Advances in Research on Compatibility of Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis in Treatment of Hypertension

Miaoxin ZHANG[1], Yunjiao YUAN[1], Chen YANG[1], Jinfeng CHEN[2]*

1. Shaanxi University of Chinese Medicine, Xianyang 712046, China; 2. Shaanxi Provincial Hospital of Traditional Chinese Medicine, Xi'an 710004, China

Abstract Based on multidisciplinary research methods, this study analyzes the mechanisms and potential of Gastrodiae Rhizoma (Tianma) and Uncariae Ramulus Cum Uncis compatibility in treating hypertension. The research confirms that components including rhynchophylline and gastrodin exert antihypertensive effects by inhibiting vascular smooth muscle proliferation and modulating calcium signaling pathways. The combination of these two herbs enhances the bioavailability of core components, synergistically regulates targets such as PTGS2 and NOS3, activates the PPAR signaling pathway, and strengthens vasodilation and antioxidant capacity. Clinical studies demonstrate that Tianma Gouteng Decoction exhibits superior efficacy in improving mitochondrial function and delaying vascular aging compared to single components. This investigation provides scientific evidence for the multi-target antihypertensive effects of traditional Chinese medicine and promotes its modern application in cardiovascular disease treatment.

Key words Gastrodiae Rhizoma (Tianma), Uncariae Ramulus Cum Uncis (Gouteng), Drug pair, Hypertension

1 Introduction

Hypertension is a common chronic disease and a risk factor for diseases with high mortality and disability rates such as stroke and myocardial infarction. Persistent progression of hypertension can easily increase the risks of other conditions including heart failure, chronic kidney disease, and atherosclerosis. With economic development and lifestyle changes, the onset of hypertension shows a trend of affecting younger populations. The *Chinese Guidelines for Hypertension Prevention and Treatment* (2018 edition) specifically listed the prevalence rates among young adults aged 18 - 44: 4.0% for 18 - 24 years old, 6.1% for 25 - 34 years old, and 15.0% for 35 - 44 years old[1]. The substantial number of young patients warrants attention. The pathogenesis of hypertension primarily involves multiple factors, including sympathetic nervous system hyperactivity, renal sodium retention, vascular endothelial cell damage, insulin resistance, and activation of the Renin - Aniotension - Aldosterone System (RAAS)[2].

Although Western medical treatments (*e.g.*, diuretics, calcium channel blockers) can effectively control blood pressure, issues such as long-term medication side effects and poor patient compliance remain prominent. Traditional Chinese Medicine (TCM) categorizes hypertension under "vertigo" and "headache," attributing its pathogenesis to liver yang hyperactivity and the close interplay of wind, fire, phlegm, and blood stasis. In recent years, national research on TCM for cardiovascular disease prevention and treatment has deepened, and the clinical efficacy of TCM in managing hypertension has become increasingly significant. The multi-link, multi-pathway, and multi-target characteristics of Chinese herbal medicine not only lower blood pressure but also improve microcirculation, protect endothelial function, and regulate vascular active substances, demonstrating considerable advantages and potential, making it a current research priority[2]. The herbal pair of Gastrodiae Rhizoma (Tianma) and Uncariae Ramulus Cum Uncis (Gouteng), a classic combination for calming the liver and extinguishing wind, has shown notable efficacy in hypertension treatment, yet its synergistic mechanisms remain to be systematically elucidated. This article integrates modern research methodologies to deeply analyze their active components, therapeutic targets, and compatibility synergy mechanisms, aiming to provide scientific evidence for the modernization of TCM.

2 Hypotensive mechanism of single drug

2.1 Uncariae Ramulus Cum Uncis (Uncaria rhynchophylla)

Has a cool nature and sweet taste, belonging to the liver and pericardium meridians. It is a commonly used medicinal herb in traditional Chinese clinical practice, known for its effects of calming wind to relieve convulsions, clearing heat, and pacifying the liver. Its antihypertensive characteristics manifest as an initial blood pressure reduction, followed by a rapid rise, and then sustained lowering of blood pressure. A study[3] employing microinjection into the femoral vein of rats combined with common carotid artery cannulation for pressure measurement found that rhynchophylline (32.1%), isorhynchophylline (42%), total alkaloids of Uncariae Ramulus Cum Uncis, and non-alkaloid components all exhibit antihypertensive effects, with rhynchophylline and isorhynchophylline identified as the primary active constituents. Further research[4] demonstrated that Uncariae Ramulus Cum Uncis alkaloids prevent and treat hypertensive vascular remodeling through the following mechanisms: inhibiting vascular smooth muscle cell (VSMC) proliferation in the thoracic aorta of spontaneously hypertensive rats (SHR); downregulating c-myc and c-fos protein expression; and reducing PDGF-B mRNA expression levels. Additionally, the total alkaloids of Uncariae Ramulus Cum Uncis

