

Chemical Composition, Pharmacological Effects and Clinical Research Progress of Hexuemingmu Tablets

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Abstract: *Hexue Mingmu tablet is a commonly used Chinese patent medicine for the treatment of retinopathy and fundus hemorrhagic diseases. It is made of 19-flavored medicine from Chuanxiong, Angelica, Red Pae, Radix, Moganlian, Nvzhenzi, Puhuang, Danpi, Danshen, Chongweizi Composition. This article reviews the chemical composition, pharmacological effects of Hexuemingmu tablets, the pharmacological effects and clinical applications of Hexuemingmu tablets, in order to provide a theoretical basis for the subsequent in-depth development and utilization and development.*

Keywords: *Hexuemingmu tablets; chemical composition; pharmacological effects; clinical application; review*

1. Introduction

The prescription of Hexuemingmu tablets is derived from the Pharmacopoeia of the People's Republic of China (2020 Edition)^[1]. It involves the combination of Siwu Decoction, Erzhi Pills, and Shengpuhuang Decoction. It has the effect of cooling the blood, removing blood stasis, stopping nourishing yin, nourishing the liver, and improving eyesight. It is mainly used to treat fundus bleeding caused by liver yin deficiency, liver yang hyperactivity, and hot wounds. It is a specialized drug used in traditional Chinese medicine to treat ophthalmological hematological conditions. Hexue Mingmu are primarily used for syndrome differentiation and treatment in traditional Chinese medicine. with modern pharmacological research, traditional Chinese medicine effectively stops bleeding in the early stages. In the middle and later stages, it promotes the absorption of blood stasis by improving circulation in the fundus. It possesses therapeutic properties such as "stopping bleeding without causing blood stasis, eliminating blood stasis without harming the blood, nourishing stagnant blood, and the blood without coagulation." This helps to achieve the goal of harmonizing qi and blood. Research shows that He Xuemingmu tablets have anticoagulant, antivascular endothelial, and hemorheological improvement properties, as well as anti-inflammatory and anti-swelling pharmacological effects. Clinically, it is mainly used to treat ophthalmic diseases such as retinal vein occlusion (RVO), diabetic retinopathy (DR), wet age-related macular degeneration (wAMD), glaucoma, anterior chamber and vitreous hemorrhage. This article aims to provide a comprehensive overview of the chemical composition, pharmacological effects, and clinical application progress of Hexuemingmu tablets. The information presented here will serve as a valuable reference for the rational clinical application and future experimental research of this medication.

2. Chemical composition

Through literature review, collation and collation of relevant compound information with representative pharmacological effects in the treatment of ophthalmic diseases, see Table 1.

