

Traditional Chinese Herbal Medicine and Lupus Nephritis

Xiaozhen Mu¹, Quan Jiang¹ and Chenchen Wang^{2*}

¹Department of Rheumatology, Guang'anmen Hospital Affiliated to China Academy of Chinese Medical Sciences, Beijing, China

²Departments of Rheumatology, Center for Complementary and Integrative Medicine, Tufts Medical Center/Tufts University School of Medicine, Boston, MA, USA

Abstract

Available treatments for lupus nephritis, a potentially fatal autoimmune disease, are limited by suboptimal efficacy and increased risk of infections and malignancies; inevitably they do not meet clinical demands. Traditional Chinese herbal medicine has recently been recognized for its potential therapeutic benefits for lupus nephritis. Encouraging evidence from clinical trials and observational studies demonstrate that Chinese herbal medicine may possess benefits for treating patients with lupus nephritis. The significant benefits of these Chinese herbal medicine modalities that have been observed and reported include improving clinical efficacy, reducing level of antibodies and proteinuria, ameliorating renal damage, diminishing the dosage of prednisone use as well as decreasing toxicity, and preventing disease flare-up. This overview aggregates the current body of medical knowledge on the therapeutic benefits of several types of Chinese herbal medicines for lupus nephritis, and these promising herbal medicines may challenge the current treatment paradigms available for lupus nephritis and inform future research and clinical practice.

Keywords: Chinese herbal medicine; Lupus nephritis; *Rhizoma alismatis*

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease with potential lethality which is incurable and requires long-term treatment [1]. Lupus nephritis, which occurs in 38%-60% of SLE patients during the course of the disease, results in significant morbidity and mortality [2,3]. SLE patients who develop lupus nephritis have a reduced life expectancy by 15 years and suffer poor health-related quality of life [2,4,5]. The rate of progression to end-stage renal disease remains high [6-8]. Current therapeutic approaches cannot meet the clinical demands of patients who have lupus nephritis and are limited by suboptimal efficacy of the treatment and increased risk of infections. Several novel biologic agents for lupus nephritis also show substantial toxicity, and the results of long-term application remain unknown [9-11]. Given the complexity, cost and apparent ineffectiveness of the therapeutic armamentarium used in lupus nephritis, complementary and integrative therapies are becoming increasingly attractive [12,13]. Chinese herbal medicine, which has been practiced for thousands of years, is still one of the main treatments in China and eastern Asia and continues to be disseminated widely around the world in the 21st century. After millennia of use and research, traditional Chinese herbal medicine has recently been recognized for its potential therapeutic benefits for patients with lupus nephritis. Clinical trials and observational studies provide encouraging evidence that Chinese herbal medicine possesses benefits for patients with lupus nephritis [14,15]. Significant benefits of Chinese herbal modalities that have been observed and reported include improving symptoms, reducing level of antibodies and proteinuria, ameliorating renal damage, diminishing the dosage of prednisone use as well as decreasing toxicity, and preventing disease flare-up [14,16,17].

In this review, we have conducted a comprehensive search of four English and Chinese biomedical databases and from inception through February 2018. These databases included PubMed, Chinese National Knowledge Infrastructure, Chongqing VIP, and WanFang Med Online. Searches were limited to human studies in English and Chinese language. We also screened the reference lists of selected studies for additional publications. Studies were grouped into the four categories which include 15 randomized controlled trials of Chinese herbal medicine for lupus nephritis (Table 1). In all these studies,

participants met 1982 or 1997 ACR criteria for classification of lupus nephritis. This overview summarizes the current body of knowledge on the therapeutic benefits of several types of Chinese herbal medicines for lupus nephritis. These promising herbal medicines may challenge the current treatment paradigms available for lupus nephritis and inform future research and clinical practice.