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Miaoxin ZHANG, master's degree candidate. *Corresponding author. Jinfeng CHEN, master's degree, deputy chief physician.

achieve vasodilation, inhibit platelet aggregation, and exert cardiovascular protective effects by elevating nitric oxide (NO) levels[5]. Network pharmacology studies[6] revealed that Uncariae Ramulus Cum Uncis (Gouteng) contains 11 active ingredients that exert efficacy through synergistic regulation of 29 hypertension-related targets, of which PTGS1 and PTGS2 are the common targets of all ingredients. Meanwhile, PTGS1 and PTGS2 are also the core targets of atherosclerosis, and flavonoids such as quercetin and kaempferol can stably combine with PTGS1 and PTGS2 to intervene in the process of atherosclerosis[7]. Studies[6] have confirmed that the active ingredients of Uncariae Ramulus Cum Uncis reduce blood pressure through multiple pathways: (i) act on PTGS1/PTGS2 to inhibit platelet aggregation; (ii) inhibit the release of Ca^{2+} through the calcium signaling pathway to relax vascular smooth muscle; (iii) block β receptors to reduce peripheral vascular resistance.

2.2 Gastrodiae Rhizoma *Gastrodia elata* is a liver-calming and wind-extinguishing medicinal herb in traditional Chinese medicine, with a sweet taste and neutral nature, primarily attributed to the liver meridian. It excels in extinguishing wind to relieve convulsions and suppressing liver yang hyperactivity, particularly effective in treating various vertigo syndromes. Its clinical compatibility for vertigo treatment is widely applied: it is often combined with Uncariae Ramulus Cum Uncis, *Cyathula officinalis*, *Haliotis discus* hannai, and others to form Tianma Gouteng Decoction, treating dizziness and headaches caused by liver yang hyperactivity, synergistically exerting heat-clearing, liver-calming, and blood-descending effects. For vertigo, headaches, chest tightness, and nausea due to wind-phlegm upward disturbance, it can also be combined with Pinelliae Rhizoma (Banxia), Atractylodis Macrocephalae Rhizoma (Baizhu), Poria (Fuling), and other spleen-strengthening and dampness-drying herbs to resolve phlegm, extinguish wind, fortify the spleen, and eliminate dampness. In treating hypertension of yin deficiency with yang hyperactivity type, Gastrodiae Rhizoma is frequently combined with Uncariae Ramulus Cum Uncis, Haliotidis Concha (Shijueming), Cyathulae Radix (Chuanniuxi), Rehmanniae Radix (Shengdihuang), Eucommiae Cortex (Duzhong), Chrysanthemi Flos (Juhua), and other heat-clearing, liver-calming, yin-nourishing, and blood-descending herbs to enhance therapeutic efficacy[8].

Cai Shunbi *et al.*[9] discovered through network pharmacology research that 14 active components in Gastrodiae Rhizoma can regulate circadian rhythm, vasoconstriction, calcium ion homeostasis, and other processes, thereby achieving antihypertensive effects. Gastrodiae Rhizoma may control blood pressure levels through a multi-component, multi-pathway, multi-target mechanism. Transcriptomic studies by Zhu Jiayu *et al.*[10] further revealed that the antihypertensive mechanism of Gastrodiae Rhizoma is closely associated with the regulation of PTGS2 (Prostaglandin-Endoperoxide Synthase 2) and NOS3 (Nitric Oxide Synthase 3) gene expression, as well as the activation of the PPAR (Peroxisome Proliferator-Activated Receptor) signaling pathway.

3 Synergistic mechanism and advantages of drug pair compatibility of Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis

