Shanxi Eye Hospital

Mission statement of in-house research fund program

Project category: Innovation Fund, Doctoral Fund ☐ Youth Fund

Microbial research team ☐
Ophthalmology specialty alliance ☐

Project number: C202302

Project name: Development of new efficacy of 7-leaf yam double glycoside eye drops and treatment of presbyopia

Project leader: Zhang Yu

Funding amount: 50,000 yuan

Made in 2023

Implementation period: From January and February 2023 to January and February 2 0 2 5

Date of filing: 2024. 1.7

Shanxi Eye Hospital

Made in 2023

Fill in the form

1. This project plan and task book is designed by the in-house research fund project of Shanxi Provincial Eye Hospital.

Ii. This task book should be printed on both sides of A4 paper. If there is not enough space in each column, please add a page by yourself, and bind it on the left side (do not use binding methods with protruding edges such as rubber ring or folder).

3. All contents of the project plan and task book should be factual and truthfully filled in one by one, and foreign words should be expressed in both original and Chinese.

Iv. The project implementation period is 2 years.

V. This project plan and task book is in duplicate. It shall become a formal contract upon being formally approved and signed by Shanxi Provincial Eye Hospital.

Project undertakers commitment:

I guarantee the authenticity of the content of the task book. I will perform my duties as the project leader, strictly abide by the provisions of the Management Measures for Scientific Research Projects of Shanxi Provincial Eye Hospital, effectively guarantee the research time, conscientiously carry out the work, and submit relevant materials on time. If the information is false or violates the regulations, I will take full responsibility.

There is no such thing as not doing scientific research, but being listed as the first person in charge and the first author of a paper. The problem of nominal registration of the first patent inventor and the first host of the award;

There is no problem of profiting from the use of someone elses name or occupation of his/her scientific research projects and achievements, so as to gain benefits in terms of job promotion, professional title promotion, talent title, bonus and performance distribution;

There is no problem of applying for multiple projects with the same or very similar research content as the project leader, illegally listing or occupying others research funds;

There is no illegal interference or intervention in various review activities such as scientific research projects, achievement awards, talent plans and professional title evaluation, and there is no problem of "talking" or "going through connections" in the above review activities; there is no other serious violation of scientific research integrity, scientific research ethics, academic norms and academic style.

Signature of the applicant: 

Project leader	surname and personal name	Zhang Yu	sex	[redacted]	date of birth	[redacted]		
	record of formal schooling	[redacted]	academic degree	[redacted]	professional ranks and titles	[redacted]	post	
	work unit	Shanxi Eye Hospital			Department of residence	pharmaceutical preparation section		
	ambit	pharmacy						
Partner information	name of organization							
	1.							
	2.							
	3.							

Background and basis of the project	(400 words limit) Presbyopia (Pb), characterized by difficulty focusing clear images on the retina when viewing nearby objects, predominantly affects individuals over 40 years old and significantly impacts daily life. However, China has yet to report the approval of presbyopia treatment drugs. The theory of presbyopia accommodation mechanism suggests that human eye regulation is closely related to ciliary muscle contraction. Studies have shown that the active ingredients in the marketed drug, Sarcosin and Digitalis Glycosides Eye Drops, can synergistically enhance ciliary muscle function. These findings suggest that Sarcosin and Digitalis Glycosides Eye Drops may improve presbyopia through enhanced ciliary muscle regulation. Nevertheless, its therapeutic effects remain unreported. This study will pioneer the first validation of Sarcosin and Digitalis Glycosides Eye Drops presbyopia treatment efficacy by comparing visual quality changes between treatment and control groups. Furthermore, we will employ optometric techniques and optical scanning methods to analyze indicators including accommodation function, anterior segment OCT, and ocular perfusion data, aiming to elucidate the therapeutic mechanism. We hope this research will bridge the gap in presbyopia drug development in China.

1. Research significance and relevance to national needs:

We are currently undergoing the Fourth Industrial Revolution, which requires our visual systems to be capable of viewing and interpreting screen information from smartphones and laptops in both work and daily life, placing higher demands on near vision. With the accelerating pace of aging, presbyopia not only causes significant inconvenience in peoples daily work and life but also hinders Chinas economic development, becoming a pressing social challenge. However, there has been no reported approval for presbyopia treatment drugs in China to date. Research shows that the marketed drug, Silymarin and Digitalis Glycosides Eye Drops, contains two active components—silymarin and digitalis glycosides—which can jointly act on the ciliary muscle to effectively enhance its regulatory function. These findings suggest that Silymarin and Digitalis Glycosides Eye Drops may also improve ciliary muscle regulation to treat presbyopia. This project will, for the first time, verify the therapeutic effects of Silymarin and Digitalis Glycosides Eye Drops on presbyopia by comparing quality changes before and after treatment between the experimental group and control group. It will elucidate the therapeutic mechanism, fill a gap in current presbyopia drug research, improve patients quality of life and work productivity, and reduce economic losses caused by presbyopia.