Liu-wei-di-huang pill for lupus nephritis

Use of the Liu-wei-di-huang pill, among the most popular Chinese herbal medicines for chronic kidney disease, was initially recorded in the earliest Chinese pediatric monograph, *Key to Therapeutics of Children's Diseases*, during the Northern Song Dynasty (960-1127 AD) [18,19]. The pill is composed of six species of medical herbs: *Radix Rehmanniae Praeparata*, *Rhizoma Dioscoreae*, *Fructus Corni*, *Cortex Moutan*, *Poria* and *Rhizoma Alismatis*. According to traditional Chinese medicine and western medicine theory, the pill is believed to have the function of 'nourishing kidney yin' and is also suggested to have anti-inflammatory and immunomodulation effects to protect kidney function [20-22].

We identified four randomized controlled trials of Liu-wei-di-huang, which comprised a total of 307 patients [23-26]. The mean age ranged from 22 to 25 years, and disease duration was 29.5-44.4 months. Average study duration was 3 to 6 months. One randomized controlled study of 33 patients with lupus nephritis administered the Liu-wei-di-huang pill (3 g, three times a day) combined with prednisone 7.5 mg/d-60 mg/d and cyclophosphamide 8-12 mg/kg via intravenous injection once every 2-4 weeks [23]. 31 patients in the control group were given prednisone and cyclophosphamide (same dosage). Compared with the

***Corresponding author:** Chenchen Wang, Department of Rheumatology, Center for Complementary and Integrative Medicine, Tufts Medical Center/Tufts University School of Medicine, Boston, MA, USA, Box 406, MA 02111, Tel: 617-636-3251; Fax: 617-636-1542; E-mail: cwang2@tuftsmedicalcenter.org

Received June 17, 2018; **Accepted** October 08, 2018; **Published** October 15, 2018

Citation: Mu X, Jiang Q, Wang C (2018) Traditional Chinese Herbal Medicine and Lupus Nephritis. *Health Care Current Reviews* 6: 230. doi: [10.4172/2375-4273.1000230](https://doi.org/10.4172/2375-4273.1000230)