In traditional Chinese medicine (TCM), hypertension in its early stages is commonly attributed to liver yang hyperactivity, with the treatment principle focusing on calming the liver and subduing yang. As the condition progresses, yang deficiency damages yin, leading to liver and kidney yin deficiency syndrome, where the therapeutic strategy shifts to nourishing yin and tonifying the kidneys. Here, calming the liver and subduing yang addresses the symptomatic manifestations, while nourishing yin and softening the liver targets the root cause. Tianma Gouteng Decoction is a frequently prescribed formula for hypertension, with Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis serving as the principal herbs. This combination synergistically calms the liver to extinguish wind, clears heat, and activates blood circulation, making it particularly suitable for patterns of excessive liver yang and liver wind disturbing the upper body. The *Essentials on disease and therapy in Plain Questions* states: "All wind-induced tremors and dizziness originate from the liver." The liver, characterized as a "rigid organ," is physically yin in substance but functionally yang in nature. Wind, a yang pathogen, tends to attack yang regions. Chronic liver and kidney deficiency leads to yin failing to control yang, resulting in liver yang hyperactivity. Hyperactive yang transforms into wind, and ascending wind-yang disturbs the brain collaterals, manifesting as headaches, vertigo, blurred vision, often triggered by emotional factors, and accompanied by insomnia, irritability, and restlessness, all hallmarks of liver yang hyperactivity. This pattern is categorized as "stagnant heat obstructing collaterals," and treatment should prioritize clearing heat, extinguishing wind, regulating the liver, and unblocking collaterals to resolve liver heat and lower blood pressure[11]. The *Convenient Reader on Materia Medica* notes: "All vine-based herbs can penetrate meridians and enter collaterals." Most vine herbs are acrid or bitter in flavor. Acridity can disperse, while bitterness can dry dampness. Herbs such as Spatholobi Caulis (Jixueteng), Uncariae Ramulus Cum Uncis, and Lonicerae Japonicae Caulis (Rendongteng) exhibit properties to regulate qi, activate blood circulation, dissipate stagnation, and unblock collaterals[12].

Experimental studies[13] have shown that the combined decoction of Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis exhibits superior antihypertensive effects compared to their respective single extracts. The mechanism may lie in: Gastrodiae Rhizoma can increase the content of isorhynchophylline (the main active component in Uncariae Ramulus Cum Uncis) and prolong the maintenance time of its effective concentration *in vivo*; while Uncariae Ramulus Cum Uncis can significantly enhance the maximum distribution concentration of gastrodin in the liver and accelerate

its absorption, distribution, and metabolic processes. Peng Yinxuan *et al.*[14] confirmed through research that Gastrodia polysaccharides promote the absorption of gastrodin in the herb pair of Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis, suggesting that polysaccharides may have certain absorption-enhancing effects on traditional Chinese medicines. This finding partially validates the rationality of the traditional water decoction method commonly used in Chinese medicine. However, most modern discussions on traditional Chinese medicine preparations remove polysaccharides as impurities during production processes, failing to consider the influence of different components on the absorption of active components[15]. Ancient and modern studies[16] have revealed that Uncariae Ramulus Cum Uncis can increase the decoction yield of active components from Gastrodiae Rhizoma, with the maximum extraction of effective components from Gastrodiae Rhizoma achieved when the compatibility ratio of Gastrodiae Rhizoma to Uncariae Ramulus Cum Uncis reaches 2 ∶ 1. This demonstrates the dissolution-enhancing characteristics and advantages of combined decoction of Chinese herbal pieces.

Modern studies suggest that Tianma Gouteng Decoction can regulate mitochondrial protein pathways, enhance their expression, and alleviate oxidative stress reactions, thereby playing a positive role in the prevention and treatment of hypertension[17-18]. For example, the study of Pan Junwei *et al.*[19] on 92 hypertensive patients demonstrated that Tianma Gouteng Decoction can regulate the expression of mitochondrial-related proteins MFN1, MFN2, and OPA1 in hypertensive patients, thereby improving oxidative stress responses, delaying vascular aging effects, and consequently controlling patients' blood pressure levels. Its antihypertensive mechanism may involve: Gastrodiae Rhizoma can activate sympathetic nerve excitability, promote the improvement of endothelin and angiotensin, and enhance microvascular and arteriolar functions; while components such as saponins, flavonoids, and alkaloids in Uncariae Ramulus Cum Uncis can inhibit the RASS system, increase serum nitric oxide content, and suppress vascular smooth muscle proliferation.

Studies have shown that the vasodilatory effects of rhynchophylline and gastrodin when used alone are far inferior to those of Tianma Gouteng Decoction[20]. However, when these two components are combined, their vasodilatory effects become comparable to those of Tianma Gouteng Decoction. This demonstrates the rationality of their roles as "sovereigns" in the Tianma Gouteng Decoction formula and provides a pharmacodynamic basis for the widespread use of this herb pair in hypertension treatment[21]. Wu Lihong *et al.*[22] analyzed from a pharmacokinetic perspective and found that the combination of Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis exhibits a characteristic pattern of "supplement first and purge later, with supplementation containing purgation." Their actions alternate between rapid and sustained effects, enabling both prompt symptom relief and long-term maintenance of therapeutic efficacy. Therefore, as "sovereign medicinals", they nourish the kidneys, soften the liver, cultivate yin, and subdue yang, addressing both symptoms and root causes. This combination facilitates the early restoration of yin-yang balance in disease progression, illustrating how the holistic treatment philosophy of Traditional Chinese Medicine is supported by substantial pharmacokinetic foundations.

