



Consensus of Experts Regarding the Clinical Utilization of Yishen Huashi Granules in Kidney Disease Management

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Abstract

Yishen Huashi Granules, initially known as “Mankidneyan,” represent a category six traditional Chinese medicine that was recently developed by Guangzhou Kangchen Pharmaceutical Co., Ltd. This medication received approval from the China Food and Drug Administration (CFDA) in March 2009. Its primary purpose is to address proteinuria, a common symptom associated with chronic glomerulonephritis characterized by a syndrome of spleen deficiency and dampness excess. This condition is typically diagnosed when serum creatinine levels (Scr) are less than 2 mg/dl. Patients with this condition often exhibit symptoms such as edema, fatigue, aversion to cold, cold limbs, and poor appetite. Over the past few years, Yishen Huashi Granules have garnered widespread recognition for their effectiveness in treating chronic kidney disease (CKD) as a result of accumulating clinical experience. However, there have also been instances of off-label use. In an effort to provide clear guidance and standardization for the clinical Utilization of Yishen Huashi Granules in CKD Management, the Chinese Association of Traditional Chinese Medicine has convened a panel of experts from various disciplines, including clinical nephrology, pharmacology, and statistics. These experts have been tasked with reviewing, summarizing, and analyzing research findings both before and after the medication’s approval for marketing. Leveraging the collective clinical experience of these experts, an “Expert Consensus on the Clinical Application of Yishen Huashi Granules in the Treatment of Kidney Diseases” has been developed. The primary objective of this consensus is to broaden the range of indications for the medication and enhance the existing application guidelines. Ultimately, this effort aims to promote the rational and well-informed clinical use of Yishen Huashi for of kidney illness.

Subject Areas

Medicine

Keywords

Yishen Huashi, Kidney, Disease and Treatment

1. Introduction

Chronic Kidney Disease (CKD) is a widespread global health challenge, affecting millions of individuals and placing a significant burden on healthcare systems worldwide. In the ever-evolving landscape of healthcare, Traditional Chinese Medicine (TCM) has emerged as a valuable and complementary approach to addressing CKD [1]. Among the various TCM remedies, Yishen Huashi Granules, originally known as “Mankidneyan,” have gained recognition for their potential to alleviate CKD symptoms and complications. Developed by Guangzhou Kangchen Pharmaceutical Co., Ltd. and approved by the China Food and Drug Administration (CFDA) in March 2009, Yishen Huashi Granules offer hope to CKD patients, particularly those with proteinuria associated with spleen deficiency and dampness excess. As their clinical application has evolved, so has the need for comprehensive guidance and standardization, leading to the creation of an “Expert Consensus on the Clinical Application of Yishen Huashi Granules in Kidney Disease Treatment.”

This journey will provide insights into the complexities of CKD, the therapeutic potential of Yishen Huashi Granules, and the collaborative efforts of experts aimed at enhancing CKD management. CKD is a global health concern characterized by a gradual loss of kidney function, leading to various complications and increased mortality risk [2]. The World Health Organization (WHO) estimates that over 850 million people worldwide are affected by CKD, making it a prevalent and concerning health issue. CKD not only manifests as a standalone condition but also contributes to associated health problems such as cardiovascular disease, hypertension, anemia, bone disorders, and a reduced quality of life. Moreover, the economic impact of CKD is substantial, straining healthcare systems and imposing financial burdens on patients and their families.

CKD progresses through distinct stages, each marked by specific clinical indicators, from early kidney damage with preserved function (Stage 1) to end-stage kidney disease (ESKD) necessitating dialysis or transplantation (Stage 5). Managing CKD requires a multifaceted approach aimed at slowing disease progression, alleviating symptoms, and addressing comorbidities. Despite advancements in conventional medical treatments, CKD management remains challenging, often requiring patients to endure frequent clinic visits, dietary restrictions, medication regimens, and potential invasive procedures. This quest for effective and holistic CKD management has led to the exploration of complementary and alternative therapies, including Traditional Chinese Medicine (TCM) [3].

