

A History of Four Chinese Herbs Used to Treat Acute and Chronic Urinary Disorders

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Introduction: Traditional Chinese Medicine (TCM) has treated Urinary Tract Infections (UTIs) for over 4 millennia. This review explores history of the classical diagnosis of "urinary syndrome (US)" in TCM and the four herbal ingredients of Huang-lian-Jiedu Decoction (HLJDD), a traditional herbal tonic, used to treat US. With increasing antibiotic resistance, alternative therapies for UTIs have gained importance. We explore the TCM concept of US and *lin* and its relevance to the modern antibiotic era.

Sources and Methods: Primary Chinese texts, translations, medical literature, and academic publications were reviewed to investigate the treatment of US with HLJDD in TCM. Botanical gardens were explored to find living versions of historic herbs used in HLJDD.

Results: The concept of US, referred to as *lin* in TCM, can be traced back to in the Yellow Emperor's *Classic of Internal Medicine* in 2600 BCE. In 610 CE, Chao Yuanfang described herbs as a treatment of US. Wang Tao, in 752 CE, classified US into five types, with Heat US corresponding to the Western diagnosis of UTI. Wang Tao also documented HLJDD as an herbal remedy for 'heat clearing'. In *The Handbook of Prescriptions for Emergencies* (220 CE), HLJDD consists of *Coptis chinensis* (Franch.)[†], *Radix scutellariae*, *Cortex phellodendri*, and *Fructus gardeniae* in a 3:2:2:3 proportion. Recent clinical trials have examined HLJDD and its ingredients, investigating their efficacy as alternative treatments for UTI. Some trials found that the herbal ingredients not only enhance the effects of antibiotics, but also prevent UTIs when taken prophylactically by postmenopausal women. Most recently, *Coptis chinensis* was found to have inhibitory activity against many uropathogenic bacteria, including *E. coli*.

Conclusions: This historical perspective provides a more complete understanding of the evolution of Heat US in TCM and its correlation to the modern diagnosis of UTI, along with the herbal ingredients of HJLDD as treatment. Modern research confirms the application of HLJDD and its ingredients as an alternative treatment for UTI.

Keywords: Traditional Chinese Medicine, Chinese Herbal Medicine, Urinary Tract Infection, Urinary Syndrome

U rinary tract infection (UTI) is diagnosed each year in approximately 400 million people worldwide.(1,2) The standard treatment for UTI is antibiotic therapy. According to the Center for Disease Control and Prevention, UTI is among the most common causes for antibiotic use. Increase in bacterial resistance to antibiotics poses a mounting threat to public health. (3) Microbial resistance motivates the exploration of alternative therapies for UTIs, particularly within the field of Traditional Chinese Medicine. Because of this growing interest, a thorough review of Chinese literature was undertaken to understand the development of a traditional herbal therapy in the context of the condition that called for it. *Lin* is a traditional Chinese medical diagnosis described as painful, dribbling, or difficult urination with associated frequency and urgency according to the *Great Dictionary of Chinese Medicine*. (4) This study examines the historical development of the traditional Chinese medical diagnosis known as *lin* and its evolution to Heat Urinary Syndrome, a close analog to the contemporary diagnosis of urinary tract infection. We also traced the history of an herbal treatment used for the Heat Urinary Syndrome, *Huang-lian-Jie-du* Decoction, and investigated modern research that spoke to the herbs' efficacy at treating symptoms of urinary tract infections.

⁺ Common botanical notation for the many species originally catalogued by the French botanist Adrien Franchet (1834-1900).

SOURCES AND METHODS

A review of primary Chinese texts with accompanied translations, medical literature and academic publications was undertaken to investigate the history of Urinary Syndrome and HLJDD in Traditional Chinese Medicine and the development of HLJDD's current application. We conducted field research at the William and Lynda Steere Herbarium (New York Botanical Gardens (NYBG), New York) and accessed NYBG resources including the Index Herbariorum (sweetgum. nybg.org/science/ih/) and the records of the LuEsther T Mertz Library (New York).

RESULTS

The History of Heat Urinary Syndrome:

