

Mechanism of Action and Clinical Research Progress of Gastrodia and Uncaria Decoction in Treating Hypertension

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Abstract: Hypertension, a major global public health issue, affects 27.9% of adults in China, with approximately 245 million patients. However, treatment and control rates stand at only 45.8% and 16.8%, respectively, indicating a significant “diagnosis and treatment gap.” While modern Western drugs form the cornerstone of antihypertensive therapy, their single-target mechanisms often induce residual symptoms like dizziness and headaches, along with long-term side effects, and provide insufficient protection for target organs. Against this backdrop, the unique advantages of Traditional Chinese Medicine (TCM)—its holistic regulation and multi-target interventions—become increasingly prominent. As a classical formula, Tianma Gou Teng Yin centers on calming liver yang and extinguishing wind, while also clearing heat, promoting blood circulation, and tonifying the liver and kidneys—aligning with the “excessive liver yang” pathogenesis of hypertension. This study systematically reviews the hypotensive mechanisms and clinical application progress of Tianma Gou Teng Yin through literature retrieval and analytical synthesis. Tianma Gou Teng Decoction regulates blood pressure through multiple synergistic pathways: First, it inhibits excessive activation of the renin-angiotensin-aldosterone system (RAAS), reducing levels of angiotensin II (Ang II) and aldosterone (ALD); Second, it modulates vascular endothelial function by upregulating nitric oxide (NO) and suppressing endothelin-1 (ET-1). Third, it inhibits inflammation mediated by the nuclear factor kappa-B (NF-κB) pathway while enhancing antioxidant enzyme activity, such as superoxide dismutase (SOD). Network pharmacology further reveals its “multi-component-multi-target-multi-pathway” characteristics. Components such as gastrodin and uncarin act on targets like AKT1 and CASP3 to regulate MAPK and PI3K-Akt signaling pathways. Combining Gastrodia and Uncaria Decoction with Western medications significantly enhances antihypertensive efficacy and alleviates symptoms like dizziness and insomnia without increasing adverse reaction risks. Its protective effects on target organs such as the heart and kidneys have also been validated: it delays left ventricular hypertrophy by inhibiting the renin-angiotensin-aldosterone system (RAAS) and reduces renal injury by lowering urinary microalbuminuria. However, current research still faces challenges including insufficient mechanistic depth, room for improvement in clinical evidence quality, and a lack of standardized formulations. Future efforts should include multicenter randomized controlled trials to optimize efficacy evaluation, integrate metabolomics and gut microbiota research to deepen mechanism analysis, and establish quality control standards for herbal materials. This study provides scientific basis for the clinical translation of Gastrodia and Uncaria Decoction and expands new perspectives for its application in complex disease management.

Keywords: Gastrodia and Uncaria Decoction, Hypertension, Mechanism of Action, Clinical Research, Review.

1. Introduction

1.1 Current Status and Challenges in Hypertension Prevention and Control

The current status of hypertension prevention and control is severe, presenting significant challenges. According to the Chinese Hypertension Prevention and Treatment Guidelines (2024 Revised Edition) and World Health Organization reports, the prevalence of hypertension among Chinese adults reaches 27.9%, affecting approximately 245 million individuals. However, the treatment rate and control rate stand at only 45.8% and 16.8%, respectively [1]. This indicates that the blood pressure of the vast majority of patients remains unmanaged, exposing them to persistent risks of damage to target organs such as the heart, brain, and kidneys. While modern drug therapies have demonstrated significant efficacy in blood pressure reduction—with calcium channel blockers and angiotensin-converting enzyme inhibitors forming the cornerstone of treatment—limitations persist. On one hand, some patients continue to suffer from clinical symptoms like dizziness, headaches, and insomnia even when blood pressure targets are met. On the other hand, long-term medication may cause side effects such as coughing and edema, and the deep

