# META-ANALYSIS OF THE EFFICACY OF BAILING CAPSULE IN THE TREATMENT OF CHRONIC ALLOGRAFT NEPHROPATHY

YiHe Wei, Shaoqun Chen*
Nephrology department, Yancheng Dafeng people's Hospital, Yancheng, 224100, China

***ABSTRACT***

*Allogeneic kidney transplantation is currently recognized as one of the effective treatments for end-stage renal disease. Chronic allograft nephropathy (CAN) usually occurs six months after kidney transplantation. Renal dysfunction is a clinical feature of CAN, which is accompanied by hypertension and proteinuria, and there is currently no effective treatment. The main ingredient of Bailing Capsule is fermented Cordyceps mycelium dry powder, which has therapeutic effects on various kidney diseases. We searched for relevant literature and finally selected five articles for inclusion in the study for meta-analysis. The results showed that compared with the control group, the condition of the Bailing Capsule test group was significantly improved. The number of cases with worsening and ineffective treatment was significantly less than that of the control group. Renal function related indicators: test group SCr (SMD -1.842, 95% CI -2.638 to -1.047 p = 0.000), BUN (SMD -0.277, 95% CI -0.482 to -0.072 p = 0.008), 24h Upro (SMD - 1.378, 95% CI -2.152 to -0.603 p = 0.000) was significantly reduced, while CCR (SMD 0.770, 95% CI 0.558-0.982 p = 000) was significantly elevated. Therefore, we can initially determine that Bailing Capsule has a good effect on CAN treatment, which can effectively improve the patient's condition, and has considerable clinical value and application prospects.*

***Keywords**: Allogeneic kidney transplantation, chronic allograft nephropathy.*

*DOI: 10.19193/0393-6384_2020_4_390*

***Received** November 30, 2019; **Accepted** January 20, 2020*

## Introduction

Compared with chronic dialysis methods, renal allografts provide better help for patients with end-stage renal disease[1]. The mortality rate of patients receiving kidney transplantation was 54% lower. Their life expectancy is 17.19 years, while the life expectancy of dialysis patients is only 5.84 years[2]. However, chronic allograft nephropathy is still an important reason for the long-term survival of kidney transplant patients. So far there is no effective treatment. The pathogenesis of CAN is complex and not fully understood, involving a variety of immunological and non-immune factors. Prevention and treatment of CAN require multidisciplinary efforts[3]. CAN is characterized by progressive renal insufficiency with chronic interstitial fibrosis, tubular atrophy, vascular occlusive changes, and glomerular sclerosis.

It is the leading cause of kidney transplant failure. Modern immunosuppressive therapy helps reduce the incidence of acute rejection, resulting in an outstanding 1-year kidney transplant survival rate of 90%-95%.

The average half-life of transplanted kidneys in the United States is about one year longer than the half-life of 1988[4]. By introducing cyclosporin and tacrolimus, the one-year survival rate of the graft has been dramatically improved. However, as the research progressed, we found that these calcineurin inhibitors produce nephrotoxicity. They are one of the leading causes of chronic graft injury[5, 6]. In the early 1980s, cyclosporin A greatly improved the survival rate of allogeneic kidney transplantation in the first year. The graft loss rate and "organ half-life" did not change after the first year. It is a significant problem in kidney transplantation[7]. Tacrolimus is a potent immunosuppressive drug that reduces the risk of

organ rejection. Akhtar used a mouse model to study the toxic effects of tacrolimus on kidney and lung[8]. After over-immunization, most kidney transplant recipients develop systemic complications (such as cardiovascular disease, malignancy, diabetes, and metabolic disorders)[9].

