Extract injection at Zúsānlǐ acupoint on arterial blood flow, hemorheology and angiogenesis index of lower extremity arteries in diabetic patients with peripheral vascular disease. *China Medical Herald* 2020; 17(18): 81-86.