protective effects on target organs remain insufficient [2]. It is precisely these “diagnostic and therapeutic gaps” and “efficacy bottlenecks” that highlight the unique advantages of Traditional Chinese Medicine (TCM) in holistic regulation and multi-targeted intervention. TCM attributes hypertension to liver dysfunction, closely linked to liver-kidney yin deficiency and liver yang hyperactivity. Treatment emphasizes “calming liver yang and nourishing liver-kidney yin.” Research indicates that classical formulas such as Gastrodia and Uncaria Decoction not only synergize with Western medications to achieve stable blood pressure reduction but also alleviate subjective symptoms, improve vascular endothelial function, and suppress inflammatory responses through multiple pathways. This demonstrates a multi-faceted, systemic therapeutic approach [3], offering a crucial complementary strategy for hypertension prevention and management.

1.2 TCM Research on Tianma Gou Teng Decoction

Tianma Gou Teng Yin, documented in Hu Guangci’s modern work *New Perspectives on the Diagnosis and Treatment of Miscellaneous Internal Diseases in Traditional Chinese Medicine*, stands as a classic representative formula for

treating Liver Yang Rising Syndrome. This formula comprises multiple herbs including gastrodia tuber (Tianma), Uncaria root (Gou Teng), raw oyster shell (Shijueming), gardenia fruit (Shan Zhi), scutellaria root (Huang Qin), Sichuan achyranthes root (Chuan Niuxi), eucommia bark (Du Zhong), motherwort herb (Yimu Cao), mulberry mistletoe (Sang Jisheng), night-blooming cereus stem (Ye Jiao Teng), and poria cocos (Fu Shen). Its formulation embodies rigorous principles: Tianma and Gou Teng serve as sovereign herbs, excelling in calming the liver and extinguishing wind. Shijueming, with its salty, cold, and heavy nature, functions as a minister herb to pacify the liver, subdue yang, clear heat, and improve vision. Chuan Niuxi directs blood downward, promotes blood circulation, and drains water, also acting as a minister herb. Gardenia and Scutellaria clear liver fire and reduce heat; Eucommia and Mulberry Parasite tonify the liver and kidneys; Leonurus promotes blood circulation and diuresis; Polygonum multiflorum and Poria calamus calm the mind and soothe the spirit. Together, these herbs achieve the effects of calming liver wind, clearing heat, promoting blood circulation, and tonifying the liver and kidneys. It is primarily indicated for headaches, dizziness, and insomnia caused by excessive liver yang and liver wind disturbing the mind. In traditional Chinese medicine theory, symptoms like headaches, dizziness, and insomnia commonly seen in hypertension patients are often attributed to liver and kidney yin deficiency. This deficiency leads to liver yang rising in excess, generating fire and wind that disturb the clear orifices—a condition known as “liver yang rising in excess.” Therefore, the syndrome pattern addressed by Tianma Gou Teng Decoction aligns closely with the clinical manifestations of hypertension. Consequently, modern clinical practice frequently employs it for treating hypertension of the liver yang hyperactivity pattern. Observations indicate that it not only assists in lowering blood pressure but also significantly improves accompanying symptoms such as dizziness, headache, and irritability.

2. Mechanism of Action of Tianma Gou Teng Decoction in Treating Hypertension

2.1 Core Pharmacological Pathways

The mechanism of action of Tianma Gou Teng Decoction in treating hypertension primarily manifests through its multi-targeted, multi-pathway pharmacological activity. Its core pharmacological pathways include systematic regulation of neuroendocrine and vascular functions, along with significant anti-inflammatory and antioxidant stress effects.

