

# Therapeutic use of traditional Chinese herbal medications for chronic kidney diseases

Yifei Zhong<sup>1</sup>, Yueyi Deng<sup>1</sup>, Yiping Chen<sup>1</sup>, Peter Y. Chuang<sup>2</sup> and John Cijiang He<sup>2</sup>

<sup>1</sup>Department of Nephrology, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China and

<sup>2</sup>Division of Nephrology, Department of Medicine, Mount Sinai School of Medicine, New York, New York, USA

Traditional Chinese herbal medications (TCHMs) are frequently used in conjunction with western pharmacotherapy for treatment of chronic kidney diseases (CKD) in China and many other Asian countries. The practice of traditional Chinese medicine is guided by cumulative empiric experience. Recent *in vitro* and animal studies have confirmed the biological activity and therapeutic effects of several TCHMs in CKD. However, the level of evidence supporting TCHMs is limited to small, nonrandomized trials. Due to variations in the prescription pattern of TCHMs and the need for frequent dosage adjustment, which are inherent to the practice of traditional Chinese medicine, it has been challenging to design and implement large randomized clinical trials of TCHMs. Several TCHMs are associated with significant adverse effects, including nephrotoxicity. However, reporting of adverse effects associated with TCHMs has been inadequate. To fully realize the therapeutic use of TCHMs in CKD, we need molecular studies to identify active ingredients of TCHMs and their mechanism of action, rigorous pharmacologic studies to determine the safety and meet regulatory standards required for clinical therapeutic agents, and well-designed clinical trials to provide evidence-based support of their safety and efficacy.

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Corticosteroid and immunosuppressive medications are cornerstone therapies for glomerular diseases. However, these medications are associated with serious side effects. Furthermore, resistance to therapy and relapse of disease after discontinuation of medication are common. For patients with chronic kidney disease (CKD), modulation of the renin–angiotensin axis provides only partial salutary effects and does not necessarily prevent the progression to end-stage renal disease and the need for renal replacement therapy.<sup>1</sup> The lack of therapeutic options for CKD has prompted patients in China and other Asian countries to seek out alternative treatment such as traditional Chinese herbal medications (TCHMs).

The practice of traditional Chinese medicine (TCM) is largely guided by the cumulative empirical experience of its practitioners. Although many small clinical studies suggest a therapeutic potential for TCHMs in CKD, large randomized trials are lacking. Some TCHMs are known to cause nephrotoxicity, which are often overlooked by some physicians and patients because of the incorrectly held belief that herbal medications are innocuous. Another major concern is that the active component(s) in most TCHM formulas and their underlying mechanism of action remain unidentified. Despite these concerns, significant progress has been made in the past decade. However, recent reviews of this topic in the English language are limited.<sup>2–4</sup>

In this review, we reviewed the current knowledge of TCHMs for the treatment of CKD based on publications in peer-reviewed journals of the English language. We also render a prospective on the direction of future investigation. Our target audience includes clinical nephrologists who care for patients being treated with TCHMs and basic scientists who are interested in the drug discovery pertaining to TCHMs.

## GENERAL THERAPEUTIC PRINCIPLES OF TCM

The overarching principle in the practice of TCM is the focus on individual assessment and treatment to coordinate the natural balance of the Yin and Yang, which are two major opposing forces of the body represented in the ancient Chinese Taoism philosophy. TCM posits that disease of the body arises from an imbalance within the body and between the body and the nature, leading to an alteration in the entire body system.

**Correspondence:** Yifei Zhong, Department of Nephrology, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 200032, China. E-mail: yifeilily@126.com or John Cijiang He, Division of Nephrology, Mount Sinai School of Medicine, One Gustave L Levy Place, Box 1243, New York, New York 10029, USA. E-mail: cijiang.he@mssm.edu

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**Table 1 | Comparison between western medicine and traditional Chinese medicine (TCM)**

