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Research Progress on the Mechanism of Stone Expulsion with Traditional Chinese Medicine: From Traditional Experience to Modern Pharmacology

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Abstract: ***Traditional Chinese medicine (TCM) has a long history of application and significant clinical efficacy in the treatment of urinary tract stones, demonstrating its multi-mechanism and multi-target therapeutic advantages. This article systematically reviews the pharmacological effects and current clinical application of TCM lithostomy. It highlights numerous challenges, including the complexity of active ingredients, unclear mechanisms of action, a lack of high-quality clinical research, lagging standardization of formulations, and the modern translation of syndrome differentiation and treatment. To address these challenges, it is proposed that future research should focus on the isolation of active ingredients and target identification, the application of multi-omics technologies in mechanism analysis, the development of novel formulations, the establishment of standardized clinical pathways, and the optimization of synergistic treatment models combining traditional Chinese and Western medicine. As a bridge connecting traditional and modern medicine, TCM lithostomy has broad development potential. Promoting its development towards precision, standardization, and internationalization will provide more scientific and efficient solutions for the comprehensive treatment of urinary tract stones.***

Keywords: TCM lithostomy, Urinary tract stones, Pharmacodynamic mechanism, Multi-omics technology, New dosage form development, Clinical pathway, Integrated TCM and Western medicine**.**

1. Introduction

Urinary stones are a common urinary system disease, and its incidence rate is increasing year by year worldwide, especially in areas with high temperatures, high protein diets, and high calcium intake [1]. According to epidemiological surveys, the lifetime prevalence of urinary stones in adults can reach 10%-15%, with a high recurrence rate and a tendency to become chronic [2]. Stones can cause severe pain, hematuria, urinary tract obstruction, and even renal damage, seriously affecting the patient's quality of life and social work ability. Although modern medicine has made significant progress in stone diagnosis and surgical treatment, drug stone removal is still an important part of clinical treatment, especially in the management of small stones, asymptomatic stones, or residual stones after surgery.

Traditional Chinese medicine has a long history and rich clinical experience in stone removal treatment. As early as in ancient medical books such as "Huangdi Neijing" and "Jingui Yaolue", disease names such as "stone stranguria" and "sand stranguria" were recorded, and treatment principles such as clearing heat and dampness, promoting stranguria and removing stones, and promoting blood circulation and removing blood stasis were proposed [3]. Doctors of all ages have accumulated a large number of effective prescriptions and medicines, such as Centella asiatica, Sea Sand, Chicken Gizzard, etc., which are widely used in clinical practice and have formed a systematic TCM stone removal theory system. With the development of modern pharmacology, more and more studies have begun to explore the scientific basis of TCM stone removal from the molecular mechanism level, promoting the transformation of traditional experience into modern medicine [4].

This paper aims to systematically sort out the research progress of TCM stone removal, starting from traditional theories and classic prescriptions, combining modern pharmacological mechanisms, clinical research data and future development directions, to explore the role and potential of TCM in stone removal treatment. The full text structure includes traditional TCM stone removal experience, commonly used TCM and its pharmacological mechanism, clinical efficacy evaluation, existing problems and research challenges, and future development trends. It is expected to provide theoretical support and practical reference for TCM stone removal research and promote the modernization and standardization of TCM in the treatment of urinary system diseases.

2. Traditional TCM Stone Removal Theory and Experience

In the TCM system, urinary stones are one of the "stranguria syndromes". TCM believes that its etiology is mainly related to factors such as damp-heat accumulation, qi stagnation and blood stasis, and kidney deficiency. Internal dampness and heat generate internally, scorching the body fluids and condensing them into sand and gravel; or due to improper diet and fatigue, internal injuries can lead to spleen and kidney deficiency, water metabolism disorder, dampness and turbidity flowing downward, and stones [5]. The pathogenesis often involves the kidney, bladder, triple energizer and other internal organs. The disease is located in the lower energizer, and the disease is of a combination of deficiency and excess. Treatment requires syndrome differentiation and treatment,

taking both the symptoms and the root cause into account [6].