Regarding neuroendocrine and vascular function regulation, Gastrodia and Uncaria Decoction inhibits excessive activation of the renin-angiotensin-aldosterone system (RAAS). Clinical studies reveal that combining this formula with Western medications significantly reduces plasma angiotensin II (Ang II) and aldosterone (ALD) levels in patients with liver yang hyperactivity-type hypertension, with greater reduction than Western medication alone [4]. Concurrently, the formula exerts distinct regulatory effects on vascular endothelial function by correcting imbalances through upregulating the vasodilator nitric oxide (NO) and suppressing the potent vasoconstrictor endothelin-1 (ET-1). Experimental studies confirm that Tianshagouteng Decoction significantly reduces

plasma ET-1 levels in spontaneously hypertensive rats (SHR) while elevating aortic NO levels and improving endothelium-dependent vasodilation [5]. This ameliorative effect is closely associated with its suppression of vascular inflammation and oxidative stress. Regarding anti-inflammatory effects, studies indicate that Tianma - Gouteng Decoction suppresses the activation of key inflammatory signaling pathways such as nuclear factor kappa-B (NF- κ B), thereby effectively downregulating the expression and release of pro-inflammatory factors like tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) [6]. Regarding antioxidant effects, this formula significantly enhances the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), while effectively reducing malondialdehyde (MDA) levels—a marker of oxidative damage end products. This strengthens the body's antioxidant defense capabilities and mitigates reactive oxygen species (ROS)-induced damage to vascular endothelium [5, 6]. Furthermore, network pharmacology studies predict that its active components (such as gastrodin and uncarin) may act on core targets including ACE, AKT1, VEGFA, and IL-6 to synergistically regulate calcium signaling pathways and PI3K-Akt signaling pathways. This provides a systemic explanation for its multi-target pharmacological basis [7].

Tianma Gou Teng Decoction exerts its effects not through a single target but via multiple pathways. These include inhibiting the overactivated RAAS, regulating vascular endothelial function, suppressing inflammatory responses, and mitigating oxidative damage. Together, these pathways form a synergistic network that stabilizes blood pressure and protects vascular target organs. This fully demonstrates the distinctive advantage of traditional Chinese medicine in treating complex diseases through multi-faceted, holistic regulation.

2.2 Target Organ Protection Effects

When treating hypertension, Gastrodia and Uncaria Decoction demonstrates efficacy not only through blood pressure reduction itself but also through distinct protective effects on key target organs such as the heart, kidneys, and blood vessels. These protective effects are partially independent of its antihypertensive action, highlighting the unique advantage of multi-target intervention in traditional Chinese medicine.

Regarding cardiac protection, Tianma Gou Teng Decoction has been proven to effectively reverse hypertension-induced left ventricular hypertrophy and myocardial fibrosis. Experimental studies indicate that this formula significantly reduces left ventricular weight (LVW) and left ventricular weight index (LVI) in rats with renovascular hypertension, while also decreasing myocardial collagen concentration. Its efficacy is comparable to that of the conventional Western medication captopril. This effect is closely associated with its mechanism of inhibiting the activation of the local renin-angiotensin-aldosterone system (RAAS). Research indicates that Tianshahouteng Decoction simultaneously reduces plasma and myocardial tissue levels of angiotensin II (Ang II) and aldosterone (ALDO) in model rats, whereas captopril only lowers Ang II without affecting ALDO. This

suggests Tianshahouteng Decoction may offer more comprehensive regulation of the RAAS [8].

Regarding vascular protection, Gastrodia and Uncaria Decoction improves vascular remodeling and delays atherosclerosis progression. Its mechanism of action results from multi-pathway synergism. First, it exhibits significant anti-inflammatory activity. Studies indicate that its active components (such as gardenoside and baicalin) synergistically inhibit the activation of the nuclear factor kappa-B (NF- κ B) signaling pathway, thereby reducing the production and release of key pro-inflammatory factors like tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) [9]. Secondly, it possesses potent antioxidant stress capabilities, enhancing the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD) and reducing malondialdehyde (MDA) levels—a marker of oxidative damage—thereby mitigating direct damage to vascular endothelium caused by reactive oxygen species (ROS) [10]. These synergistic effects collectively contribute to restoring vascular endothelial function, inhibiting abnormal proliferation and migration of vascular smooth muscle cells, and thereby delaying the progression of hypertensive vascular lesions.