	Traditional Chinese medicine	Western medicine
Development Principles of practice	Based on empirical experience of practicing TCM. Balancing Yin-Yang and the five major elements.	Based on the scientific knowledge and practice experience. Understanding the molecular and cellular pathophysiology of disease and targeting therapy to normalize the underlying disease process.
Disease perception	Disease is the result of interactions among different parts of the body and the environment.	Disease is engendered by alterations in the cellular and molecular processes.
Nomenclature of the organ	Organ system is named by the organ and its related tissues. For example, kidney usually means the kidney and related organs such as bone, ear, and so on.	Each organ has a unique name.
Diagnostic approach	Diagnosis involves inspection, auscultation and smelling, inquiry, pulse-taking, and palpation. <sup>a</sup>	Diagnosis relies on history, physical examination, and diagnostic testing of biological samples (pathology, blood tests, and radiographic imaging).
Principle of therapy	Apart from treatment of disease, TCM also focuses on the reaction of the body to herbs. Prescription is adjusted frequently based on signs and symptoms during follow-up visits.	Emphasis is on targeted therapy that normalizes the underlying disease pathogenesis. Efficacy of treatment is evidence based. The dose of medications is adjusted or medications are changed if the effect is not achieved.
Therapy with medications	Prescription is based on the combination of multiple herbs and their interaction in order to regulate the whole body system and minimize toxic effects of herbs.	Drugs are designed based on the individual target with defined molecular identity. Most patients are first treated with one drug and a second drug is added if the first medication is not efficacious.
Physician training	Based on individual experiences that have been accumulated over years of practice.	Understanding of basic medical knowledge and familiarity with clinical trials and guidelines.

<sup>a</sup>Inspection means observation of patient's general condition including physical appearance and activity, body movement, skin color and condition, color and appearance of the tongue, and body secretions (urine and feces). Auscultation means listening to the voice, respiration, coughing, and so on. Smelling means to smell the odors from patients' body, urine, and feces. Inquiry is to get patients' current and past medical history. Pulse-taking is a diagnostic method performed by pressing patients' radial artery to examine the strength and variability of the pulse. Palpitation is to touch, feel, and press the skin and muscle, hand and foot, and chest and abdomen in order to detect pathological changes.

The syndrome differentiation and treatment approach is a principle that has been used to understand, diagnose, and treat diseases based on the theories of TCM. The diagnostic procedure involves an analysis of the clinical data regarding symptoms, physical signs, and disease history, together with information obtained from application of the four diagnostic methods, which consist of inspection, auscultation and smelling, inquiry, and pulse-taking and palpation (see Table 1). These four diagnostic methods allow the differentiation of syndromes, which in turn dictates the approach to clinical treatment. The patient's response to a specific clinical treatment plan then informs the correctness of the deduced differentiation. These three key aspects of the syndrome differentiation and treatment approach form the basis of diagnosis and treatment in TCM.

In the practice of TCM, it is generally considered that multiple herbal medications are more effective than a single herbal agent. Therefore, prescriptions of TCHMs usually combine several herbs in which a few components contribute to the main effect of the prescription, and these herbs are referred to as 'ruler drugs.' In addition, another group of herbs known as 'minister drugs' provide an additive effect to the 'ruler drugs,' and the remaining constituents of the herbal prescription are called 'assistant drugs and messenger drugs.' Physicians practicing TCM usually prescribe formulas that combine several types of herbs or minerals, where one herb represents the principal component and others serve as adjunctive agents, assisting the effects or facilitating the delivery of the principal component. In China, more than 3200 herbs and 300 mineral and animal extracts are

used in more than 400 different formulas.<sup>5</sup> Adjustment of individual components of the herbal prescription by the practitioner is based on patients' signs and symptoms, with an overall goal of restoring the balance of Yin and Yang. At each follow-up visit, physicians usually change either the herbal components or their relative percentage in the prescription.

Differences in the practice and principles of TCM and western medicine are summarized in Table 1. These differences largely stemmed from their different historical backgrounds. Concepts of TCM related to organ function, disease pathogenesis, and treatment approach were formulated in the absence of our current molecular understanding of disease and were deeply influenced by social, religious, and cultural factors in these historical periods. One can debate the validity and scientific merits of the TCM approach. However, one should not immediately discount the empiric knowledge accumulated over centuries of treating patients with different decoctions of herbal mixtures. With recent integration of TCM and western medicine, diagnosis of CKD by practitioners of TCM has supplemented traditional diagnostic approach with western molecular and imaging diagnostic tools. The current treatment of CKD in TCM is often achieved by combining TCHMs and western pharmacologic agents. Owing to the rapid economic growth and scientific development over the past decade, the Chinese government has supported studies to examine the scientific basis of TCM using advanced cell and molecular biology approaches. A rapid development of TCM is expected over the next decade.

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