TCM, one of the world’s oldest and enduring systems of medicine, has a history spanning millennia. Rooted in ancient philosophical principles and holistic

health perspectives, TCM encompasses a diverse range of modalities, such as acupuncture, herbal medicine, dietary therapy, and qi gong. It places a strong emphasis on balancing vital energies (qi) and promoting harmonious bodily function. TCM's holistic approach and personalized treatments continue to be relevant in modern healthcare. In the context of CKD, TCM offers a unique perspective on understanding the disease's causes, progression, and management.

Yishen Huashi Granules, originally named "Mankidneyan," have emerged as a notable TCM remedy for CKD management. Developed by Guangzhou Kangchen Pharmaceutical Co., Ltd. and granted CFDA approval in 2009, these granules encapsulate the essence of traditional Chinese herbal medicine. They have shown promise in alleviating symptoms and slowing CKD progression, especially in cases characterized by proteinuria linked to spleen deficiency and dampness excess. The formulation of Yishen Huashi Granules draws from a rich tradition of herbal knowledge, combining specific herbs known for their therapeutic effects on the kidneys and related systems. Given the multifactorial nature of CKD, TCM's holistic approach aligns well with the need for comprehensive management strategies.

As the clinical application of Yishen Huashi Granules in CKD management has evolved, a growing body of clinical experience and research has emerged. However, their use has encountered challenges, including off-label usage and treatment variations. These issues underscore the importance of clear guidelines and standardized protocols. In response, the Chinese Association of Traditional Chinese Medicine recognized the need to consolidate knowledge, experience, and research findings. A panel of esteemed experts from various fields, including clinical nephrology, pharmacology, and statistics, was convened to comprehensively review, summarize, and analyze existing research on Yishen Huashi Granules and their clinical application in CKD treatment. The result of their collaboration is the "Expert Consensus on the Clinical Application of Yishen Huashi Granules in Kidney Disease Treatment," representing a significant milestone in CKD management and traditional Chinese medicine. This consensus document provides comprehensive guidelines and recommendations for the rational and evidence-based use of Yishen Huashi Granules [4] [5].

We will delve into Yishen Huashi Granules, exploring their formulation, mechanisms of action, evolving role in CKD treatment, and the critical insights offered by the Expert Consensus. We will examine the research, clinical experiences, and perspectives that have shaped the application of this TCM remedy in CKD management. Our exploration will encompass multiple disciplines, including clinical nephrology, pharmacology, and statistical analysis. We will also consider CKD management within the broader context of traditional Chinese medicine, where holistic approaches and personalized treatments are fundamental principles. Through this journey, we will gain a deeper understanding of CKD's complexities, the potential of Yishen Huashi Granules, and the pivotal role of collaborative expertise in shaping the future of CKD treatment. The Ex-

pert Consensus will serve as a guiding light, leading us toward more effective, evidence-based, and patient-centered approaches to CKD management, ultimately improving the lives of those affected by this challenging condition. The development of this expert consensus adheres strictly to the “Technical Specifications for Expert Consensus in the Revision of Clinical Practice Guidelines in Traditional Chinese Medicine” and utilizes the Nominal Group Technique (NGT). It was jointly chaired by Professor Wang Yaoxian, the Chairman of the Kidney Disease Branch of the Chinese Association of Traditional Chinese Medicine, and Professor Yang Hongtao, Vice Chairman and Secretary-General of the branch. The consensus development process involved two rounds of meetings for evaluating, discussing, reevaluating, and discussing the consensus content, ultimately resulting in the initial draft of the consensus. After forming the initial draft, input and opinions were solicited from a wide range of clinical experts in the field of kidney disease. Subsequent discussions and deliberations led to the final consensus. The sources of evidence for this expert consensus were obtained from various databases, including SCI, google scholar Wanfang, VIP, Sino-Med, PubMed, Embase, and the Cochrane Library, with a search period spanning from January 2009 to March 2022. The included study types encompassed randomized controlled trials, non-randomized controlled trials, cohort studies, and case-control studies. Additionally, the consensus considered pharmacological and toxicological studies of Yishen Huashi Granules and clinical studies conducted before its market approval (Phase II and Phase III trials).