2. Research content, new methods and technical routes to be adopted, key problems to be solved, test scale and main indicators:

【 research contents 】

(1) Changes in subjective visual quality and objective visual quality of subjects and control group before and after treatment, as well as contrast sensitivity function (CSF), diffusion function (PSF), modulation transfer function (MTF) and so on.

(2) Effects of different pupil diameters (PD) and frequency bands on higher-order aberrations (HOA) under different presbyopia conditions with different severity.

(3) Research on the influence of adjustment function and higher order aberration on visual quality and discussion on related mechanism.

(4) The dose-effect relationship between treatment course and effect under different severity of presbyopia conditions.

[Research Programme]

Research object: 30 cases of presbyopia patients who visited our hospital and met the inclusion criteria of this study.

Exclusion criteria: ① Age 40-55 years; ② After cycloplegic refraction, exclude cases if one eye has a refractive power greater than-0.5D~2.0D or astigmatism exceeding 1.0D; ③ For uncorrected distance vision (UDVA) below 1.25 or uncorrected near vision (UNVA) above 0.8 in both eyes, exclude cases using standard logarithmic visual acuity charts; ④ Use slit-lamp examination according to LOCS protocol

The three-tier screening criteria for cataract development are as follows: ① Exclusion criteria include: NO3-NC3 lens opacity or more severe opacities detected, or presence of ocular surface diseases, visual fatigue, any corneal conditions (dry eye syndrome, corneal injury, corneal opacity, keratoconus, or history of refractive surgery); ② Exclusion criteria for subjects who have used digitoxin digoxin diphosphate eye drops within two weeks, or those with known/suspected allergies to digitalis drugs, or taking insulin, anti-anxiety medications, antidepressants, antipsychotics, antihistamines, antispasmodics, or diuretics.

This project has been approved by the ethics committee of this hospital.

Research and work in

Experimental protocol: The treatment group received Eclipta Paridis Dioscin Eye Drops (Suiduling Pharmaceutical Co., Ltd., Germany), while the control group received normal saline (Otsuka Pharmaceutical Co., Ltd., China). Administration was 1 drop per eye per application, three times daily, for both eyes. Each treatment course lasted two weeks, with a total of two courses administered. All patients discontinued other similar medications, glucocorticoids, and analgesics during treatment.

Subject withdrawal or termination: The subject has the right to voluntarily withdraw from this study at any time for any reason without specifying the specific reason. In each follow-up visit, if ocular surface disease signs or unilateral or bilateral IOP higher than 21mmHg are found, the case will be excluded.

Statistical analysis: SPSS19.0 software was used for statistical analysis, and Spearman correlation coefficient was used to analyze the correlation.

Observation method:

(1) The short-range activity visual questionnaire (NAVQ) was used to investigate the quality of life of patients.

(2) Instrumental examination. Before and after treatment: ① Measure uncorrected visual acuity under 30 lux and 180 lux conditions, including 5m uncorrected distance vision (UDVA), 80cm intermediate vision (UIVA), 30cm near vision (UNVA), and corrected vision using the same examination method after subjective refraction, including multiple measurements

Far vision (CDVA), corrected intermediate vision (CIVA), corrected near vision (CNVA), DCNVA, far corrected intermediate vision (DCIVA and CSF, refractive power (D), astigmatism (DC) and so on.

② Total higher-order aberrations, spherical aberration,慧差 and three-leaf aberration of the whole eye and lens in the frequency regions of 3c/d, 6c/d and 12~18c/d with pupil diameters of 3mm and 6mm, recording PSF and MTF. ④ OCT sweep frequency anterior pupillary diameter (PD), lens thickness (LT) and lens dome height

(LV), anterior chamber depth (ACD), anterior and posterior surface curvature, etc.

Therapeutic evaluation:

(1) Therapeutic effect and evaluation of therapeutic effect according to different severity.

(2) Calculation of the rate of removing glasses: the rate of removing glasses = the number of patients who removed glasses/total number ×100%, which is calculated to calculate the rate of removing glasses in close reading after treatment.