4 Conclusions

The compatibility of Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis demonstrates significant advantages in hypertension treatment through synergistic effects involving multiple components, targets, and pathways. Its mechanisms may involve various aspects such as vasodilation, anti-oxidative stress, and delaying vascular aging, which not only validate the scientific validity of traditional Chinese medicinal compatibility but also provide directions for the development of novel antihypertensive drugs. Future research should further explore their dose-effect relationships and long-term medication safety to facilitate clinical translation.

References

[1] WANG Z, CHEN Z, ZHANG L, *et al.* Status of hypertension in China: Results from the China Hypertension Survey, 2012-2015[J]. Circulation, 2018, 137(22): 2344-2356.

[2] YANG HY, HE YY, ZHU Y, *et al.* Research progress of efficacy and mechanism of traditional Chinese medicine in treatment of essential hypertension[J]. Basic Traditional Chinese Medicine, 2024, 3(8): 110-117. (in Chinese).

[3] SONG CQ, FAN Y, HUANG WH, *et al.* Different hypotentive effects of various active constituents isolated from *Uncaria rhynchophylla*[J]. Chinese Traditional and Herbal Drugs, 2000, 31(10): 44-46. (in Chinese).

[4] SUN JC, QI DM, ZHOU HL, *et al.* Effects of Uncaria alkaloids on apoptosis and proliferation of thoracic aortic smooth muscle cells in spontaneously hypertensive rats[J]. Chinese Pharmacological Bulletin, 2011, 27(7): 925-929. (in Chinese).

[5] PAN WH, JIANG HQ, LI YL. Effects of Guoteng (*Uncaria rhynchophylla*) extracting solution on urine metabolomics in spontaneously hypertensive rats[J]. Journal of Traditional Chinese Medicine, 2019, 60(1): 62-66, 71. (in Chinese).

[6] MA XC, LUO TT, YI FL, *et al.* Mechanism of *Uncaria rhynchophylla* for hypertension based on network pharmacology[J]. Central South Pharmacy, 2019, 17(5): 671-675. (in Chinese).

[7] WANG T, LAN Q, MA GD, *et al.* Study on the effective components and mechanism of Uncaria in the treatment of atherosclerosis based on network pharmacology and molecular docking[J]. Chinese Journal of Arteriosclerosis, 2023, 31(2): 110-121. (in Chinese).

[8] TIAN LF, WANG XQ, ZHAI ZG. Analysis of compatibility pattern of rhizoma gastrodiae in the treatment of hypertension of Yin deficiency and Yang excess type[J]. Chinese Journal of Basic Medicine in Traditional Chinese Medicine, 2017, 23(6): 868-871. (in Chinese).

[9] CAI SB, QIN S. Exploring the hypotensive mechanisms of action of tianma based on network pharmacology[J]. Journal of Modern Medicine & Health, 2024, 40(23): 3967-3972. (in Chinese).

[10] ZHU JY, YANG X, WANG RJ, *et al.* Exploring the molecular mecha-

nism of Guizhou tall gastrodis tuber in treating hypertension based on transcriptomic analysis[J]. Information on Traditional Chinese Medicine, 2024, 41(11): 23-28. (in Chinese).

[11] REN FJ, ZHANG YN. Characteristics of Chinese medicinal materials used by YE Tianshi in treatment of collateral disease from "analogy" [J]. Journal of Tianjin University of Traditional Chinese Medicine, 2019, 38(5): 442-444. (in Chinese).

[12] JI ZZ, QI XZ, YU ZQ. Yu Zhiqiang's clinical experience in using vine medicines[J]. Inner Mongolia Journal of Traditional Chinese Medicine, 2020, 39(12): 68-69. (in Chinese).

[13] JIANG H, XIE Q, WANG L, *et al.* Research progress of liver-yang suppressing medicines in hypertension[J]. Lishizhen Medicine and Materia Medica Research, 2019, 30(12): 2965-2967. (in Chinese).

[14] PENG YX, WANG X, YANG J, *et al.* Influence of polysaccharide of tall gastrodia tuber on absorption of effective components in medicine suits of tall gastrodia tuber and gambir plant nod[J]. Global Traditional Chinese Medicine, 2015, 8(12): 1452-1454. (in Chinese).