TCM syndrome differentiation mainly includes dampness and heat flowing downward, qi stagnation and blood stasis, and kidney deficiency and blood stasis. The dampness and heat flowing downward is characterized by short and dark urine, burning and stinging pain, and distension and pain in the waist and abdomen. Treatment should be to clear away heat and dampness, and to relieve stranguria and expel stones. The qi stagnation and blood stasis is often accompanied by severe colic, hematuria, and urinary tract obstruction. Treatment should be to regulate qi and activate blood circulation, and to remove blood stasis and dredge the meridians. The kidney deficiency and blood stasis is characterized by soreness and weakness in the waist and knees, fatigue, and repeated stone attacks. Treatment should be to tonify the kidney and replenish qi, and to remove blood stasis and expel stones. The treatment principle emphasizes clearing heat and removing dampness as the basis, combined with methods such as relieving stranguria, promoting blood circulation, and replenishing deficiency, in order to achieve the comprehensive goals of removing stones, relieving pain, and preventing recurrence [7].

In terms of traditional medicine, Chinese medicine has accumulated a large number of effective prescriptions and single-ingredient drugs. Bazhengsan is a representative prescription for treating stranguria caused by damp heat, which has the functions of clearing heat and purging fire, promoting diuresis and removing stranguria, and is often used to remove stones in the acute stage. Centella asiatica is an important medicine for removing stones. It is sweet and mild in nature and enters the liver, kidney, and bladder meridians. It has the functions of clearing heat and removing dampness, removing stranguria and removing stones, detoxifying and reducing swelling. Modern research has confirmed that it can promote urine flow, relax the ureter, and inhibit stone formation [8]. Sea sand is good at promoting diuresis, removing stranguria, removing stones, and relieving pain. It is often used in combination with Centella asiatica and chicken's gizzard lining [9]. In addition, chicken's gizzard lining can strengthen the spleen and digestion, dissolve hard masses and disperse nodules. Talcum, plantain, and stonewort are also commonly used in stone-removing prescriptions, forming a multi-drug synergistic treatment system that treats both the symptoms and the root cause [10]. Traditional Chinese medicine's experience in stone removal not only demonstrates the flexibility of syndrome differentiation and treatment, but also provides rich material and theoretical foundation for modern pharmacological research. With the in-depth study of the active ingredients of traditional Chinese medicine, these classic prescriptions are gradually transforming from empirical therapies to modern medicine with clear mechanisms and controllable efficacy.

3. Commonly used Chinese Medicines for Stone Removal and Their Modern Pharmacological Studies

With the development of modern pharmacology, the mechanism of action of traditional Chinese medicines for stone removal has gradually been revealed, showing the therapeutic advantages of multiple targets and multiple links. These Chinese medicines are not only widely used in clinical practice, but also show good biological activity in experimental studies, providing scientific support for the theory of stone removal in traditional Chinese medicine. Lysimachia christinae is one of the most widely used drugs in stone removal treatment. Its main pharmacological effects include diuresis, anti-inflammatory, antioxidant, and relaxation of ureteral smooth muscle. Studies have shown that Lysimachia christinae can significantly increase urine volume and promote stone excretion, while inhibiting the expression of inflammatory factors such as TNF-α and IL-6, and reducing urinary mucosal edema and irritation. In addition, its extract can reduce urinary calcium and urinary oxalic acid levels, intervening in the key links of stone formation. Some studies have also found that the flavonoids and triterpenoids in Lysimachia christinae have the effect of inhibiting the aggregation and adhesion of calcium salt crystals, which helps prevent stone recurrence [11]. Lygodium japonicum has a good effect on urinary tract urination and stone removal. Its pharmacological mechanisms mainly include promoting urine flow, inhibiting crystal formation and adhesion, and relieving ureteral spasm. The steroid and flavonoid components in Lygodium japonicum can interfere with the aggregation and growth of crystal nuclei during stone formation and reduce the saturation of stone formation in urine. At the same time, its diuretic effect helps dilute urine and reduce stone deposition. When used in combination with other drugs, it can enhance the stone removal effect [12]. Gallus gallus domesticus gizzard lining is used in traditional Chinese medicine to "dissolve hard masses". Modern research has found that it contains a variety of proteases and digestive enzymes, which can promote stone dissolution and improve digestive function. Chicken gizzard lining can enhance intestinal and renal metabolic function, indirectly regulate urine composition, and reduce the risk of stone formation [13]. Talc and plantain are mainly used for diuresis, stranguria, heat-clearing and detoxification. The silicate component in talc can reduce crystal adhesion, while plantain is rich in polysaccharides and flavonoids, which have anti-inflammatory and antioxidant effects and help improve the urinary tract microenvironment [14].