Therefore, there is an urgent need to find an immunomodulatory drug as an aid to reduce dose and side effects. Cordyceps Sinensis is a traditional Chinese herbal medicine that can effectively improve immune defense function and regulate immune status. In recent years, as an immunomodulator, it has been widely used in post-transplant patients in China. CS has a two-way immunomodulatory effect and is used alone as an immunosuppressive agent. It can prolong the survival time of the graft[10, 11]. More and more scholars have studied the supporting role of CS in clinical kidney transplantation. Li found that the use of CS may reduce the dose and concentration of cyclosporin, thereby reducing side effects without increasing the risk of acute rejection. Also, Cs and low doses of cyclosporin can reduce proteinuria and delay the progression of the disease[12].

Ding studied Cs in a rat model. A potential synergistic effect of Cs and cyclosporin in allogeneic kidney transplantation was also found. The cyclosporine dose reduction further avoids the associated side effects[13]. Cordyceps Sinensis is widely used, but the production of Cordyceps sinensis is limited and cannot be widely applied. The cultivated Cordyceps sinensis and the natural Cordyceps sinensis have similar chemical compositions[14]. Bailing Capsule is a dry powder of Cordyceps sinensis mycelium, which also has the functions of regulating immune function, protecting liver and kidney function, promoting hematopoiesis, improving hypoproteinemia and hyperlipidemia, reducing infection and reducing proteinuria[15].

Based on the combined results of serum creatinine value, BUN, urine protein and other related indicators, we evaluated the efficacy of Bailing Capsule in the treatment of chronic allograft nephropathy, in order to provide a theoretical basis for clinical diagnosis.

## Materials and method

### *Standard of research*

The two authors independently completed the screening of the included studies and finally summarized them. For controversial research, they decide after discussion. Bailing Capsule is a clinical study for the treatment of chronic allograft nephropathy as an adjuvant drug for immunological preparations. We combined these studies to evaluate the therapeutic effects of Bailing Capsules.

*The inclusion criteria were as follows:*

• All included studies were eligible for CAN diagnosis;

• All clinical studies were of randomized controlled trials, and the patients involved in the study were unrestricted in age and gender. Patients in the control group and the experimental group were randomly assigned, and essential indicators (including gender, age, blood pressure, blood lipids, survival time, initial serum creatinine, blood urea nitrogen, creatinine clearance, 24h urine protein) were started at the beginning of the study. There was no significant difference in time;

• All patients in each study must receive the same immunosuppressive intervention;

• The data included in the study needs to be complete; otherwise, subsequent analysis cannot be performed;

• Ensure that there is no duplication in each study to avoid unreasonable analysis results.

### *Data retrieval*

In the database (Medline, ScienceDirect, Cochrane Library, China National Knowledge Infrastructure, Wanfang, Weipu Electronics), we searched all the Bailing Capsules for the treatment of CAN clinically related research from 2000 to the present. We also manually searched the initial study and meeting abstracts, which were not recognized by other searches. Filtering the reference list of all retrieved articles helps us to obtain other potential research. The search terms are as follows: Cordyceps, Cordyceps Sinensis, Bailing capsule, chronic allograft nephropathy.

### *Data extraction*

When extracting data, the two authors also completed independently, and finally summarized them, and decided after a controversial joint discussion. Data included author, time of publication, type of study, number of cases per study, age of patient, intervention, and the dose of Bailing Capsule.

The main observations were SCr, 24 h Upro, BUN, and CCr. For the number of patients with worsening and the number of stable and improved patients in each study, we extracted clinical prognosis results and performed statistics and mergers, and then evaluated the therapeutic effect of Bailing Capsules.

***Data analysis and research quality evaluation***

Meta-analysis was performed on the data summarized by each study using Stata version 12.0. For continuous variables, the summary results (SCR, 24 h Upro, BUN, and CCr,) are expressed as normalized mean difference (SMD), and the confidence interval is 95% CI. The statistical significance of all results was set at $p<0.05$. The corresponding research model was selected according to the size of heterogeneity between studies. A fixed effect model was used for the heterogeneity between studies, and a random effect model was used for heterogeneity[16]. The methodological quality of the included studies was evaluated using the Cochrane bias risk tool and was discussed by two authors.