(3) Satisfaction assessment: Questionnaires were used to investigate and evaluate whether the subjects had visual interference symptoms and their satisfaction degree after treatment.

(4) Safety assessment: evaluate whether adverse reactions such as stinging, conjunctival congestion, photophobia, redness and so on occurred during medication. Grouping method:

Implementation of Centralized Randomized Blinding: Statistical professionals independent of the research team generate randomized allocation sequences based on study protocols. Group information is sealed in opaque envelopes. After participants are enrolled and baseline assessments completed, researchers follow procedures to open the envelopes and deblind the groups. This ensures that group assignment remains concealed during enrollment and baseline data collection phases, thereby preventing selection bias.

blind method ：

Double-blind design: subjects, investigators (including efficacy assessment and data recording personnel), and statisticians were unaware

Group Information. Both drug groups use identical containers and packaging with identical dosing instructions to maintain blinding. Group information is managed by an independent third party using sealed password-protected envelopes and a central randomization system. Blinding is only lifted by the third party following

predefined protocols after data lock-up at study completion or in the event of serious adverse events. Blinding information is not disclosed to the research team.

The treatment group received a seven-leaf digitoxin total glycoside eye drop (Pharma Stulln GmbH, Import Drug Registration No.: 0909803; H20130295). Patients were instructed to use one drop in each affected eye three times daily, strictly following aseptic techniques. Care was taken to prevent contact between the dropper and the ocular surface.

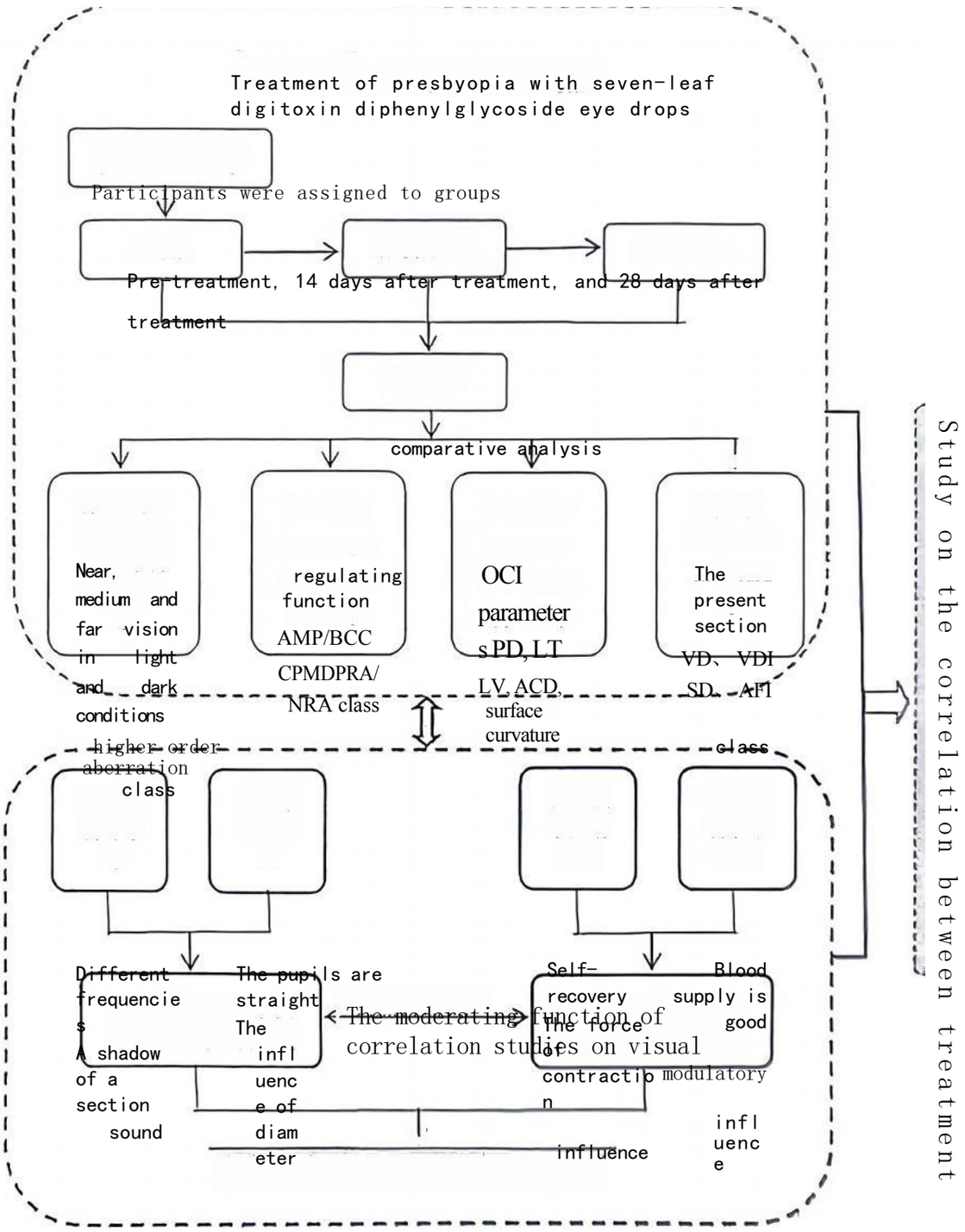
The control group received an equal amount of sterile, preservative-free and non-irritating saline solution. The containers were packaged in the same appearance, specifications, and labels as the treatment group. Only the designated personnel responsible for group management in the research team knew the grouping information, while the subjects were unaware of their own group to maintain the double-blind status. Both groups received treatment for one month.