[15] MIAO HC, SHEN YS. Antihypertensive effect of polysaccharides substracted from *Gastrodia elata* Blume[J]. Chinese Journal of Hypertension, 2006, 14(7): 531-534. (in Chinese).

[16] GU J. Study on chemical characteristic spectrum and content changes of active components in Gastrodia-Uncaria herb pair[J]. Journal of Clinical Medical Literature, 2019, 6(97): 188-190. (in Chinese).

[17] ZHOU ZN, DUAN JR, TENG ZY. Clinical efficacy of Tianma Gouteng decoction combined with enalapfil maleate folate tablets and vitamin B12 in the treatment of vascular dementia with H-type hypertension[J]. Sichuan Journal of Physiological Sciences, 2024, 46(1): 157-160. (in Chinese).

[18] GAO XH, CHEN DY, LIU XS, *et al.* Effect of serum containing Tianma Gouteng Decoction on expressions of serum inflammatory factors and apoptosis related factors in brain tissue around hematoma in rats with intracerebral hemorrhage[J]. Chinese Archives of Traditional Chinese Medicine, 2022, 40(3): 232-235, 259. (in Chinese).

[19] PAN JW, PAN Q, LUO XF. Mechanism and efficacy of Tianma Gouteng Decoction in treating hypertension by regulating mitochondrial protein pathway[J/OL]. Chinese Archives of Traditional Chinese Medicine, 1-8[2025-04-15]. http://kns.cnki.net/kcms/detail/21.1546.R.20241205.1403.012.html. (in Chinese).

[20] LIU R, BIAN XH, XU JY, *et al.* Study on the vasodilator effect of components combination of Chinese materia medica[J]. West China Journal of Pharmaceutical Sciences, 2011, 26(6): 551-553. (in Chinese).

[21] LI XQ. Study on distribution of active components in large blood vessels and gene expression before and after compatibility of Uncaria and Gastrodia[D]. Chengdu: Southwest Jiaotong University, 2012. (in Chinese).

[22] WU LH, HOU J, WANG J, *et al.* Effect of combination of gastrodia and uncaria on pharmacokinetics of gastrodin and rhynchophylline[J]. China Journal of Chinese Materia Medica, 2017, 42(13): 2577-2582. (in Chinese).

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References

[1] DING K, LANG BX, LI T. Clinical study on micro-needle-knife therapy combined with abdominal acupuncture and traction for lumbar disc herniation[J]. New Chinese Medicine, 2025, 57(1): 121-126. (in Chinese).

[2] LI SZ, GUO J, LIU WP, *et al.* Observation on selection of traction weight in the treatment of lumbar disc herniation with electric traction [J]. Chinese and Foreign Medical Research, 2024, 22(34): 161-164. (in Chinese).

[3] YI BX. Effects of electropuncture and moxibustion combined with lumbar traction in treatment of patients with lumbar disc herniation[J]. Medical Journal of Chinese People's Health, 2024, 36(21): 117-119, 123. (in Chinese).

[4] ZHANG Y, SUN SX, HAN F, *et al.* Clinical effect observation of acupuncture combined with traction rehabilitation training on lumbar disc herniation[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2024, 39(11): 6259-6262. (in Chinese).

[5] YANG JG, DING JX, LIN XZ, *et al.* Clinical efficacy of electroacupuncture point stimulation combined with lumbar traction in the treatment of lumbar disc herniation[J]. Shenzhen Journal of Integrated Traditional Chinese and Western Medicine, 2024, 34(20): 43-46. (in Chinese).

[6] CHEN FT, WU FY. Influence of Tuina traction combined with lumbar back muscle rehabilitation training on patients with lumbar disc herniation[J]. Shenzhen Journal of Integrated Traditional Chinese and Western Medicine, 2024, 34(16): 50-53. (in Chinese).

[7] YANG XY, ZHOU BB, SU T, *et al.* A meta-analysis of the effect of shockwave therapy on lumbar disc herniation[J]. Clinical Journal of Chinese Medicine, 2024, 16(24): 121-127. (in Chinese).

[8] XU XW, LYU LL. Effect of lumbar traction combined with physiotherapy in the treatment of lumbar disc herniation[J]. Chinese Journal of Urban and Rural Enterprise Hygiene, 2024, 39(7): 102-104. (in Chinese).

[9] ZHAO WF. Influence of traditional Chinese medicine orthopedic Tuina combined with lumbar traction intervention on lumbar function and pain degree of patients with lumbar disc herniation[J]. Modern Diagnosis and Treatment, 2024, 35(13): 1921-1923. (in Chinese).