Regarding renal protection, Tianma-Gouteng Decoction demonstrates ameliorative effects on early renal injury. Research has focused on its impact on sensitive markers of early renal damage, such as urinary microalbumin (mALB) and urinary β 2-microglobulin (β 2-MG). Experimental evidence indicates that spontaneously hypertensive rats (SHR) treated with the modified Tianma Gou Teng Decoction exhibited significantly reduced urinary excretion of mALB and β 2-MG [11]. This finding suggests that Tianma-Gouteng Decoction may exert a protective effect on the kidneys and delay the progression of hypertensive nephropathy by mitigating the damage caused by hypertension to the glomerular filtration barrier and tubular reabsorption function.

Through synergistic multiple pharmacological mechanisms including local RAAS inhibition, anti-inflammatory effects, and antioxidant activity, Tianma-Gouteng Decoction effectively controls blood pressure while exerting distinct protective effects on the heart, blood vessels, and kidneys affected by hypertension. This provides a robust pharmacological foundation for its broad clinical application.

2.3 Modern Pharmacological Research

Network pharmacology research strategies have profoundly revealed the synergistic characteristics of Tianma-Gouteng Decoction in treating hypertension through a “multi-component-multi-target-multi-pathway” approach from a systems biology perspective. The core approach involves screening active components and action targets of the formula through public databases, intersecting them with hypertension disease targets to construct a complex “component-target-pathway-disease” network [12].

Research indicates that the chemical composition of Gastrodia and Uncaria Decoction is highly complex. One analysis identified 1,272 chemical constituents in the formula, with 73 bioavailable components further detected in the serum of

Parkinson’s disease mice post-administration. Among these, 15 compounds were predicted to potentially cross the blood-brain barrier and exert effects [13]. These serum-bound components, considered potential pharmacologically active constituents, encompass diverse structural types including phenolic acids, flavonoids, and alkaloids. Separate studies on gastrodin monotherapy suggest parishin-type compounds, nucleosides, and organic acids (e.g., adenosine, ferulic acid) may constitute its key antihypertensive active ingredients [14].

At the target level, network prediction results showed exceptional richness. Intersection analysis identified 135 disease-related core targets, with nodes such as JUN, AKT1, TP53, RELA, and CASP3 occupying pivotal positions in the network [15]. These targets do not operate in isolation but form a complex interaction network (protein-protein interaction network), jointly regulating multiple biological processes including apoptosis, inflammatory response, and proliferation [16].

Further pathway enrichment analysis (KEGG) revealed that the antihypertensive effects of Gastrodia and Uncaria Decoction are closely associated with multiple signaling pathways. These pathways extensively involve cancer-related pathways, endocrine resistance, lipid and atherosclerosis, IL-17 signaling pathways, TNF signaling pathways, etc. [12]. Notably, pathways directly linked to hypertension pathogenesis—cAMP signaling, calcium signaling, and MAPK signaling—were also significantly enriched [15]. This suggests that Tianma-Gouteng Decoction may achieve systemic blood pressure regulation by modulating vascular smooth muscle contractility, influencing neurotransmitter release, and intervening in inflammatory and apoptotic processes.

Molecular docking techniques provide robust support for these predictions. Studies indicate that key active components in Tianma-Gouteng Decoction, such as quercetin, kaempferol, and luteolin, exhibit strong binding affinity with core targets including JUN, AKT1, and CASP3 [12]. For instance, ferulic acid exhibits high binding stability with the transcription factor NFE2L2 [13], computationally validating the reliability of network predictions.

Network pharmacology research links the traditional efficacy of Gastrodia and Uncaria Decoction (calming liver wind) to modern molecular mechanisms, elucidating its complex network of multi-target regulation through synergistic actions of components like gastrodin, uncarin, quercetin, and others on AKT1, CASP3, IL-6, thereby regulating multiple signaling pathways including MAPK, PI3K-Akt, and cAMP. This provides modern scientific evidence for understanding the holistic regulatory effects of traditional Chinese medicine formulas.