Copyright: © 2018 Mu X, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Source [Ref]	Number (Female %)	Mean Age (year)	Disease Duration (month)	Intervention	Control	Study Duration	Results
Liu-wei-di-huang pill							
Zheng, [23]	64 (90.6%)	24	44.4	Liu-wei-di-huang pill, 3 g three times a day; Cyclophosphamide, 8-12 mg/kg, intravenous injection once every 2-4 weeks; Prednisone, 7.5 mg/d-60 mg/d.	Cyclophosphamide, 8-12 mg/kg, intravenous injection once every 2-4 weeks; Prednisone, 7.5 mg/d-60 mg/d.	3 months	↓ 24 h urine protein, ESR s ↑ C3, Alb s ↓ Scr ns Adverse effects, recurrence rate s
Huang, [24]	51 (45.1%)	22	38.4	Liu-wei-di-huang pill, 3 g, three times a day; Mycophenolate mofetil, 0.5 g/d-2.0 g/d; Prednisone, 7.5 mg/d-60 mg/d.	Mycophenolate mofetil, 0.5 g/d-2.0 g/d; Prednisone, 7.5 mg/d-60 mg/d.	3 months	↓ 24 h urine protein s ↑ C3, Alb s ↓ Scr ns Adverse effects s
Xian, [25]	120 (NR)	NR	29.5	Liu-wei-di-huang decoction, 200 ml, twice a day; Tripterygium glycosides tablet, 20 mg, three times a day; Cyclophosphamide, 0.4 g, intravenous injection once every 2-4 weeks; Prednisone, 7.5 mg/d-1.2 mg/kg/d.	Cyclophosphamide, 0.4 g, intravenous injection once every 2-4 weeks; Prednisone, 7.5 mg/d-1.2 mg/kg/d.	6 months	↓ 24 h urine protein, ESR s ↓ dsDNA, ANA s ↓ SLEDAI s ↓ Scr ns ↑ Alb ns Adverse effects ns
Bai, [26]	72 (87.5%)	25	33.9	Liu-wei-di-huang decoction, 200 ml, twice a day; Cyclophosphamide, 0.6 g-1.0 g, intravenous injection once every 4 weeks; Prednisone, 7.5 mg/d-1 mg/kg/d.	Cyclophosphamide, 0.6 g-1.0 g, intravenous injection once every 4 weeks; Prednisone, 7.5 mg/d-1 mg/kg/d.	6 months	↓ 24 h urine protein, Scr s ↑ C3, Alb s ↓ ESR ns Adverse effects s
Artemisinins							
Lu, [31]	61 (93%)	44	4.3	Artemisinin powder, 0.2 g, three times a day; Cordyceps powder, 1 g, three times a day.	Tripterygium glycosides tablet, 1 mg/kg/d; Baoshenkang tablet, 150 mg, three times a day.	36 months	↓ 24 h urine protein, Scr, BUN s ↑ C3, Alb, CCr s β2-MG ns
Huang, [32]	60 (92%)	29	46	Class I/ class II, Artesunate tablet, 25 mg, twice a day; Class I: Artesunate tablet, 25 mg, twice a day, and prednisone, 0.5 mg/kg/d.	class I /class II : Tripterygium glycosides tablet, 10 mg, three times a day; class III: Tripterygium glycosides tablet, 10 mg, three times a day, and prednisone 0.5 mg/kg/d.	2 months	↓ 24 h urine protein, ESR, CD8+ s ↑ C4, IL-2 s ↑ C3 ns ↓ IgG, ds-DNA ns CD3+, CD4+ ns
Cordyceps sinensis							
Wang, [35]	118 (83%)	31	21.3	Cordyceps sinensis capsule, 1.0 g, three times a day; Tacrolimus capsule, the first dose of 0.05 mg/kg, twice a day for 3 days, then maintain the blood concentration at 5-15 ug/L.	Tacrolimus capsule, the first dose of 0.05 mg/kg, twice a day for 3 days, then maintain the blood concentration at 5-15 ug/L.	12 months	↓ 24 h urine protein, urine RBC s ↑ C3, Alb s ↓ SLEDAI s ↓ Scr, dsDNA ns Adverse effects s
Zhu, [36]	120 (89%)	50	NR	Cordyceps sinensis capsule, 1.0 g, three times a day; Cyclophosphamide, 0.5-1.0 g/m ² , intravenous injection once every 3-4 weeks; Prednisolone, 0.5-1 mg/kg/d.	Cyclophosphamide, 0.5-1.0 g/m ² , intravenous injection once every 3-4 weeks; Prednisolone, 0.5-1 mg/kg/d.	12 months	↓ 24 h urine protein, urine RBC s ↑ C3, Alb, IL-2 s ↓ SLEDAI s ↓ Scr, dsDNA, ANA ns Infection rate s Adverse effects ns
Yang, [37]	136 (84%)	51	NR	Cordyceps sinensis capsule, 1.0 g, three times a day; Cyclophosphamide, 0.5-1.0 g/m ² , intravenous injection once every 3-4 weeks; Prednisolone, 0.5-1 mg/kg/d.	Cyclophosphamide, 0.5-1.0 g/m ² , intravenous injection once every 3-4 weeks; Prednisolone, 0.5-1 mg/kg/d.	12 months	↓ 24 h urine protein, urine RBC s ↑ C3, Alb s ↓ SLEDAI s ↓ Scr, dsDNA, ANA ns Infection rate s Adverse effects ns
He, [38]	41 (87.8%)	31	11.4	Cordyceps sinensis capsule, 1.0 g, three times a day; Low molecular heparin, 5000U, hypodermic injection once a day; Prednisolone, 1 mg/kg/d.	Low molecular heparin, 5000U, hypodermic injection once a day; Prednisolone, 1 mg/kg/d.	2 months	↓ 24 h urine protein, Scr, BUN s ↑ Alb s Adverse effects ns
Li, [39]	50 (90%)	38	82	Cordyceps sinensis capsule, 1.65 g, three times a day; Prednisone, 1 mg/kg/d.	Prednisone, 1 mg/kg/d.	2 months	↓ 24 h urine protein, ESR, CD8+ s ↑ C3, C4, CD4+ s ↓ SLEDAI s ↑ CCr ns ↓ dsDNA, sIL-2R, CD3+ ns
Wu, [40]	42 (66.7%)	34	53.5	Cordyceps sinensis capsule, 1.0 g, three times a day; Prednisolone, 1 mg/kg/d.	Prednisolone, 1 mg/kg/d.	2 months	↓ 24 h urine protein, Scr, BUN s ↓ dsDNA s ↑ C3 s
Tripterygium glycosides							