## Results

***Research observation***

We searched the clinical research on the treatment of kidney transplantation with Cordyceps sinensis and Bailing Capsule in an electronic database (Medline, ScienceDirect, Cochrane Library, CNKI), and initially selected 186 articles. We screened six articles about the effects of 100 capsules and Cordyceps Sinensis on CAN. Lai[17] explored the clinical efficacy of mycophenolate mofetil combined with low-dose cyclosporine A and Bailing capsules in the treatment of CAN. Compared with the control group, the test group not only increased the Bailing capsule, but also increased the mycophenolate mofetil, and the amount of cyclosporine A was also different from the control group[18].

In all the trials, the test group and the control group received three identical immunologic treatments. There will be one more drug (Bai Ling capsule) in the test group. Zhang[19] studied the effects of angiotensin-converting enzyme inhibitor enalapril and Cordyceps Sinensis fermented preparation Bailing capsule on renal function in patients with CAN. We only extracted the data from the treatment group of Bailing Capsule and the control group to ensure that the analysis results were more accurate. The study involved 463 patients, including 189 in the control group and 232 in the experimental group. The dose of the Bailing capsules ingested by the patients in the test group was 2-9 g/day.

***Research quality evaluation***

Of the five studies, four of them[17, 18, 19], and[20] were randomized controlled trials. We [18] explicitly pointed out the use of random number tables to generate random assignments. The other three studies did not describe the method of random assignment. Another study[21] did not explicitly report the method of grouping. The results of the five studies provide relatively complete data and individual studies. The various research implementations were not reported in detail. Therefore, we believe that the study of all pre-specified results mentioned in the reporting method section does not selectively report bias. None of the five studies were lost to follow-up.

Although most studies do not explicitly report methods of random assignment. There were no significant differences in baseline data between the experimental and control groups in each study, so we defaulted to a lower risk of publication bias. Conclusively, the degree of bias we included in the study was moderate and mild.

***Effect of bailing capsule on CAN patients***

Three studies[22, 19, 20] reported the number of cases with worsening conditions and the number of solid and improved cases in the experimental and control groups, respectively.

They also reported[21] the number of cases in which the trial and control groups were effective and ineffective. The results of treatment failure and deterioration of the disease in the four studies were combined. The results of the treatment are effective, and the condition is stable and improved. The combined results were OR 0.229, 95% CI 0.138-0.382 p=0.000, I2=47.6% p=0.126.

It showed that the degree of deterioration and treatment ineffective in the experimental group was significantly lower than that in the control group. That is, Bailing Capsule is effective in treating patients with CAN, which can effectively improve the patient's condition (Figure 1).

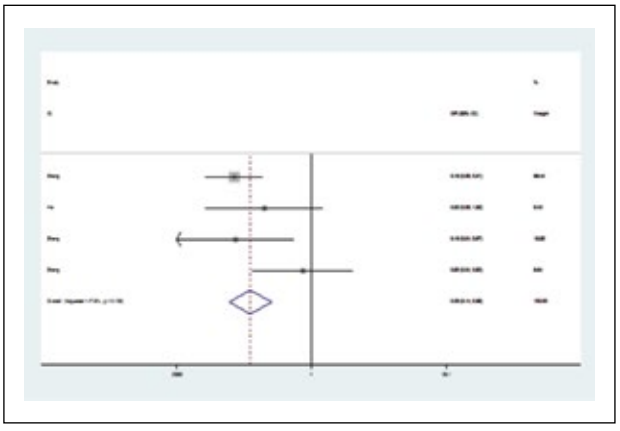

**Figure 1:** Bailing capsule treatment CAN effect meta-analysis forest map.
*Note: OR: odds ratio, CI: confidence interval.*

***Renal function index and urine protein***

Five studies reported post-intervention levels (SCr, BUN, CCr, urine protein, 24h Upro).