Table 1: The main chemical components of He Xue Ming Mu Tablet

Category	Compound	Molecular Formula	Relative molecular mass	CAS Number	Source	Literature
Flavonoids	Puxin glycoside	C34H42O20	770.68	104472-68-6	Puhuang	[2]
	Plumin-3-O-new orange peel glycoside	C28H32O16	624.54	55033-90-4	Puhuang	[2]
	Plumin-3-O-rutin glycoside	C28H32O16	624.54	604-80-8	Puhuang	[2]
	Wood rhinoceros	C15H10O6	286.24	491-70-3	Ink dry lotus, chrysanthemum	[3,4]
	Acacia acacia	C16H12O5	284.26	480-44-4	Ink dry lotus	[3]
	Nayphenol	C15H10O6	286.24	520-18-3	Sadako, hawthorn	[3,5]
	Quercetin	C15H10O7	302.24	117-39-5	Chrysanthemum, hawthorn	[4,5]
	Celery vegetarian	C15H10O5	270.24	520-36-5	Chrysanthemum Root of large-flowered skullcap	[4]
	Scutellin	C21H18O11	446.36	21967-41-9	Root of large-flowered skullcap	[6]
	Scutellaria	C15H10O5	270.24	491-67-7	Root of large-flowered skullcap	[6]
	Salvia miltamine I	C18H12O3	276.29	568-73-0	Root of red-rooted salvia Root of red-rooted salvia	[7]
	Salvia miltamine IIA	C19H18O3	294.34	568-72-9	Root of red-rooted salvia	[7]
	Danpiol	C9H10O3	166.17	552-41-0	Danpi and Danshen	[7,12]
Phenolic acids	Danol Acine A	C26H22O10	494.45	96574-01-5	Danshen	[7]
	Danol Acid B	C36H30O16	718.61	115939-25-8	Danshen	[7]
	Rosemary acid	C18H16O8	360.31	20283-92-5	Danshen	[7]
	Salvia miltiorrhiza rophylic acid	C9H10O5	198.17	76822-21-4	Danshen	[7]
	Original catechin acid	C7H6O4	154.12	99-50-3	Red peony	[8]
	Feruric acid	C10H10O4	194.18	1135-24-6	Scouring rush Chuanxiong	[9,10]
	Caffeic acid	C9H8O4	180.16	331-39-5	Scouring rush	[9]
	Neochlo	C16H18O9	354.31	327-97-9	Chuanxiong, Angelica	[10,11]
Phenylphthalein	Gaoben lactone	C12H14O2	190.24	81944-09-4	Chuanxiong, Angelica	[10,11]
	Yangchuan lactone A	C12H16O2	192.25	62006-39-7	Chuanxiong, Angelica	[10,11]
	Yangchuan lactone H	C12H16O4	224.25	94596-27-7	Chuanxiong, Angelica	[10,11]
	Yangchuan lactone I	C12H16O4	224.25	94596-28-8	Chuanxiong, Angelica	[10,11]
Monoterpenes	Paeoniflorin	C23H28O11	480.46	23180-57-6	Red peony	[8]
	Benzoyl peony glycoside	C30H32O12	584.57	38642-49-8	Danpi	[12]
	Benzoyl oxidized peony glycoside	C30H32O13	600.57	72896-40-3	Danpi	[12]
Tanned	five galactyl glucose	C41H32O26	940.68	14937-32-7	Red peony	[8]
Quinones	Meijue Mingzi	C16H12O5	284.26	477-85-0	Cassia seed	[13]
	Orange-yellow cassia	C17H14O7	330.29	67979-25-3	Cassia seed	[13]
	Huang Jue Mingsu	C19H18O7	358.34	70588-06-6	Cassia seed	[13]
Alkaloid	Chuanxiangzine	C8H12N2	136.19	1124-11-4	Chuanxiong	[10]

3. Pharmacological effects

Up until now, there has been no research conducted on the pharmacological mechanism of

Hexuemingmu tablets in the treatment of fundus hemorrhagic diseases. Therefore, this paper discusses the pharmacological effects of anticoagulants, substances that are active in the vascular endothelium, improvement of hemorheology, anti-inflammatory properties, and reduction of swelling in the treatment of various ophthalmic conditions using Xuemingmu tablets.

3.1. Anticoagulation

At present, it is widely recognized that the common indicators reflecting the coagulation function of the human body are prothrombin time (PT), activated partial thromboplastin time (APTT), and thrombin time (TT). Guo Qi et al. [14] conducted studies that found high compatibility between paeonol and peony glycoside. The high dose group (Danpiphem 50 mg·kg⁻¹ + peony glycoside 12.5 mg·kg⁻¹), medium dose group (Danpiphem 25mg·kg⁻¹+ peony glycoside 6.25mg·kg⁻¹), and low dose group (Danpiol 12.5 mg·kg⁻¹+ peony glycoside 3.125 mg·kg⁻¹) were able to significantly inhibit adenosine diphosphate (ADP) and anodylene tetraenic acid-induced platelet aggregation in rabbits. Furthermore, the high and medium-dose combination of paony was found to significantly prolong the TT and total coagulation time. Cui Guozhen et al. [15] found that *Salvia miltiorrhiza* can reduce thrombin-induced platelet aggregation by regulating platelet-associated proteins and decreasing coagulation factor activity. In addition, quinone compounds, michin glucoside, orange deamine glucoside, and xanrin glucoside all inhibit platelet aggregation [16].