2. Traditional Chinese Medicine Theory behind the Formula

The kidneys are considered the water organ in traditional Chinese medicine (TCM), responsible for storing, receiving, and governing bodily fluids. They play a crucial role in storing essence and transforming it into vital energy (Yuan Qi), which is not only the driving force of life activities but also a cornerstone for building the body’s defense mechanisms. The essence and vital energy within the kidneys depend on the nurturing and nourishing of the subtle essence derived from water and grains through the spleen and stomach’s digestive processes. This process ensures a continuous supply of essence, which is then transformed into vital energy. Therefore, the spleen is considered the foundation for generating vital energy.

Simultaneously, the kidneys are responsible for the storage of essence, allowing the essence produced by the spleen and stomach to be retained within the body. The spleen and stomach work in synergy with the kidneys, mutually supporting each other. The spleen and stomach are located in the middle burner of the body and have a direct relationship, with the spleen’s upward function complementing the stomach’s downward function. When the spleen is functioning correctly, the stomach is harmonious, and when there is stomach dysfunction, the spleen becomes weakened. The spleen’s role is to ascend, while the stomach’s role is to descend. This coordinated movement of Qi, fluids, and substances promotes the digestion and absorption of food and nutrients.

If external factors, such as dampness, invade the body and hinder the upward movement of spleen Yang Qi or if factors like fatigue and overeating damage the spleen's function, it can result in spleen and stomach weakness, leading to an imbalance in the ascending and descending functions. This can lead to water and dampness retention, the formation of phlegm and dampness, and ultimately result in conditions like edema. Furthermore, the presence of "dampness evil" is a continuous factor in chronic kidney disease [6].

In TCM, the spleen governs the ascending clear Qi and has the role of controlling and managing. The kidneys govern the descending functions and the storage of essence. When the clear Yang Qi ascends smoothly, and the governing function is appropriate, it prevents the loss of vital substances (such as proteins). When the spleen and stomach efficiently transform dampness, and the kidney's water function is normal, there is less likelihood of fluid retention and the development of edema. Therefore, in clinical treatment, strengthening the spleen, nourishing the stomach, and promoting Yang are important for maintaining the balance of Qi, fluids, and dampness, which can alleviate symptoms associated with water retention.

Professor Zhang Qi's academic thoughts emphasize that spleen and kidney deficiency is the key pathological mechanism of proteinuria in kidney disease. The accumulation of dampness and damp heat between spleen and kidney is the main pathological product of proteinuria in kidney disease. Spleen and kidney Qi and Yin deficiency, as well as the coexistence of cold and heat, are the basic characteristics of the evolution of the pathological mechanisms in kidney disease. Strengthening the spleen and tonifying the kidneys are the fundamental methods for treating proteinuria in kidney disease.

Yishen Huashi Granules are based on the classical formula "Shengyang Yifei Tang" from Li Dongyuan's "Piwei Lun" (Treatise on the Spleen and Stomach). The original formula primarily treats lung disorders caused by spleen and stomach Qi deficiency. Ingredients such as Astragalus, Ginseng, Atractylodes, and Licorice nourish the source Qi and strengthen the spleen and stomach, promoting the ascending of Qi. On the other hand, herbs like Qianghuo, Duhuo, Chaihu, and Fangfeng have a light and dispersing nature, helping to raise the Qi and resolve dampness. This combination of herbs balances the function of replenishing and dispersing, achieving the effects of tonifying Qi, lifting Yang, strengthening the spleen, nourishing the stomach, and resolving dampness and heat. It is suitable for conditions characterized by spleen and stomach Qi deficiency, blocked Yang Qi, and the formation of damp heat [7].

Even though "Yishen Huashi Granules" is derived from the formula "Shengyang Yifei Tang," which primarily focuses on treating the spleen and stomach, it is applicable to kidney diseases due to the fundamental interconnection between the spleen and kidneys in TCM theory. The kidneys rely on the spleen's digestive processes to nurture and nourish essence, which is crucial for the production of vital energy. As kidney diseases progress, dampness and moisture retention become common, and the spleen and stomach's ability to generate es-

sence is compromised. Yishen Huashi Granules, with their combination of herbs, effectively address these imbalances, strengthening the spleen, nourishing the kidneys, and resolving dampness and heat, making them a suitable treatment option for chronic kidney diseases associated with spleen and kidney deficiency and dampness retention.