In recent years, the study of the synergistic effects of traditional Chinese medicine compound preparations has become a hot topic. The combined use of multiple stone-removing traditional Chinese medicines can achieve complementary and synergistic effects. For example, the combination of Centella asiatica and Lycopodiella ternata can simultaneously exert diuretic, anti-inflammatory and anti-stone effects; the combination of chicken gizzard lining and talc can take into account both stone removal and stranguria. Compound preparations such as "Stone-Removing Granules" and "Tonglin Mixture" are widely used in clinical practice. Studies have shown that they have significant advantages in improving the stone expulsion rate, relieving pain and reducing the recurrence rate. In terms of mechanism, each drug in the compound acts on stone formation, expulsion and inflammatory response through different pathways, reflecting the "multi-target, multi-mechanism" therapeutic characteristics of traditional Chinese medicine. Commonly used stone-removing traditional Chinese medicines have shown good biological activity and clinical potential in modern pharmacological research [15]. In-depth exploration

of its effective ingredients and mechanism of action will help promote the development of TCM stone removal treatment towards precision and standardization.

4. Discussion on the Mechanism of Action of TCM Stone Removal

The therapeutic mechanism of TCM stone removal embodies the concept of "holistic regulation and treatment of both the symptoms and the root cause" in traditional Chinese medicine. Its pharmacological effects cover multiple links such as diuresis, anti-inflammatory, antispasmodic, anti-stone formation, and stone dissolution, forming a systematic treatment network. Modern pharmacological research has gradually revealed the molecular basis of these mechanisms, providing scientific support for traditional experience [16]. First, diuresis and promotion of urine flow are one of the basic mechanisms of TCM stone removal. The formation and retention of stones in the urinary tract are closely related to the urine flow rate. TCM such as Centella asiatica, Plantago asiatica, Talc, and Selaginella ternata have significant diuretic effects, which can increase urine volume, dilute urine, and speed up flow, thereby reducing the chance of stone adhesion and deposition [17]. The diuretic effect not only helps the natural excretion of small stones or gravel, but also reduces the saturation of stone formation in urine and reduces the risk of crystal aggregation. Secondly, anti-inflammatory and mucosal edema reduction play an important role in relieving symptoms and promoting stone excretion. Stones in the urinary tract can cause mechanical stimulation of the mucosa, inducing local inflammatory reactions, manifested as pain, hematuria, frequent urination and other symptoms. Traditional Chinese medicines such as Centella asiatica, Lycopodiella ternata, and Selaginella ternata contain active ingredients such as flavonoids and triterpenes, which can inhibit the expression of inflammatory factors such as TNF-α, IL-6, COX-2, reduce mucosal edema and congestion, and improve urinary tract patency. The anti-inflammatory effect can also reduce the risk of urinary tract infection induced by stones and improve the overall treatment effect [18]. Thirdly, relaxing smooth muscle and relieving spasm are important auxiliary mechanisms of traditional Chinese medicine for stone excretion. When stones are embedded in the ureter or bladder outlet, they often cause severe spasmodic pain, affecting the excretion of stones. Studies have found that drugs such as Centella asiatica, Lycopodiella ternata, and Gallus gallus domesticus can act on urinary tract smooth muscle, reduce tension and spasm, dilate the urinary tract, and make stones easier to pass. Some Chinese medicines can also regulate calcium ion channels and neurotransmitter release, achieving smooth muscle relaxation at the molecular level [19].

In addition, inhibiting stone formation and crystal aggregation is an important mechanism for Chinese medicine to prevent recurrence. The formation process of urinary stones includes crystal nucleation, crystal growth, aggregation and adhesion. Chinese medicines such as Centella asiatica, Sea Sand, and Chicken's Endothelial Gizzard can interfere with the nucleation and growth process of crystals such as calcium oxalate and calcium phosphate, reducing the saturation of stone formation in urine. Some drugs can also change the pH value and ion concentration of urine, inhibit crystal adhesion to the urinary tract mucosa, and reduce the physical basis for stone formation. Promoting stone dissolution and excretion is the ultimate goal of Chinese medicine stone removal [20]. The protease and digestive enzyme components in Chicken's Endothelial Gizzard are believed to have a certain ability to decompose stones, especially for gallstones and uric acid stones. Combined with diuretic, anti-inflammatory, and antispasmodic effects, Chinese medicine can achieve the natural dissolution and excretion of stones, reducing damage to the urinary tract and the need for intervention [21]. Traditional Chinese medicine for stone removal often uses compound preparations, with multiple drugs acting synergistically to form a "multi-target, multi-mechanism" treatment system. For example, the combination of Centella asiatica and Lygodium japonicum can simultaneously exert diuretic, anti-inflammatory, and anti-stone formation effects; the combination of Chicken Gizzard Stone and Talc can achieve both stone removal and stranguria relieving effects. Compound preparations such as "Stone Removal Granules" and "Tonglin Mixture" are widely used in clinical practice. Studies have shown that they have significant advantages in improving stone removal rates, relieving pain, and reducing recurrence rates [22].