3.2. Antivascular endothelial active substance

Blood stasis syndrome is often associated with the secretion of vascular activity factors by vascular endothelial cells. Lena et al. [17] found that paeoniflorin, a chemical compound found in paeony, primarily regulates vascular endothelial function in rats. It increases the content of nitric oxide (NO) and reduces the level of endothelin-1 (endothelin), thereby improving the condition of blood stasis syndrome. NO and ET-1 are a pair of interacting vascular active substances. ET-1 has a strong effect on constricting blood vessels, while NO has the effect of dilating blood vessels, improving microcirculation, and altering cell adhesion [18]. In addition, tanshinone I, tanshinone IIA, tanthylphenolic acid A, and tanthanoic acid B can act on key targets related to blood stasis, such as thrombin, plasminogen activator inhibitor-1, peroxidase prolifer activator α , and 3-hydroxy-3-methylpentadiyl coenzyme A reductase. This action helps to activate blood circulation and remove blood stasis [19].

3.3. Improving hemorheology

Hemorheology mainly includes indicators such as blood viscosity and red blood cell deformation ability. Whole blood viscosity (WBV), plasma viscosity (PV), erythrocyte sedimentation rate (ESR), and packed cell volume (PCV) are commonly used indicators of blood viscosity. Red blood cells, platelets, and plasma can affect the viscosity of whole blood. Li Wei et al. [20] found that paeonol can significantly enhance the deformability of red blood cells by reducing whole blood viscosity (WBV) and packed cell volume (PCV), as well as inhibiting erythrocyte aggregation and platelet adhesion. This, in turn, affects hemorheology indicators. In addition, Xie et al. [21] found that peony glycoside, peony lactone glycoside, galonyl glucose, and prophyllic acid can significantly reduce whole blood viscosity (WBV), plasma viscosity (PV), erythrocyte sedimentation rate (ESR), and packed cell volume (PCV).

3.4. Anti-inflammatory

Yang Huan et al. [22] used lipopolysaccharide (LPS) to induce an inflammatory response in BV2 cells. It was found that the activation of Toll-like receptors (TLR4) reduces the release of inflammatory factors such as tumor necrosis factor alpha (TNF- α) and interleukin-1 β (IL-1 β), thereby improving the inflammatory response. Danshinone IIA may inhibit LPS-induced nuclear factor-kappaB (NF- κ B) by suppressing signaling pathways, such as mitogen-activated protein kinase (MAPK), to exert anti-inflammatory activity [23]. Quercetin can exert an anti-inflammatory effect by inhibiting the expression of cytokines and inducible nitric oxide synthase (iNOS) through the NF- κ B pathway [24].

4. Clinical application

4.1. Retinal vein occlusion

RVO is a retinal vascular disease characterized by retinal edema, bleeding, blood stasis, and vein dilation. Most of the patients are accompanied by complications, such as macular edema, which can be very harmful to visual function. At present, the exploration of the optimal treatment for retinal vein occlusion remains a focal point and a hot topic in clinical research. Traditional Chinese medicine has demonstrated promising prospects in its treatment. Li Jianhua^[25] randomly divided 108 patients with retinal vein occlusion (RVO) into two groups. The control group was treated with Jingdi Danhong injection, while the observation group received oral Xuemingmu tablets. The results showed that the overall efficiency of the observation group was 98%, which was 82% higher than the overall efficiency of the control group ($P<0.05$). The observation group could better promote the absorption, which can effectively improve the patient's vision. Zhuang Jingling^[26] used Xuemingmu tablets in combination with Leizhuzumab to treat retinal vein occlusion (RVO) accompanied by macular edema. The results showed that the total efficiency of the observation group, which received combined drugs, was 93.48%, which was significantly better than the control group that received Leizhuzumab alone 80.43% ($P<0.05$). The observation group treated symptoms such as blurred vision, dark shadow, visual deformation, macular edema, and retinal hemorrhage. Additionally, the group showed improvement in retinal circulation time, macular central concave retina thickness, and vision compared to the control group. Zhao Dongxian et al.^[27] selected 80 patients with macular edema caused by retinal vein occlusion (RVO) and randomly divided them into two groups. The control group received retinal laser photocoagulation, while the observation group received retinal laser photocoagulation along with blood eye tablets in addition to the control group. The results showed that the clinical efficacy, vision, and blood flow density of the deep retinal capillary layer were observed to have a significant improvement ($P<0.05$). Additionally, the levels of serum inflammatory factors (IL-1 β , TNF- α) and VEGF (vascular endothelial growth factor) in the observation group were significantly reduced ($P<0.05$). In summary, He Xue Mingmu tablets have a significant curative effect on patients with RVO (Retinal Vein Occlusion), and the medication is convenient, making it worthy of clinical promotion and application.