Dai, [41]	91 (89%)	NR	NR	Tripterygium glycosides, 20 mg, three times a day; Prednisone, 0.8 mg/kg/d.	Leflunomide, 20 mg/d; Prednisone, 0.8 mg/kg/d.	6 months	↓ 24 h urine protein, Scr ns ↑ C3, Alb ns ↓ SLEDAI ns Adverse effects s Menstrual disorder s
Hong, [42]	82 (74.4%)	30	25.6	Tripterygium glycosides, 0.5 mg/kg, three times a day; Prednisone, 10 mg, three times a day.	Prednisone, 10 mg, three times a day.	3 months	↓ 24 h urine protein, dsDNA s ↑ Platelet, C3, C4 s Adverse effects ns
Wang, [43]	84 (95.2%)	33	NR	Tripterygium glycosides, 20 mg, twice or three times a day; Prednisone, 10 mg, once a day.	Azathioprine, 1-2 mg/kg/d; Prednisone, 10 mg, once a day.	24 months	↓ 24 h urine protein, Scr ns ↑ Alb ns Adverse effects, infection rate ns Menstrual disorder s

Ref= reference; NR=no relevant; s= significant; ns= no significant;
Alb= albumin; BUN= blood urea nitrogen; C3=complement 3; C4=complement 4; CCR=creatinine clearance rate; ESR=erythrocyte sedimentation rate;
Scr= serum creatinine; SLEDAI=systemic lupus erythematosus disease activity index.

Table 1 Randomized controlled trials of chinese herbal medicine for lupus nephritis.

control group, the Liu-wei-di-huang pill interventions significantly improved 24-hour proteinuria, erythrocyte sedimentation rate, and complement 3 and plasma albumin levels. Notably, the recurrence rate of the treatment group was significant lower than that of the control group within a year of follow-up. Similar results were found in another study of 51 lupus nephritis patients given the Liu-wei-di-huang pill (3 g, three times a day) combined with prednisone (7.5 mg/d-60 mg/d) and mycophenolate mofetil (0.5 g/d-2.0 g/d) [24]. In addition, the study found that Liu-wei-di-huang pill therapy could significantly reduce the occurrence of adverse effects, such as diarrhea, adiposity, liver damage, infection, and leukocyte descent. The other two RCTs treated participants with 6-month Liu-wei-di-huang decoction, combined with prednisone and cyclophosphamide, and found that Liu-wei-di-huang decoction reduced 24-hour urine protein, decreased serum creatinine level, and improved disease activity scores [25,26]. These clinical studies indicate that Liu-wei-di-huang formulation combined with western medicine has better efficacy with fewer adverse events compared to western medicine alone.

Artemisinin for lupus nephritis

Artemisinin family drugs are extracted from the plant *Artemisia annua* L. (qing hao), a traditional Chinese herbal medicine that has been used to treat malaria for more than two thousand years in China [27]. Recently, it has been found that artemisinin family drugs also have anti-inflammatory [28] and complex immunosuppressive effects [29]. Artemisinin derivatives show therapeutic effects for SLE, similar to other anti-malarial drugs such as hydroxychloroquine and chloroquine [30]. Two unique randomized controlled trials of artemisinins were identified for lupus nephritis. The course of treatment ranged from 8 weeks to three years. One randomized study of 61 patients with inactive lupus nephritis randomly assigned participants into two groups, each receiving three years of treatment. Artemisinin (0.2 g, three times a day) and cordyceps sinensis were given to the treatment group, and tripterygium glycosides tablets and Bao Shen Kang tablets were given to the control group. Compared to the control group, the treatment group showed significant improvement after treatment in 24-hour urine protein content, creatinine clearance rate and level of complement 3. The study concluded that artemisinin and cordyceps sinensis may delay the recurrence of lupus nephritis, protect renal function and improve the quality of life of patients with lupus nephritis [31]. Similar findings of improvement in renal function and the immune system from artesunate were reported in another randomized controlled study of 60 lupus nephritis patients [32]. Together, artemisinin derivatives may decrease antibody and creatinine levels, erythrocyte sedimentation rate, and urinary protein, as well as improve the level of complement,

whether the afflicted patient has class I, II, or III lupus nephritis. Overall, the clinical studies demonstrate that artemisinins have the potential to preserve kidney health in patients with lupus nephritis. Long term application of artemisinins may also alleviate renal lesions and prevent the recurrence of lupus nephritis.