2.1. Mechanisms of Action of Yishen Huashi Granules

Research has shown that Yishen Huashi Granules can improve BUN (Blood Urea Nitrogen), Scr (Serum Creatinine), and kidney hypertrophy index in diabetic nephropathy rats. This effect is likely achieved by reducing the expression of FoxO1 in the renal glomeruli, thereby decreasing glomerular apoptosis and ultimately protecting the kidneys and improving kidney function [8]. Another study has indicated that Yishen Huashi Granules upregulate the expression of nephrin and podocin, both of which are critical components of the renal podocyte structure, in diabetic nephropathy mice. Additionally, it reduces the expression of Platelet-Derived Growth Factor Receptor Beta (PDGFR β), resulting in decreased urinary protein excretion in diabetic nephropathy mice. This suggests that Yishen Huashi Granules have a renal protective effect [9].

The extracellular signal-regulated kinase (ERK) pathway plays a crucial role in the development and progression of diabetic nephropathy. Research conducted that Yishen Huashi Granules effectively reduce the activation of ERK in the renal cortex of diabetic nephropathy rats, thereby exerting a protective effect on the kidneys [10].

These studies collectively suggest that Yishen Huashi Granules may operate through various pathways to protect the kidneys. While the existing research primarily focuses on diabetic nephropathy, further investigation is needed to understand the mechanisms by which Yishen Huashi Granules protect against other forms of chronic kidney disease.

2.2. Clinical Applications of Yishen Huashi Granules

Chronic (Glomerular) Nephritis: Chronic glomerular nephritis is a chronic inflammatory reactive disease with an increasing incidence in recent years. Its clinical manifestations mainly include hematuria, proteinuria, edema, and hypertension. Without timely treatment, the disease can progress to chronic kidney failure, endangering the patient's life.

Results from Phase II and III clinical trials have shown that after 8 weeks of treatment, Yishen Huashi Granules have a good therapeutic effect on chronic glomerular nephritis with a pattern of spleen deficiency and dampness. They significantly reduce symptoms and signs such as edema, fatigue, poor appetite or loose stools, aversion to cold, and lumbar pain. Yishen Huashi Granules also reduce proteinuria, hematuria, stabilize kidney function, and are more effective in reducing proteinuria compared to the control group. Several observational clinical studies have also indicated that, in addition to a low-salt, low-fat, high-quality low-protein diet and basic treatments like antihypertensive, anti-

coagulant, and kidney function protection measures, the use of Yishen Huashi Granules can significantly reduce urinary albumin excretion in patients with chronic glomerular nephritis [11].

Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (ARB) are commonly used antihypertensive drugs in clinical practice, such as benazepril, losartan, and valsartan. Clinical practice has shown that these antihypertensive drugs can effectively lower blood pressure and reduce urinary protein excretion. Yishen Huashi Granules combined with losartan, valsartan, or benazepril can significantly improve patients' kidney function and clinical symptoms while alleviating adverse reactions. Additionally, some researchers have found that combining Yishen Huashi Granules with a spleen-invigorating and kidney-benefiting formula is effective in treating chronic nephritis, improving the condition, and enhancing the quality of life.

Yishen Huashi Granules are recommended for patients with chronic (glomerular) nephritis with a pattern of spleen deficiency and dampness. The recommended dosage is 1 packet per dose, 3 times a day, for a common treatment period of 2 to 3 months. They can reduce proteinuria in patients with chronic glomerular nephritis, regulate the body's immune function, promote diuresis, tonify yang, invigorate the spleen, and resolve dampness. Yishen Huashi Granules can be used in combination with ACEI or ARB without significant adverse reactions [12].

Diabetic Nephropathy: Diabetic nephropathy (DN) is one of the microvascular complications of diabetes, characterized by glomerular microcirculatory disorders and thickening of the glomerular basement membrane, leading to diabetic glomerulosclerosis. The probability of developing DN increases with the duration of diabetes, and it can result in continuous proteinuria, edema, hypertension, and eventually kidney failure.