4.2. Diabetic retinopathy

DR (Diabetic Retinopathy) is one of the common chronic complications of diabetes. The clinical manifestations include symptoms such as flying mosquito disease, blurred vision, diplopia, vision loss, and even blindness. Zhang Yurong and colleagues^[28] discovered that Xuemingmu tablets can significantly enhance the visual function of patients, yielding significant results. Wang Xuemei et al.^[29] demonstrated that Xuemingmu tablets, when combined with prostir, have a positive clinical effect in the treatment of DR. The overall effective rate of the treatment group was 91.84%, whereas the effective rate of prostir treatment alone was only 70.83%. The treatment group was found to be superior to the control group ($P<0.05$) in terms of maintaining retinal blood flow stability, reducing levels of inflammatory factors IL-2, IL-10, and TNF- α , improving retinal microcirculation, and reducing fundus lesions. Zhou Liwen^[30] studied the clinical effect of diabetic retinopathy (DR) with fundus hemorrhage. On the basis of receiving conventional hypoglycemic drugs, 160 patients were randomly divided into two groups: the Hexuemingmu tablet group and the hemostatic aromatic acid group. The results showed that the therapeutic effect of Hexuemingmu tablets was superior to that of hemostatic aromatic acid, and the rate of adverse reactions was low. These findings suggest that Hexuemingmu tablets are a promising option for clinical use. Yin Li et al.^[31] observed the efficacy of laser photocoagulation therapy combined with Xuemingmu tablets in the treatment of DR with macular edema and its effect on serum vascular endothelial growth factor (VEGF). The results showed that the combined treatment group was able to significantly reduce the serum VEGF level in patients, improve retinal edema and macular edema, and consistently enhance the visual function of patients. These findings are noteworthy and merit clinical recommendation.

4.3. Wet age-associated macular degeneration

wAMD refers to retinal edema, exudation, bleeding, and other symptoms that occur due to the presence of choroidal neovascular or retinal neovascular vessels in the macular area. It may also be accompanied by scar-like changes in the macular area. The pathogenesis is still unclear, and the rate of vision loss is as high as 90%^[32]. wAMD has become one of the leading causes of blindness in the elderly. At present, antivascular endothelial growth factor (anti-VEGF) has become the primary

treatment for patients with wet age-related macular degeneration (wAMD). However, during the treatment process, there is a risk of macular atrophy progression, formation of fundus scars, and the patient's vision returning to the baseline level within five years after treatment. In addition, there is a risk of infection with multiple vitreous injections and numerous challenges^[33]. He Xuemingmu tablets have a positive impact on retinal hemorrhagic edema caused by wAMD, with minimal side effects, and can reduce the duration of the patient's illness. It has been recommended as a therapeutic drug in the Clinical Application Guide for Proprietary Chinese Medicine in the Treatment of Age-related Macular Degeneration (Wet)^[34]. Xu Chao et al.^[35] collected 96 patients with wet age-related macular degeneration (wAMD). Patients in the treatment group were orally administered Xuemingmu tablets in combination with Leizhu intraglobular injection, while patients in the control group were given Lehumuzumab intraglobular injection. By comparing the best correction of vision, the thickness of the retina in the macular area, macular bleeding area, exudation area, cumulative damage area, and the recurrence of macular edema, the treatment group showed a more significant improvement in these indicators ($P < 0.05$). This suggests that the combination of Xuemingmu tablets and Leizhumab in the treatment of wAMD can reduce the extent of fundus damage and delay the recurrence of macular edema and bleeding. At the same time, it is cost-effective and safe, making it suitable for clinical promotion and application. Zhan Yu et al.^[36] collected 104 patients with wet age-related macular degeneration (wAMD) and randomly divided them into two groups. The control group received a vitreous injection of antivascular endothelial growth factor drugs, while the treatment group was administered Xuemingmu tablets in addition to the same injection given to the control group. The results showed that the total efficiency of the treatment group was significantly higher than that of the control group, with a percentage of 94.23%. Additionally, the treatment group demonstrated better improvement in vision, posterior ciliary artery blood flow, central concave thickness, and choroid neovascular area of choroids compared to the control group ($P < 0.05$). It shows that He Xuemingmu tablets can regulate blood flow in the eyes. Combined use of treatment in patients with wet age-related macular degeneration (wAMD) and macular hemorrhage can promote absorption of fundus hemorrhage, reduce the thickness of the macular center, stabilize the neovascular area, and improve corrected vision. This treatment approach is safe and reliable.