[Key issues to be resolved]

(1) The correlation between higher-order aberrations (tHOA), differential spherical aberration (TSA), cloverleaf aberration (TT), and慧差 (TC) and adjustment functions such as adjustment amplitude (AMP), adjustment response (BCC), adjustment sensitivity (CPM), and positive/negative adjustment (PRA/NRA).

(2) The variation of wavefront higher-order aberration (WA) and its mechanism during the treatment.

【 technology roadmap 】



3. Expected project results (including publishing relevant papers, applying for invention patents, training talents, making contributions to the construction of academic degrees, etc.)

[Expected Research Results]

(1) Theoretical achievements: The therapeutic effect of saponin dioscin eye drops on presbyopia was clarified, the therapeutic mechanism was elucidated, and the therapeutic effect of the same degree of presbyopia was scientifically evaluated, providing a new direction for the treatment of presbyopia.

(2) Publication of papers: Publish 2 high-quality academic papers.

(3) Academic conferences: Participate in one domestic academic conference.

(4) Talent training: teach 1-2 interns.

4. Project schedule by stage (time is accurate to month)

temporal interval	The schedule of the project and the main research work to be completed
2023.12～2024.12	Continue to collect clinical subjects, complete the selection and grouping of subjects, clinical treatment and observation data collection, experimental data summary, data analysis.
2025.01～2025.12	Write and publish papers, summarize projects.

6. Project budget unit: 10,000 yuan			
Budget of source of funds		Budget of expenditure	
subject	Budget figures	subject	Budget figures
Total project investment	5	Budget expenditure summary	5
(1) Application for grants	5	1. Equipment costs	
(2) Other funds		2. Material cost	0.9
		3. Test, laboratory and processing costs	
		4. Fuel and power costs	
		5. Travel costs	0.2
		6. Conference costs	0.3
		7. Collaborative research and exchange fees	
		8. Publication/literature/information dissemination/intellectual property affairs fee	0.9
		9. Labor costs	1.7
		10. Expert consultation fees	
		11. Compensation for subjects and other	1.0

		expenses	

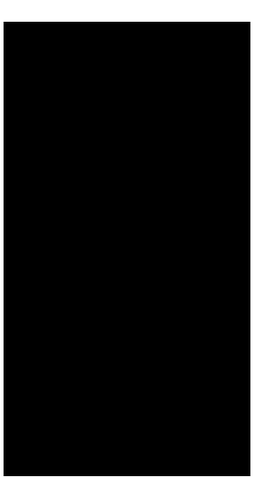
7. Expected social and economic benefits after the completion of the project

This groundbreaking project addresses the critical pathological mechanism where ciliary muscle regulation influences presbyopia development, while addressing Chinas current shortage of presbyopia treatment options. It establishes the feasibility of using the marketed drug Erythromycin Dihydrochloride Eye Drops for presbyopia management. This innovation not only provides a simple, safe, and effective medication selection for presbyopia treatment, alleviating the work-life inconveniences caused by myopia complications, but also significantly enhances quality of life and productivity. Furthermore, it demonstrates substantial market potential and economic value in the field.

8. Form, content and opinions of the cooperative unit

1. Forms and contents of cooperation

2. Opinions of the cooperative unit (on the content, form of cooperation, quality of participants and guarantee of working conditions, etc.) sign specific opinions:



9. Sign the task book

Project Manager (signature)

[redacted]

January 8, 2024

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Opinions of project undertaking unit:

agree

Unit responsible [redacted]
person
(signature)

[redacted] ter Date: 18th
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