5. Clinical Research and Efficacy Evaluation of Traditional Chinese Medicine for Stone Expulsion

Clinical research on traditional Chinese medicine for stone expulsion has gradually become standardized in recent years, and the efficacy evaluation system has become increasingly refined. With the development of evidence-based medicine, an increasing number of studies have used methods such as randomized controlled trials (RCTs) and prospective observational studies to systematically evaluate the efficacy, safety, and mechanisms of traditional Chinese medicine for stone expulsion. In terms of clinical trial design and efficacy indicators, commonly used evaluation indicators include stone expulsion rate, pain relief, recurrence rate, changes in urine composition, and imaging findings. In the combination of traditional Chinese medicine and Western medicine, traditional Chinese medicine is often used in conjunction with α-blockers (such as tamsulosin) to enhance stone expulsion. Western medicine can promote stone expulsion by relaxing ureteral smooth muscle, while traditional Chinese medicine plays a role in diuresis, anti-inflammatory effects, and regulation of urine composition. Multiple clinical studies have shown that combined treatment groups are superior to monotherapy groups in terms of stone expulsion rate, pain relief rate, and urinary tract infection incidence, demonstrating the advantages of synergistic traditional Chinese and Western medicine [23-24].

Tonghua stone expulsion treatment is generally mild, but the toxic and side effects of individual drugs still need to be considered. For example, high doses or long-term use of Lycopodiella vulgaris may cause gastrointestinal discomfort, and Centella asiatica should be used with caution in patients with liver and kidney dysfunction. Therefore, in clinical applications, attention should be paid to dose control, treatment course management, and individual differences, and personalized adjustments should be made based on the patient's constitution and condition. Some studies recommend

regular monitoring of liver and kidney function, urine composition, and imaging changes during TCM treatment to ensure the safety and effectiveness of treatment. In addition, TCM lithotripsy also has unique advantages in postoperative management and recurrence prevention. Postoperative residual stones or small stones are often difficult to completely remove through surgery. TCM can be used as an auxiliary treatment to promote the excretion of residual stones, improve the urinary tract environment, and reduce the risk of recurrence [25]. In long-term management, TCM can also regulate renal function, improve metabolic status, and improve the quality of life of patients. TCM lithotripsy has shown good efficacy and safety in clinical practice, especially in the treatment of small stones, postoperative residual stones, and recurrence prevention. In the future, we should strengthen the development of multicenter, randomized controlled trials, improve the efficacy evaluation system, and promote the development of TCM lithotripsy towards evidence-based medicine. At the same time, combining modern pharmacological research with new technologies will further enhance the scientific nature, standardization, and international influence of Traditional Chinese Medicine (TCM) stone removal.

6. Existing Problems and Future Research Directions

Although TCM has demonstrated promising efficacy and a broad clinical application base in stone removal treatment, its development still faces numerous challenges. First, the active ingredients are complex, and the mechanisms are not yet fully understood. Traditional Chinese medicines are often compound preparations containing multiple active ingredients, and their efficacy often relies on the synergistic effects of multiple targets and pathways. While current research on herbs such as Lysimachia chinensis, Lygodium japonicum, and Gallus gallus domesticus has revealed some anti-inflammatory, diuretic, and antispasmodic mechanisms, the overall pathway of action remains unclear. In particular, technical bottlenecks remain in target identification and pathway analysis at the molecular level.