4.4. Glaucoma

Glaucoma is a disease that causes blindness in the eye. It is characterized by progressive damage to the optic nerve and visual field defects, which are caused by increased pressure inside the eye. It is the second leading cause of blindness in the world, after cataracts. Although drug treatment and surgery have effectively controlled intraocular pressure in some patients, the damage to the optic nerve continues to increase in others. Therefore, the reduction of intraocular pressure, protection of the optic nerve, and emphasis on optic nerve regeneration are the focal points and challenges of ophthalmological research. Chen Yanting et al.^[37] found that Xuemingmu tablets, when combined with sodium cytocholine, can effectively reduce intraocular pressure, improve vision, modify visual evoked potential, regulate eye hemodynamic indicators, decrease serum beta endorphins, and increase serum epithelial factor levels. It has a positive clinical effect on patients with glaucoma and does not increase the occurrence of adverse drug reactions. It is a safe and effective treatment plan. Huang Heling et al.^[38] used Xuemingmu tablets in combination with Mi Kebao to treat patients following glaucoma surgery. It was found that the average sensitivity of the postoperative visual field in patients was reduced. The edema of the optic nerve fiber layer in postoperative patients was also reduced. Additionally, the retinal nerve fiber layer was observed to thin over an extended period of time. These findings suggest that the treatment has a certain protective effect on the postoperative optic nerve function of glaucoma patients.

4.5. Blood accumulation in the anterior chamber

Anterior chamber bleeding caused by blunt eye trauma is the most common type of bleeding. It is primarily caused by the rupture of iris ciliary vessels or increased vascular permeability. Another cause is the rupture of the scleral venous sinus, leading to bleeding into the anterior chamber. Typical clinical manifestations include elevated intraocular pressure and decreased vision. Most of the blood accumulation in the anterior chamber can be absorbed on its own. When there is a significant amount of bleeding, it can lead to severe complications such as corneal blood staining and secondary glaucoma. These complications can cause eye pain, headaches, and vision loss in patients, ultimately impacting their quality of life. Li Xunyi et al.^[39] conducted a study in which 46 patients with traumatic level I and level II anterior chamber effusion were randomly divided into two groups. The control group received

symptomatic treatment, including the reduction of intraocular pressure and local eye anti-infection. The treatment group, in addition to the same treatment as the control group, was also administered Xueming tablets. It was found that the treatment group was able to significantly promote blood circulation and absorption, accelerate the patient's vision recovery, improve patient satisfaction, and have a significant impact. Zhang Haifang et al. [40] found that He Xue Mingmu tablets have a significant impact on the treatment of anterior chamber hematocephalus caused by blunt eyeball contusion and can be widely utilized.

4.6. Glass volume blood

Glass volume blood is a refractive interstitial vitreous opacity caused by eye trauma and fundus vascular lesions. It is a common eye disease. Xiangyang et al. [41] found that the treatment of vitreous hemorrhage with Xuemingmu tablets combined with Walitin tablets can enhance retinal circulation and the absorption of vitreous hemorrhage, improve retinal metabolism, and exhibit significant anti-inflammatory effects. This treatment approach reduces the formation and contraction of anterior retinal membranes and significantly shortens the treatment duration. Therefore, He Xuemingmu tablets are an effective drug treatment for vitreous hemorrhage in the early and middle stages.

5. Conclusions

In recent years, there have been numerous studies on the medicinal effects of various ingredients in the Hexue Mingmu tablet group. However, research on the interaction between the components of the entire group, the basis of the medicinal substance, and the metabolic process in the complete prescription is still lacking. Existing research on Hexue Mingmu tablets primarily focuses on clinical efficacy observation. In addition, attention should also be paid to the compatibility of Xuemingmu tablets' prescriptions. This will provide a theoretical basis for the comprehensive clinical application and subsequent research and development of related preparations.

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