3. Clinical Research and Application of Gastrodia and Uncaria Decoction

3.1 Synergistic Effects in Integrated Chinese-Western Medicine Treatment

Multiple rigorously designed clinical studies confirm that

Tianma Gou Teng Yin, when combined with conventional Western medications (such as calcium channel blockers and angiotensin-converting enzyme inhibitors), produces a clear synergistic effect. Its advantages are evident in enhancing antihypertensive efficacy, improving clinical symptoms, and ensuring medication safety.

Regarding enhanced antihypertensive efficacy, a randomized controlled trial involving 80 patients with primary hypertension of the liver yang hyperactivity pattern demonstrated that the experimental group receiving Tianma-Gouteng Decoction in addition to conventional Western medication achieved significantly greater reductions in both systolic and diastolic blood pressure compared to the control group receiving Western medication alone. The study also found that combined therapy more effectively improved vascular endothelial function, manifested by a significant decrease in plasma levels of the potent vasoconstrictor endothelin (ET) and a significant increase in nitric oxide (NO), which has vasodilatory effects [17]. Another study in elderly hypertensive patients further confirmed that Tianma-Houteng Decoction combined with nifedipine not only effectively lowered blood pressure levels but also significantly improved 24-hour ambulatory blood pressure parameters. This included reductions in 24-hour mean systolic blood pressure, mean diastolic blood pressure, and their diurnal variation coefficients, thereby helping restore normal circadian blood pressure rhythms and enhancing the stability of blood pressure control quality [18].

The advantages of Gastrodia and Uncaria Decoction are particularly prominent in improving patients' clinical symptoms and quality of life. Results from a community hospital study showed that the combined treatment of Gastrodia and Uncaria Decoction with Western medicine achieved a clinical total effective rate of 95% for treating hypertension with liver yang hyperactivity pattern, significantly higher than the 77.5% rate in the Western medicine-only group [19]. Combination therapy demonstrated remarkable efficacy in alleviating typical symptoms of liver yang hyperactivity—including dizziness, headache, tinnitus, insomnia, irritability, and soreness in the lower back and knees—significantly reducing Traditional Chinese Medicine syndrome scores. This is primarily because the formula adheres to the therapeutic principle of “calming liver yang, extinguishing wind, clearing heat, and promoting blood circulation,” directly targeting the core pathogenesis of liver yang hyperactivity in hypertensive patients. This achieves a shift from merely treating symptoms to addressing the root cause.

Regarding drug safety, all aforementioned clinical studies reported that the incidence of adverse reactions when Tianma Gou Teng Yin was used in combination with Western medications showed no statistically significant difference compared to the Western medication-only group. No significant drug interactions were observed, indicating that this combination regimen possesses good safety and tolerability [17,19]. This provides important safety assurance for long-term clinical application.

3.2 Clinical Intervention for Target Organ Damage

The profound value of Gastrodia and Uncaria Decoction in hypertension treatment lies in its potential protective effects on target organs such as the heart and kidneys, which are crucial for delaying disease progression and improving long-term patient outcomes.

Regarding cardiac protection, its clinical effects are closely associated with established mechanisms such as inhibiting excessive activation of the renin-angiotensin-aldosterone system (RAAS) and exerting anti-inflammatory and antioxidant stress effects. Clinical studies reveal that Gastrodia and Uncaria Decoction significantly reduces plasma levels of angiotensin II (Ang II) and aldosterone (ALD) [20], key factors driving myocardial hypertrophy and fibrosis. By inhibiting this system, the decoction helps delay the onset and progression of hypertensive heart disease at its source. Supplementary evidence from animal studies indicates that Gastrodia and Uncaria Decoction reduces collagen fiber deposition and myocardial cell apoptosis in spontaneously hypertensive rats, thereby effectively reversing the pathological process of left ventricular hypertrophy [21].