Second, the lack of high-quality randomized controlled trials and long-term follow-up data has hampered the accumulation of evidence-based medical evidence for the efficacy of TCM stone removal. Most clinical studies have small sample sizes, poorly designed designs, lack of control groups and blinding, and inconsistent efficacy evaluation indicators, making it difficult to develop generalizable treatment guidelines. At the same time, long-term follow-up data is scarce, and there is still a lack of systematic evaluation of the sustained effects of traditional Chinese medicine in preventing stone recurrence and improving renal function. The development of standardized preparations and dosage forms is lagging behind. Traditional Chinese medicine decoctions lack ease of administration and ingredient stability, impacting patient compliance and consistent efficacy. Currently, the variety of Chinese patent medicine preparations on the market is limited, with inconsistent quality control standards and a lack of a unified efficacy evaluation system. Furthermore, innovation in dosage forms for traditional Chinese medicine is still in its infancy, and a technical system compatible with modern pharmaceutical formulations has yet to be established. The challenges of modern translation of individual differences and syndrome differentiation and treatment also pose significant challenges to traditional Chinese medicine stone removal research. Traditional Chinese medicine emphasizes individualized treatment plans, resulting in highly personalized treatment plans, while modern medicine pursues standardization and replicability. This conceptual difference creates difficulties in developing clinical pathways, evaluating efficacy, and compiling guidelines for traditional Chinese medicine. Modern translation is urgently needed while maintaining the distinctive characteristics of traditional Chinese medicine.

To promote the scientific and standardized development of traditional Chinese medicine stone removal treatment, future research could focus on the following areas. First, the isolation of active ingredients and target research in traditional Chinese medicines are fundamental. Modern pharmacological techniques, such as high-performance liquid chromatography, mass spectrometry, and molecular docking, can identify key active ingredients in traditional Chinese medicine (TCMs), clarify their targets and mechanistic pathways, and provide a basis for drug development and dosage form optimization. Secondly, the application of multi-omics technologies in mechanistic analysis will become a research hotspot. Metabolomics, proteomics, and transcriptomics can comprehensively reveal the regulatory networks of TCMs on the body, exploring their systemic effects on stone formation, inflammatory responses, and urine metabolism. By integrating omics data, it is possible to construct a map of the effects of TCMs on stone removal, enabling precise mechanistic analysis. Thirdly, the development of new dosage forms of TCMs is key to enhancing their clinical value. Modern pharmaceutical technologies, such as sustained-release formulations, transdermal formulations, and nanoformulations, can improve the bioavailability, targeting, and stability of TCMs, enhancing treatment efficiency and patient compliance. Furthermore, standardized production and quality control systems for TCM preparations must be established to ensure consistent efficacy and safety.

Establishing standardized clinical pathways and evaluation systems is crucial for the promotion of TCM stone removal. Unified syndrome differentiation criteria, treatment processes, and efficacy evaluation indicators should be developed, combined with modern clinical trial design methods to create a replicable and scalable treatment plan. Multicenter, long-term follow-up clinical studies will provide a solid evidence-based foundation for TCM stone removal. Optimizing the synergistic treatment model of traditional Chinese medicine and Western medicine is a key direction for future development. By deeply studying the synergistic mechanisms and interactions between traditional Chinese medicine and Western medicine (such as α-blockers and diuretics), the advantages and risks of combined treatment can be clarified, and a patient-centered comprehensive treatment system can be established to maximize efficacy and minimize side effects.

7. Conclusion

As an important component of traditional medicine, TCM

stone removal has accumulated rich experience and practical results in the treatment of urinary stones. Its treatment philosophy emphasizes holistic regulation and syndrome differentiation. Its pharmacological effects encompass diuresis, anti-inflammatory, antispasmodic, and anti-stone formation, demonstrating the combined advantages of multiple mechanisms and targets. With the advancement of modern pharmacological and clinical research, the efficacy of TCM stone removal has been scientifically validated, and it shows broad application prospects in the treatment of small stones, residual stones after surgery, and recurrence prevention.

However, the development of traditional Chinese medicine for stone removal still faces challenges such as unclear efficacy mechanisms, insufficient clinical research, and lagging dosage forms. Future efforts should strengthen research on active ingredients, elucidation of mechanisms, innovative dosage forms, and standardized clinical pathways to promote the precise, standardized, and international development of traditional Chinese medicine for stone removal. Through the synergistic integration of traditional Chinese and Western medicine, it is hoped that a more scientific, efficient, and safe comprehensive system for the treatment of stone disease will be established, providing patients with higher-quality medical services and injecting new impetus into the modernization of Traditional Chinese Medicine.

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