Patients with DN who receive Yishen Huashi Granules in addition to conventional Western medical treatment can significantly improve early proteinuria symptoms, reduce urinary albumin excretion, and lower blood urea nitrogen. Yishen Huashi Granules have been found to reduce the expression of inflammatory markers like hs-CRP and IL-8 in early-stage DN patients, thereby inhibiting inflammation. Additionally, they can lower the levels of visceral adiposity factor (visfatin), an independent influencing factor for urinary albumin excretion.

In recent years, ACEIs and ARBs have been found not only to lower blood pressure but also to protect the kidneys. Yishen Huashi Granules have the effects of tonifying yang, benefiting the kidneys, and eliminating dampness. The combination of both can significantly lower blood pressure, relieve kidney stress, repair the glomerular charge barrier, and prevent thrombosis formation. This combination therapy can also prevent vasoconstriction, improve blood microcirculation, and reduce adverse reactions associated with antihypertensive medications [13].

Yishen Huashi Granules are recommended for diabetic nephropathy, especially in early-stage and elderly diabetic nephropathy patients. The recommend-

ed dosage is 1 packet per dose, 3 times a day, for a common treatment period of 2 to 4 months. They can improve symptoms, reduce serum creatinine, blood urea nitrogen, urinary protein, and inflammatory reactions. Yishen Huashi Granules can be used in combination with RAS inhibitors (ACEI or ARB), antithrombotic drugs, and microcirculation-improving medications. Their kidney-protective effects are superior to using Western medicine alone, and they can reduce the incidence of adverse reactions.

3. Other Kidney Diseases

Chronic kidney disease (CKD) patients generally have a state of micro-inflammation, which intensifies with worsening kidney function and exacerbates renal damage. Yishen Huashi Granules have been shown to significantly reduce the levels of hs-CRP, IL-6, and TNF- α in CKD stages 2 - 3 patients, while also reducing MDA and increasing SOD, thereby inhibiting inflammation and reducing oxidative stress damage.

Proteinuria directly affects the progression and prognosis of IgA nephropathy, making strict control of proteinuria crucial. Yishen Huashi Granules, when combined with potassium sparing diuretic losartan, can significantly reduce 24-hour urinary protein excretion in IgA nephropathy patients.

Nephrotic syndrome is a clinical syndrome caused by multiple factors, characterized by increased glomerular basement membrane permeability, leading to massive proteinuria, hypoalbuminemia, severe edema, and hyperlipidemia. Adding Yishen Huashi Granules to the conventional treatment significantly improves clinical outcomes, reduces the side effects of hormone therapy, and is especially effective for refractory nephrotic syndrome. When combined with renal ion importing formulas, Yishen Huashi Granules can achieve definite clinical efficacy and effectively improve kidney function [14].

Purpura nephritis, mainly characterized by necrotizing small vessel vasculitis, often accompanies various degrees of renal damage and can lead to kidney failure. Purpura nephritis tends to relapse, and treatment with corticosteroids alone is often ineffective. Combining Yishen Huashi Granules with corticosteroid treatment significantly reduces the recurrence rate of purpura nephritis and decreases 24-hour urinary protein excretion.

Yishen Huashi Granules are recommended for the treatment of IgA nephropathy, refractory nephrotic syndrome, and purpura nephritis. They can reduce 24-hour urinary protein excretion, improve kidney function, and reduce disease recurrence. The recommended dosage is 1 packet per dose, 3 times a day, with the treatment duration determined by the clinical physician based on the patient's response [15].

4. Chronic Kidney Function Decline and End-Stage Kidney Disease

Chronic kidney function decline is a syndrome of progressive kidney function

damage caused by various kidney diseases. Effectively delaying its progression and improving its symptoms is the key to treatment. Combining Yishen Huashi Granules with benazepril can significantly reduce blood creatinine, blood urea nitrogen, and 24-hour urinary protein quantification in patients with chronic kidney failure, improving kidney function and reducing proteinuria, thus delaying kidney damage.