Within Traditional Chinese Medicine, the treatments for symptoms associated with the modern diagnosis of a urinary tract infection have a history that dates back four millennia. To help identify traditional alternative treatments that could be advantageous for urinary tract infections, it is imperative to identify traditional diagnoses with a similar clinical picture. The most closely associated disease in traditional texts to our current diagnosis of a UTI is *lin*, translated as urinary syndrome. Predictably, the accounts of *lin* appear before its treatment. The term *lin*, first appears as a term for urinary syndrome in the Yellow Emperor's *Classic of Internal Medicine* in 2600 BCE.(5) Around this same time, urinary syndrome was referenced in both the medical manuscripts at Mawangdui, before 168 BCE, and Wuwei, in the first century CE.(6) Over time, the diagnosis of lin became more refined. Hua Tuo (140–208 CE) distinguished eight types of Urinary Syndrome: Cold, Hot, Qi, Fatigue, 'Sticky', Sand, Deficient and Excess types.(7) The imperial physician of the Sui Dynasty, Chao Yuanfang, explicitly recorded the subtypes of *lin* and its treatments in *Treatise on the* Etiology and Symptoms of Diseases.(8) Chao Yuanfang's treatment were described as a complex intervention that combined herbs, daoyin (exercises), and lifestyle changes as important components. In 752 CE, Wang Tao added to this knowledge in The Medical Secrets of an Official where he differentiated five types of Urinary Syndrome, i.e. Stone, Qi, 'Sticky', Fatigue and Hot.(8) These five types of Urinary Syndrome were agreed upon and the subtypes studied for the proceeding centuries. Now, it is understood that different types of urinary syndrome correlate generally with the following Western pathologies.(9)

- Heat Urinary Syndrome: acute infection of urinary tract (UTI), acute nephritis, cystitis
- Blood Urinary Syndrome: tuberculosis of kidney, carcinoma of bladder or kidney
- Stone Urinary Syndrome: urinary calculi
- 'Sticky' Urinary Syndrome: urethritis
- Fatigue Urinary Syndrome: chronic prostatitis.

Species	Active Ingredient	Traditional Name	Associated Plant	Medicine Source
Cortex Phillodendri	barberine	Huangbai	Amur Cork Tree	Bark
Fructus Gardeniae	genipin	Zhi Zi	Gardenia jasminoides	Dried Fruit
Coptis chinensis	Coptidis alkaloids	Duěn è huánglián	<i>Rhizoma Coptidis</i> or Chinese Goldthread	Rhizome
Radix scutellariae	Flavones	Huang Qin	<i>Scutellaria baicalensis</i> or Chinese skullcap	Root

Table. Chinese herbs of HLJDD and their potential chemical and botanical properties, in continuous use as part of traditional chinese medicine (TCM) for at least 2000 years.



Figure 1A (left). *Coptis Chinensis (Franch.)* or Chinese Goldthread, whose rhizome provided important alkaloids in HLJDD. **Figure 1B (right)**. *Scutellaria baicalensis*, or Chinese skullcap, collected by H Swift, August, 1939, regarded as similar to *radix sutelariae*, or Huang Qin, whose roots are used in HLJDD. Both courtesy New York Botanical Gardens, NY.

While Heat Urinary Syndrome is most synonymous with acute (UTI), it is important to note that there is never an exact correspondence between Chinese and Western Medicine. This manuscript is cautious to retrospectively diagnose a UTI in those with Heat Urinary Syndrome due to the lack of physical evidence.(10) It aims to establish a connection between the two diagnoses to provide historical context and elucidate why the herbal treatment of *lin* was considered for a UTI.

In the 12th century, Zhu Dan Xi wrote, "In *lin* disease with dribbling of urine and difficult urination there is always Heat and one must clear Heat to free urination."(11) This idea was reinforced by Zhu Dan Xi in 1418 in *The Essential Methods of Dan Xi*, when he wrote, "There are five types of Urinary Syndrome but all have Heat."(12) The symptom of Heat, what is known as burning on urination, is foundational in diagnosing and treating urinary syndromes. Given its frequency, the treatment of heat became principal to treating all subtypes of urinary syndromes. In 752 CE, Wang Tao, the same author known for differentiating the five types of Urinary Syndrome, documented Huang-lian-Jie-du Decoction (HLJDD) as a prescription for Heat clearing and detoxifying.(8)

History of Huang-lian-Jie-du Decoction and contemporary research:

Huang-lian-Jie-du Decoction (HLJDD) was first

discovered in the Handbook of Prescriptions for Emergencies written between 206 BCE- 220 CE, but it was first explicitly recorded by Wang Tao in Arcane Essentials from the Imperial Library.(13,14) The ingredients of HLJDD and their proportions are as follows: Huang Lian (Coptis chinensis), Huang Qin (Radix scutellariae) Huang Bo (Cortex phellodendri), and Zhi Zi (Gardenia fructus), in a 3:2:2:3 proportion. Despite the diverse treatments of lin used throughout history, HLJDD has been applied and improved upon over time. Today, HLJDD and several of its herbs have been studied and validated through contemporary clinical trials as a treatment for different conditions, including urinary tract infections. Modern research confirms the potential applications of HLJDD and its properties, including antiinflammatory, antioxidant, antithrombotic, hypoglycemic, hypolipidemic, hypotensive, and antitumoral effects.(15-17) In 1984, the Journal of Chinese Medicine published a clinical trial that treated a portion of patients diagnosed with Heat Urinary Syndrome with either the herbal remedy of Ba Zheng San, Eight Upright Powder, or Huang Lian Jie Du Tang Coptis Resolving Toxin Decoction. Of the 125 subjects, 79.8% were found to be cured.(18)