Cordyceps sinensis for lupus nephritis

Cordyceps sinensis has been known to have the function of ‘strengthening kidney and lung, enhancing vigor and vitality’ in traditional Chinese medicine theory. It has been suggested that Cordyceps sinensis can regulate the immune system bidirectionally, reduce renal tubulointerstitial damage, inhibit renal fibrosis and improve kidney function [33,34]. Six RCTs totaling 507 patients tested the effects of Cordyceps sinensis on lupus nephritis [35-40]. The treatment duration ranged from 2 to 12 months. Patients in the control groups received glucocorticoid (methylprednisolone or prednisone) and immunosuppressive agents (cyclophosphamide or tacrolimus), while the treatment groups received Cordyceps sinensis preparation (1 g or 1.65 g, three times a day) and the same dose of western medicine. Compared with western medicine controls, the combination treatment of Cordyceps sinensis preparation significantly improved clinical symptoms and disease activity scores, and decreased 24-hour urine protein, anti-ds DNA antibody and serum creatinine levels. Furthermore, the infection and adverse reaction rates in the treatment group were significantly lower than those in the control group. Therefore, Cordyceps sinensis may have a potential role in improving the immune function of patients with lupus nephritis, and have potential clinical therapeutic effectiveness when combined with western medication.

Tripterygium glycosides for lupus nephritis

In Chinese herbal medicine, the extract of *Tripterygium wilfordii* Hook. f. roots, named Tripterygium glycosides, has been widely used to treat autoimmune diseases including lupus nephritis [41-43]. Several randomized controlled trials have examined the therapeutic effects of Tripterygium Glycosides in patients with lupus nephritis. The results of these studies showed the effects of Tripterygium glycosides (20 mg, three times a day) were similar to the effects of leflunomide (20 mg, once a day) and azathioprine (1-2 mg/kg once a day). In addition, treatment of Tripterygium glycosides combined with prednisone demonstrated better clinical efficacy than prednisone (10 mg, three times a day) alone. Adverse effects due to the use of Tripterygium glycoside did not increase except for incidence of menstrual disorder. Thus, Tripterygium glycosides have therapeutic potential in patients with lupus nephritis, but the signs of menstrual disorder should be monitored during use.

In summary, lupus nephritis remains a therapeutically challenging chronic condition to manage. While evidence regarding the use of traditional Chinese herbal medicine modalities for lupus nephritis remains limited, the data outlined above suggest that Chinese herbal medicine may have synergistic effect with western medicine. The potential therapeutic benefits of certain Chinese herbal medicines may challenge the current treatment paradigms available for lupus nephritis and warrant a new strategy to include Chinese herbal medicine.

Acknowledgments

Dr. Wang is supported by the National Center for Complementary and Integrative Health (K24 AT007323). Dr. Mu is supported by the China academy of Chinese medical sciences, Guang'anmen Hospital, Beijing. The contents of this manuscript are solely the responsibility of the authors and do not necessarily represent the official views of the National Center for Complementary and Integrative Health of the National Institutes of Health. The organizations above did not have any role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication. The investigators are solely responsible for the content of the manuscript and the decision to submit for publication. The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