Compared with the control group, the test group had Scr (SMD -1.842, 95% CI -2.638 to -1.047 p = 0.000, I2 = 89.0% p = 0.000), BUN (SMD -0.277, 95% CI -0.482 to -0.072 p =0.008, I2 = 27.8% p = 0.245), 24h-Upro (SMD - 1.378, 95% CI - 2.152 to -0.603 p = 0.000, I2 = 89.8% p = 0.000) was significantly reduced. CCR (SMD 0.770, 95% CI 0.558-0.982 p=000, I2=43.5% p=0.151) was significantly elevated. (Table 1). Sensitivity analysis showed that the heterogeneity of the study of Zhang[22] was significantly reduced. (Table 2).

## Discussion

Organ transplantation is currently the best treatment option for the treatment of various end-organ diseases. The survival rate of allografts after transplantation has dramatically improved over the past few decades. This is because we have enhanced the immunosuppressive regimen and reduced the rate of acute rejection. Infectious complications have been well prevented and treated[23, 24]. CAN is the most common cause of graft dysfunction in the first decade after transplantation. It has a high incidence of kidney transplant recipients. Advances in immunosuppressive therapy have improved graft

| Author | Issuing time | Country | Type of study | Number of cases | Age | Intervention | | Capsule dose (bailing) | Evaluation index |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Control group | Test group | | |
| Zhang[18] | 2011 | CHINA | Randomized controlled trial | 231 cases, 109 cases in the control group, 122 cases in the test group | 39.2±13.2 years old | Cyclosporine + azathioprine/ mycophenolate mofetil + prednisolone. | Bailing capsules, cyclosporine, azathioprine or mycophenolate mofetil, and prednisolone. | 2.0g /day | SCr, BUN, CCr, 24 h Upro |
| Shen[19] | 2013 | CHINA | Randomized controlled trial | 41 cases, 19 cases in the control group and 22 cases in the experimental group | Test group 37.5±14.1 years old Control group 36.8±13.2 years old | Cyclosporin A + mycophenolate mofetil + prednisone | Valsartan, Bering capsule, cyclosporin A + mycophenolate mofetil + prednisone | 2.0g /day | SCr, 24 h Upro |
| He[20] | 2006 | CHINA | Randomized controlled trial | 51 cases, 15 cases in the control group, 36 cases in the experimental group | Test group 43.6±15.9 years old Control group 48.3±17.7 years old | Cyclosporine + azathioprine + prednisone | Bailing Capsule + cyclosporine + azathioprine + prednisone | 9.0g /day | BUN, SCr, CCr, 24h Upro |
| Zhang[21] | 2007 | CHINA | Randomized controlled trial | 56 cases, 25 cases in the control group, 31 cases in the test group | 34.3±15.5 years old | Cyclosporine A + azathioprine/ mycophenolate mofetil + prednisone | Bailing Capsule + Cyclosporine A + azathioprine/ mycophenolate Ester + prednisone | 6.0g /day | SCr, BUN, CCr, 24 h Upro |
| Zhang[22] | 2008 | CHINA | Randomized controlled trial | 84 cases, 21 cases in the control group, 21 cases in the test group of Bailing Capsule | 34.3±15.5 years old | Cyclosporine A/Prograf + azathioprine/ mycophenolate + prednisolone | Bailing Capsule + cyclosporine A/Prograf + azathioprine/ mycophenolate + prednisolone | 6.0g /day | SCr, BUN, CCr, 24h Upor |