Regarding renal protection, Tianma-Gouteng Decoction also demonstrates clear improvement in early hypertensive kidney injury. Clinical observations reveal that patients taking this decoction exhibit significantly reduced levels of urinary microalbumin (mALB) and urinary β 2-microglobulin (β 2-MG) [22]. These two indicators are sensitive markers for early assessment of impaired glomerular filtration barrier function and tubular reabsorption function. These findings suggest that Tianma Gou Teng Decoction may protect renal microarchitecture by alleviating inflammatory responses and oxidative stress in the kidneys, thereby exerting positive intervention and protective effects against hypertensive renal damage.

Extensive clinical evidence demonstrates that combining Tianma Gou Teng Decoction with conventional Western medication for treating liver yang hyperactivity-type hypertension fully embodies the integrated advantages of Chinese and Western medicine. This regimen not only achieves the “symptomatic” goals of synergistic blood pressure reduction and stabilization of blood pressure fluctuations but also significantly improves patients' subjective symptoms and quality of life. Through mechanisms such as RAAS system regulation, anti-inflammatory effects, and antioxidant properties, it provides profound protection against hypertension-induced damage to key target organs like the heart and kidneys. With its excellent safety profile, it represents a highly clinically valuable therapeutic strategy.

4. Summary and Outlook

As a classic TCM formula for treating liver yang hyperactivity syndrome, Tianma Gou Teng Yin's efficacy in “calming liver yang and extinguishing wind, clearing heat and activating blood, and tonifying liver and kidney” aligns closely with traditional TCM theory. Modern pharmacological research has progressively revealed its multi-component, multi-target, and multi-pathway action characteristics. Studies indicate that this formula possesses effects such as lowering blood pressure, inhibiting myocardial remodeling, and enhancing antioxidant capacity,

demonstrating favorable efficacy for cerebrovascular diseases including hypertension, stroke, and Parkinson's disease. Clinically, Gastrodia and Uncaria Decoction is widely applied in treating cardiovascular and cerebrovascular diseases like hypertension. Treatment typically involves integrated traditional Chinese medicine approaches, with close monitoring of blood pressure changes and adverse reactions. This demonstrates the intrinsic logical connection and scientific value of the formula, spanning traditional Chinese medical theory to modern pharmacology and clinical practice.

Current research still faces several limitations. First, regarding depth of mechanism, the complex pharmacological actions of Gastrodia and Uncaria Decoction have been primarily studied using serum pharmacology methods. Experimental indicators are relatively lagging, with many repetitive studies and few breakthrough advances. Second, the quality of clinical evidence requires improvement. Existing clinical research generally exhibits low methodological rigor, with efficacy evaluations often relying solely on subjective symptom improvement rather than objective measures. A systematic review on Gastrodia and Uncaria Decoction for treating hypertension due to liver yang hyperactivity also noted insufficient evidence in current studies, highlighting the low standardization of clinical research and a high likelihood of bias. Furthermore, efforts to standardize formulations are urgently needed. Research on the pharmacologically active components underlying the efficacy of the Tianma-Gouteng Decoction compound remains insufficient. Identifying these active components is essential for elucidating its therapeutic effects, mechanisms of action, safety profile, and quality control.

Future research on Gastrodia and Uncaria Decoction should pursue breakthroughs in multiple directions. The primary task is to conduct high-quality clinical research. Rigorous, large-scale, multicenter, randomized, blinded, placebo-controlled clinical trials are needed to further validate its efficacy and safety. Concurrently, cutting-edge technologies should be leveraged to deepen mechanistic exploration. Future efforts should include in-depth investigation of the mechanisms underlying Dendrobium-Uncaria Decoction's effects on neurological disorders such as Parkinson's disease and epilepsy, while also undertaking holistic research on its pharmacodynamic foundation. Furthermore, advancing the standardization of herbal materials and formulations is crucial. Establishing precise quality specifications for herbal ingredients will provide benchmarks for evaluating Tianma-Gouteng Decoction's quality, thereby ensuring the stability and reliability of its clinical efficacy. Collaborative efforts among multiple teams to conduct large-scale, high-quality clinical efficacy studies will undoubtedly provide a more robust scientific foundation for the clinical application of Tianma-Gouteng Decoction.

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