For end-stage kidney disease patients, hemodialysis is the conventional treatment method, but it cannot address issues such as abnormal blood phosphorus, blood calcium, parathyroid hormone, and C-reactive protein levels, as well as vascular calcification caused by these abnormalities. Using Yishen Huashi Granules in conjunction with hemodialysis can improve the above-mentioned indicators to varying degrees. Combining Yishen Huashi Granules with valsartan can protect residual kidney function in uremic patients, reduce the levels of inflammatory factors such as CRP, IL-6, and TNF- α , and improve the micro-inflammatory state of patients [16].

Gastrointestinal symptoms are the earliest and most prominent symptoms in patients with chronic kidney function decline, mainly due to gastrointestinal motility disorders, gastrointestinal mucosal inflammation and edema, uremic toxins, gastrointestinal hormones, and metabolic acidosis, among other factors. Traditional Chinese medicine emphasizes the treatment of early-stage chronic kidney function decline by invigorating the spleen, eliminating dampness, and preventing the accumulation of dampness and toxins. Yishen Huashi Granules have the effects of tonifying yang, benefiting the kidneys, eliminating dampness, and promoting diuresis. Clinical observational studies have shown that Yishen Huashi Granules can significantly improve gastrointestinal symptoms in patients with chronic kidney function decline, with an effective rate of 91.7%, significantly higher than the control group (effective rate: 72.9%).

Yishen Huashi Granules are recommended for chronic kidney failure and end-stage kidney disease. The recommended dosage is 1 packet per dose, 3 times a day, and they can improve kidney function, relieve gastrointestinal symptoms, invigorate the spleen, benefit the kidneys, eliminate dampness, and remove turbidity. In addition, they can also improve the micro-inflammatory state in patients with chronic kidney function decline and correct biochemical indicators such as blood phosphorus and blood calcium. No significant adverse reactions have been observed with long-term use.

5. Safety of Yishen Huashi Granules

5.1. Preclinical Safety Studies

In preclinical safety studies, mice were orally administered Yishen Huashi Granules at a dose of 200 g of herbal medicine/kg (approximately 266.7 times the clinical dose). Most of the animals exhibited reduced activity and were less active, but there were no other abnormal behavioral changes. There were no abnormal secretions from the mouth, nose, or eyes, and the animals' water and

food intake remained normal. There were no significant changes in respiration, and the color of urine and feces was slightly darker on the first day but returned to normal within a week. No animal deaths were reported within one week. Animals that survived for one week were euthanized, and upon dissection, no significant changes were observed in the organs.

In another study with rats, Yishen Huashi Granules were orally administered at a dose of 75 g of herbal medicine/kg (approximately 100 times the clinical dose). Most of the animals exhibited reduced activity, but there were no tremors or piloerection. There were no abnormal secretions from the mouth, nose, or eyes, and respiration remained unchanged. The color of urine and feces was slightly darker on the first day, but there was no constipation or diarrhea. The animals' response to external stimuli did not show significant changes, and no animal deaths were reported within one week. Animals that survived for one week were euthanized, and upon dissection, no significant changes were observed in the organs [17].

In a long-term toxicity test in rats, three different doses of Yishen Huashi Granules (10 g, 20 g, and 45 g of herbal medicine/kg) were administered (approximately 13 times, 26 times, and 60 times the clinical dose, respectively). Rats were continuously orally administered the granules for six months (with some rats in the high-dose group receiving a three-month live dissection control period and a one-month recovery period after discontinuation of treatment). The results showed that, except for male rats in the high-dose group having lower weight gain compared to the control group (with no significant difference during the recovery period), there were no significant abnormalities observed in general observations, blood routine, blood biochemistry, organ coefficients, or histopathological examination of 24 organs. These findings indicated that Yishen Huashi Granules at a dose of 45 g of herbal medicine/kg (approximately 60 times the clinical dose) did not exhibit toxicity [18].