Reference

- Davis LS, Reimold AM (2017) Research and therapeutics-traditional and emerging therapies in systemic lupus erythematosus. *Rheumatology* 56: 100-113.
- Hanly JG, O'Keeffe AG, Su L, Urowitz MB, Romero-Diaz J, et al. The frequency and outcome of lupus nephritis: Results from an international inception cohort study. *Rheumatology* 55: 252-262.
- Mok CC (2012) Understanding lupus nephritis: Diagnosis, management and treatment options. *Int J Womens Health* 4: 213-222.
- Mok CC, Kwok RC, Yip PS (2013) Effect of renal disease on the standardized mortality ratio and life expectancy of patients with systemic lupus erythematosus. *Arthritis Rheum* 65: 2154-2160.
- Jolly M (2005) How does quality of life of patients with systemic lupus erythematosus compare with that of other common chronic illnesses? *J Rheumatol* 32: 1706-1708.
- Dall'Era M (2017) Treatment of lupus nephritis: Current paradigms and emerging strategies. *Curr Opin Rheumatol* 29: 241-247.
- Menez SP, El Essawy B, Atta MG (2018) Lupus nephritis: Current treatment paradigm and unmet needs. *Rev Recent Clin Trials* 13: 105-113.
- Tang KT, Tseng CH, Hsieh TY, Chen DY (2018) Induction therapy for membranous lupus nephritis: A systematic review and network meta-analysis. *Int J Rheum Dis* 21: 1163-1172.
- Margiotta DPE, Basta F, Batani V, Afeltra A (2018) Belimumab and low-doses of mycophenolate mofetil as induction therapy of class IV lupus nephritis: Case series and literature review. *BMC Nephrol* 19: 54.
- Venuturupalli S (2016) Rethinking biologics in lupus nephritis. *Lupus* 25: 1102-1110.
- Oon S, Huq M, Godfrey T, Nikpour M (2018) Systematic review, and meta-analysis of steroid-sparing effect, of biologic agents in randomized, placebo-controlled phase 3 trials for systemic lupus erythematosus. *Semin Arthritis Rheum* pp: 30579-30586.
- Greco CM, Nakajima C, Manzi S (2013) Updated review of complementary and alternative medicine treatments for systemic lupus erythematosus. *Curr Rheumatol Rep* 15: 378.
- Hajja AJ, Schulz SW (2011) The role and effect of complementary and alternative medicine in systemic lupus erythematosus. *Rheum Dis Clin North Am* 37: 47-62.
- Heng M, Tu J, Hao Y, Zhao Y, Tian J, et al. (2016) Effects of integrated traditional Chinese and western medicine for the treatment of lupus nephritis: Ameta-analysis of randomized trials. *Evid Based Complement Alternat Med* 2016: 1-7.
- Choi TY, Jun JH, Lee MS (2018) Integrative medicine for managing the symptoms of lupus nephritis: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)* 97: e0224.
- Jiao B, Gao J (2013) Intensive research on the prospective use of complementary and alternative medicine to treat systemic lupus erythematosus. *Drug Discov Ther* 7: 167-171.
- Zhong LL, Bian ZX, Gu JH, Zhou X, Tian Y, et al. (2013) Chinese herbal medicine (Zi Shen Qing) for mild-to-moderate systemic lupus erythematosus: A pilot prospective, single-blinded, randomized controlled study. *Evid Based Complement Alternat Med* 2013: 1-10.
- Hu Xinying (2012) A review of clinical applications of Liu-wei-di-huang pill. *J Practical Chinese Med* pp: 244-245.
- Wu YM, Li P (2014) A review of pharmacological action and clinical application of Liu-wei-di-huang pill. *World J Integrated Traditional Chinese and Western Medicine* pp: 1023-1025.
- Nie L (2009) Protective effect of Liu-wei-di-huang pill on rats with experimental chronic renal disease. *Clinical J Traditional Chinese Med* 21: 321-322.
- Chen J, Xie LH, Li SQ, Xu HQ, Chen SN, et al. Relationship between JAK/STAT pathway and immunomodulatory effects of Liu-wei-di-huang pills on postmenopausal osteoporosis patients with syndrome of deficiency of kidney yin. *China J Traditional Chinese Medicine and Pharmacy* 32: 1747-1750.