**Table 1:** Basic characteristics of the included studies.
*Note: SCr: serum creatinine, 24h Upro: 24 h urine protein, BUN: blood urea nitrogen, CCr: creatinine clearance.*

| Evaluation index | Number of studies | SMD and 95% CI | p-value | Heterogeneity test | | Analysis model |
|---|---|---|---|---|---|---|
| | | | | $I^2$ | p-value | |
| SCr | 5 | -1.842 (-2.638 to -1.047) | 0.000 | 89.0% | 0.000 | Random effect model |
| CCr | 4 | 0.770 (0.558 to 0.982) | 0.000 | 43.5% | 0.151 | Fixed effect model |
| BUN | 4 | -0.277 (-0.482 to -0.072) | 0.008 | 27.8% | 0.245 | Fixed effect model |
| 24h Upro | 5 | -1.378 (-2.152 to -0.603) | 0.000 | 89.8% | 0.000 | Random effect model |
| Sensitivity analysis result | | | | | | |
| SCr | 4 | -1.567 (-2.215 to -0.919) | 0.000 | 72.6% | 0.012 | Random effect model |
| CCr | 3 | 0.458 (0.149-0.882) | 0.005 | 0.0% | 0.677 | Fixed effect model |
| BUN | 3 | -0.521 (-0.858 to -0.183) | 0.002 | 0.0% | 0.617 | Fixed effect model |
| 24h Upro | 4 | -1.080 (-1.525 to -0.636) | 0.000 | 49.5% | 0.115 | Fixed effect model |

**Table 2:** Metabolic analysis results of renal function indicators.
*Note: SCr: serum creatinine, 24h Upro: 24 h urine protein, BUN: blood urea nitrogen, CCr: creatinine clearance, SMD: Standardized mean difference, CI: Confidence interval.*

survival by one year[25]. Analysis of serum creatinine concentrations indicates that at least 80% of kidney transplant patients experience a gradual loss of renal function. They also began to show signs of chronic graft nephropathy (CAN). At least, within ten years after transplantation, 50% of kidney transplant patients have the characteristics of CAN[26].

We evaluated the effect of Bailing Capsule as an immunosuppressive drug in the treatment of CAN. Participants in the control group and the experimental group were given the same immunosuppressive agent. We also provided Bailing Capsule to the experimental group as an auxiliary drug for immunosuppressants. Using the Stata software, we can combine the extracted data, and we found that the renal function recovery of the experimental group was significantly better than the control group.

Compared with the control group, the SCR, BUN, and Upro (24h) of the test group were significantly decreased, while the CCr was significantly increased. According to these indicators, Bailing Capsule was significantly associated with renal function recovery in the experimental group. For the control group, they only used immunosuppressive drugs such as cyclosporine. Without the use of Bailing Capsule for treatment, the recovery of renal function was relatively weak. Therefore, we believe that the Bailing Capsule has a particular clinical value in the treatment of CAN. A randomized study (15-year follow-up) on the continued use of cyclosporin with early discontinuation of cyclosporin indicated that calcineurin inhibitors initially provided more significant benefit. However, subsequent calcineurin inhibitor toxicity leads to more severe graft loss[27]. Specific histological features of calcineurin inhibitor toxicity include plaque fibrosis and hyaline arteriolar disease. It is one of the main factors leading to the development of CAN. Within ten years after transplantation, 100% of adults showed some histological evidence of CNI toxicity[28]. Modern biochemical experimental methods have proved that Cordyceps Sinensis has active ingredients such as mannitol, nucleosides, ergosterol, aminophenols and trace elements. Cordyceps has a wide range of medical effects. Its immunoregulatory function plays an essential role in anti-tumor effects, organ transplantation and prevention of kidney, liver and heart diseases[29].

Chiu found that the polysaccharide component of Cordyceps Sinensis regulates renal dysfunction in rats with endotoxemia. The polysaccharide component of Cordyceps Sinensis can improve renal dysfunction caused by nephrotoxicity in rats through anti-oxidation, anti-apoptosis, and anti-autophagy mechanisms[30, 31]. Bailing Capsule, as a dry powder preparation of Cordyceps sinensis, can effectively prevent rejection after kidney transplantation, protecting kidney function and liver function, stimulating hematopoietic function, improving hypoproteinemia and hyperlipidemia, and reduce infection[32]. We analyzed the results of five studies and obtained the combined results of renal function related indicators. Bailing Capsule has a significant effect on CAN treatment, but the data we have included is far from enough. The long-term effect of Bailing Capsule in the treatment of CAN has not been mentioned, so we can not evaluate the long-term effects of Bailing Capsule on CAN.