5.2. Clinical Studies

According to Phase II and III clinical trials and published clinical observational studies, the main adverse reactions when using Yishen Huashi Granules alone to treat kidney diseases are dry mouth and bitter taste. Clinical observational studies have reported that when Yishen Huashi Granules are used in combination with steroids, immunosuppressants (such as cyclophosphamide and mycophenolate mofetil), the main adverse reactions are skin rash, leukocyte decrease, and liver function impairment. When Yishen Huashi Granules are used in combination with ACE inhibitors (such as benazepril) or ARBs (such as potassium losartan and valsartan), the main adverse reactions are dizziness, headache, dry cough, and orthostatic hypotension. These adverse reactions are primarily caused by the concomitant medications [19] [20].

The results of animal studies suggest that Yishen Huashi Granules have good safety within the therapeutic dose range, and there is also clinical research evi-

dence indicating their good safety profile with no reports of severe adverse reactions. However, a more comprehensive and systematic safety evaluation would require further large-scale studies.

6. Conclusion and Outlook

Since the approval of Yishen Huashi Granules in 2009, it has been used in clinical practice for nearly 14 years. Over this decade, we have accumulated extensive clinical experience with Yishen Huashi Granules, and its therapeutic efficacy is well-established. It has shown significant effects, particularly in reducing proteinuria, improving edema, alleviating fatigue, cold limbs, and poor appetite. In addition to the indications mentioned in the product instructions, which include “proteinuria due to spleen deficiency and dampness-heat syndrome in chronic glomerulonephritis (Scr < 2 mg/dl),” Yishen Huashi Granules can be used in the treatment of various chronic kidney diseases with Traditional Chinese Medicine differentiation patterns such as spleen deficiency with dampness-heat, spleen-kidney deficiency, sinking of qi with elevated urinary protein, and conditions like diabetic nephropathy, IgA nephropathy, refractory nephrotic syndrome, and purpuric nephritis, among others. From the perspective of “diagnosing the mechanism and determining treatment,” it can also be applied to patients with stage 4 - 5 chronic kidney disease or end-stage renal disease undergoing renal replacement therapy to improve their symptoms and prognosis. When used in combination with common clinical medications like RAS inhibitors (ACEI/ARB), anticoagulants (e.g., clopidogrel), and microcirculation-improving drugs (e.g., cilostazol), no clear adverse reactions have been reported, and it can provide better therapeutic effects while potentially reducing the side effects of Western medications. The typical dosing regimen is 1 packet per time, three times a day, and long-term adherence to the treatment has not shown significant adverse reactions. The specific duration of treatment should be determined by clinical physicians based on the severity of the patient’s condition and treatment outcomes.

However, it’s important to note that this consensus is based on existing research data and has several limitations:

There is a relative lack of systematic foundational research on the use of Yishen Huashi Granules in treating various chronic kidney diseases. Further research is needed to investigate the onset time and targets of Yishen Huashi Granules in different chronic kidney diseases to explore its efficacy and mechanisms of action.

Existing literature is predominantly in Chinese and often suffers from small sample sizes, short observation periods, poorly designed clinical trial protocols, lack of randomization and blinding, and the absence of hard endpoints. High-quality clinical research data is lacking. Large-scale, high-quality, rigorously designed clinical evidence is urgently needed to assess the efficacy and safety of Yishen Huashi Granules in the treatment of various chronic kidney diseases.

Despite being on the market for many years, further evaluation of the safety profile in larger populations and post-market assessments are still necessary. Randomized controlled trials or real-world studies are needed to further validate its effectiveness and safety in treating CKD, providing valuable references for the rational and standardized use of Yishen Huashi Granules in clinical practice.

In conclusion, to address the issue of incomplete information in the drug's instructions and to provide guidance to healthcare providers and patients on the proper and standardized use of this traditional Chinese medicine, we convened a panel of renowned experts in both traditional Chinese and Western medicine. This expert consensus was developed considering the unique characteristics of the product, along with the experts' years of knowledge and experience. Through multiple expert meetings, workshops, and offline discussions, this consensus was formulated after a preliminary research phase, consensus formation stage, and iterative refinement stage. We hope that by promoting this consensus, users will have a clearer understanding of the drug's indications and main treatment effects, enabling them to make more targeted medication choices. Additionally, it can serve as a foundation and guide for further research and development of the product, providing a clear direction for future endeavors.

Conflicts of Interest

The authors declare no conflicts of interest.

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