- Wei Q, Zhou P (2017) Effect of Liu-wei-di-huang pill on cellular immunity and senescence in the elderly. *Practical Clin Medicine* 18: 20-21.
- Zheng WC, Hu SJ, Fang Qi, Zhang TY, Zhang Li, et al. (2005) Intervention of Liu-wei-di-huang pill on lupus nephropathy treated with cyclophosphamide and glucocorticoids. *Chinese J Integrated Traditional and Western Medicine* 25: 983-985.
- Huang GY, Zhong XJ (2007) Effects of Liu-wei-di-huang pill on lupus nephropathy combined with mycophenolate mofetil and glucocorticoids. *J Guangdong Medical College* 25: 638-637.
- Wei X, Kun S, Jing T (2012) Clinical observation of lupus nephritis treated by Liu-wei-di-huang decoction added with tripterygium glycosides. *Chinese J Medicinal Guide* 14: 166-170.
- Wenhan B, Xiangfu G (2013) 37 cases of lupus nephritis treated with combined Chinese medicine. *J Shanxi College of Traditional Chinese Medicine* 36: 51-53.
- Lu YQ (2012) The discovery and research progress of artemisinin. *Life Science Res* 16: 260-265.
- Wang XQ, Liu HL, Wang GB, Wu PF, Yan T, et al. (2011) Effect of artesunate on endotoxin-induced uveitis in rats. *Invest Ophthalmol Vis Sci* 52: 916-919.
- Ho WE, Peh HY, Chan TK, Wong WS (2014) Artemisinins: Pharmacological actions beyond anti-malarial. *Pharmacology & Therapeutics* 142: 126-139.
- Wang C, Fortin PR, Li Y, Panaritis T, Gans M, et al. (1999) Discontinuation of antimalarial drugs in systemic lupus erythematosus. *J Rheumatol* 26: 808-815.
- Lu Lan (2002) Study on effect of artemisinin and Cordyceps sinensis in preventing recurrence of lupus nephritis. *Chinese J Integrated Traditional and Western Medicine* 22: 169-171.
- Huang XX (2011) Clinical study of artesunate on immune function in patients with SLE. *Lishizhen Medicine and Materia Medica Res* 22: 1673-1674.
- Xiao Y, Hu XF, Tao SC, Qian ZM, Mei QX, et al. (2018) Advance in pharmacological research of fresh Cordyceps sinensis. *Asia-Pacific Traditional Med* 14: 80-85.
- Gao SS, Chen YZ (2015) Study on the immune function of Cordyceps sinensis to protect liver and kidney. *Traditional Chinese Med Res* 28: 77-80.
- Wang XY, Wang GH, Zhang XX, Gong YN, Li YS, et al. (2017) Clinical study on Bailing capsules combined with tacrolimus in treatment of lupus nephritis. *Drugs and Clinics* 32: 1065-1069.
- Zhu PJ, Ke SS, Xu f (2016) Effect of Bailing capsules on interleukin-2, complement and infection rate in patients with lupus nephritis. *Chinese J Modern Applied Pharmacy* pp: 364-368.
- Yang ZH, Liu B, Lu Jian, Hou XX, Yin J (2015) A multicenter prospective study of the effect of Bailing capsules on clinical efficacy and infection rate in the patients with lupus nephritis. *Heilongjiang Medicine* 28: 1205-1208.
- He Y, Huang JP, Wu RY, Tan F (2013) Clinical efficacy of Bailing capsule combined with low molecular weight heparin in the treatment of lupus nephritis. *Asia-Pacific Traditional Medicine* pp: 207-208.

-
39. Li Gang, Cheng Gong, Chen Zhejun, Chen Hao (2009) Clinical research of aweto in improving the immune function of patients with lupus nephritis. *Journal of Military Surgeon in Southwest China* 11: 412-413.
40. Wu Ge (2007) Methyprednisolon with Bailing capsule in treatment of lupus nephritis. *J Med Forum* 28: 38-39.
41. Dai H, Liu W (2018) Efficacy and safety of tripterygium glycosides combined with prednisone in the treatment of lupus nephritis. *Xinjiang Medical J* 48: 20-22.
42. Hong L (2018) Effect of tripterygium glycosides combined with prednisone on lupus nephritis. *China Higher Medical Education* pp: 140-141.
43. Wang JJ, Liu ZZ, Chen YH, Hu WX, Liu ZH (2015) Tripterygium wilfordii and azathioprine in maintenance therapy for lupus nephritis-a randomized controlled trial of single center. *J Nephrol Dialy Transplant* 24: 429-434.