More recently, a 2019 study was conducted to analyze the phytochemical and pharmacokinetics of HLJDD with the hypothesis that herbs create synergic interactions among one another and improve pharmacological activities better than single drugs. The study concluded



Figure 2A (left) and B (right, close up). *Gardenia jasminoides*, equivalent to *Fructus gardeniae*, or Zhi Zi, thought to contribute, among other phytochemicals, genipin, in HLJDD, from its dried fruit. From the Enid Haupt Conservatory House 3, New York Botanical Gardens (IJUH Archives, 2023).

that HLJDD possessed certain pharmacokinetic properties that potentiated better pharmacological effects than a single drug or couplet medicine.(2)

Three of the four herbs in HLJDD, Coptis chinensis, Radix scutellariae, and Cortex phellodendri have been included in various clinical trials testing their efficacy in treating UTIs over the past twenty years. Coptis chinensis was found to have anti-inflammatory properties and inhibitory activity against several uropathogenic bacteria, including E. coli.(19) An in vitro study evaluated the antimicrobial properties of three different berberine alkaloids (the major active component of Coptis chinensis) and found that the growth rate constant of E. coli was reduced with all berberine alkaloids studied (berberine, coptisine and palmatine).(20) A 2007 randomized control trial conducted by Shen et al. gave postmenopausal female subjects with symptoms of a UTI and positive bacterial urine culture a treatment known as Er Xian Tang (EXT). The decoction included two of the four herbs included in HLJDD: Cortex phellodendri and Coptis chinensis.(21) Compared to the control group of four weeks of antibiotic capsules alone, EXT treatment was as effective at four weeks and at 3 month recurrence rates. The findings suggested that the herbs may provide more effective treatment than antibiotics alone for acute UTI episodes and potential prophylactic use for longterm management of recurrent infections. A 2011 trial

conducted by Ma et al. tested a decoction that included *Radix scutellariae* and produced similar findings for postmenopausal women in the acute and prophylactic setting.(22)

Chen et al. and Luo et al. performed randomized clinical trials (RCTs) comparing a *Cortex phellodendribased* approach plus antibiotics with antibiotics alone in the treatment of UTI symptoms.(23,24) Chen et al. used a modified erxian decoction plus antibiotics in middle-aged and postmenopausal women, finding that the Chinese Herbal Medicine (CHM) approach was as effective as antibiotics in the acute management of UTI as well as in longer-term prophylaxis.(23) Similarly, Luo et al. used a bushen tonglin decoction on females with chronic UTI and concluded it may have potentiated the standard role of antibiotics.(24)

A 2018 systematic review confirmed that the decoctions tested in Chen 2008 and Luo 2011, which utilized *Cortex phellodendri*, may provide effective treatment during the acute phase of UTI and prevent recurrence in the six months following treatment when given prophylactically (25). Another study concluded, however, that the two RCTs were of sub-optimal quality limiting their generalizability either as a sole intervention or as an adjunct to antibiotics in treating symptoms of recurrent UTIs in postmenopausal women.(8)



Figure 3. The Amur corktree or *Phellodendron amurense* closely related to its cousin *P. chinense*, the barks of which are collectively referred to as Huang Bai in TCM and are thought to contribute the phytochemical barberine in HLJDD. From the grounds of the NYBG, July 2023 (IJUH Archives).

CONCLUSIONS

The use of herbal therapies to treat *lin* and urinary difficulties in China has been documented for more than two thousand years. In our modern era of increasing antibiotic resistance, the efficacy of traditinal Chinese herbal approaches has taken on renewed interest. Components of the original Huang-lian-Jie-du Decoction including Coptis chinensis, Radix scutellariae, and Cortex phellodendri, have been included in some contemporary clinical trials but will require more rigorous RCTs to establish their role as an adjunct or replacement of antibiotic therapy. The precise roles of Coptis chinensis, Radix scutellariae, and Cortex phellodendri have yet to be discovered; they have may have been in more continuous use by health care practitioners in treating urinary difficulties than any other compounds in history. They may yet hold an even more promising role in the treatment of urinary tract infection in the future.

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Figure 4. Leaves of *Phellodendron amurense* or the Amur corktree displaying the classical pinnately compound, pointed, ovals with wavy margins. While the crushed leaves had a fragrance of turpentine, it is the dried bark of the corktree which is used in HLJDD. From the grounds of the NYBG, July 2023 (IJUH Archives).