The therapeutic effect of Bailing Capsule requires more data to study and improve. Although kidney transplantation is the preferred method to improve survival in patients with end-stage renal disease, the impact of chronic allograft nephropathy (CAN) and the long-term effectiveness of transplantation remain significant challenges for clinicians and researchers[33]. We systematically evaluated and analyzed the effect of Bailing Capsule on the treatment of CAN, and initially determined that Bailing Capsule has a particular clinical value in the treatment of CAN, and provides a theoretical basis for the treatment of CAN.

## References

1) Jagdale, A., et al., Chronic dialysis in patients with end-stage renal disease: Relevance to kidney xenotransplantation. Xenotransplantation, 2019. 26(2): p. e12471.
2. Oniscu, G.C., H. Brown, and J.L. Forsythe, Impact of cadaveric renal transplantation on survival in patients listed for transplantation. J Am Soc Nephrol, 2005. 16(6): p.1859-65.
3) Li, C. and C.W. Yang, The pathogenesis and treatment of chronic allograft nephropathy. Nat Rev Nephrol, 2009. 5(9): p.513-9.
4) Kedzierska, K., et al., Effects of immunosuppressive treatment on protein expression in rat kidney. Drug Des Devel Ther, 2014. 8: p.1695-708.
5) Nojima, M., et al., Immunosuppression Modification by Everolimus With Minimization of Calcineurin Inhibitors Recovers Kidney Graft Function Even in Patients With Very Late Conversion and Also With Poor Graft Function. Transplant Proc, 2017. 49(1): p.41-44.

6) Nankivell, B.J., et al., The natural history of chronic allograft nephropathy. N Engl J Med, 2003. 349(24): p.2326-33.
7) Pascual, M., et al., Chronic rejection and chronic cyclosporin toxicity in renal allografts. Immunol Today, 1998. 19(11): p.514-9.
8) Akhtar, T., et al., Tacrolimus induced nephrotoxicity and pulmonary toxicity in Wistar rats. J Biol Regul Homeost Agents, 2017. 31(4): p.1061-1066.
9) Caletti, C., et al., Impact of 3 Major Maintenance Immunosuppressive Protocols on Long-term Clinical Outcomes: Result of a Large Multicenter Italian Cohort Study Including 5635 Renal Transplant Recipients. Transplant Proc, 2019. 51(1): p.136-139.
10) Zhang, Z. and S.S. Xia, Cordyceps Sinensis-I as an immunosuppressant in heterotopic heart allograft model in rats. J Tongji Med Univ, 1990. 10(2): p.100-3.
11) Ding, C., et al., Efficacy of Cordyceps sinensis in long term treatment of renal transplant patients. Front Biosci (Elite Ed), 2011. 3: p.301-7.
12) Li, Y., et al., Clinical application of Cordyceps sinensis on immunosuppressive therapy in renal transplantation. Transplant Proc, 2009. 41(5): p.1565-9.
13) Ding, C., et al., The synergistic effects of C. Sinensis with CsA in preventing allograft rejection. Front Biosci (Landmark Ed), 2009. 14: p.3864-71.
14) Xu, H. and S. Li, [Pharmacological effects of Bailing capsule and its application in lung disease research]. Zhongguo Zhong Yao Za Zhi, 2010. 35(20): p.2777-81.
15) Wang, W., et al., Effects of Bailing capsules for renal transplant recipients: a retrospective clinical study. Chin Med J (Engl), 2013. 126(10): p.1895-9.
16. Chaimani, A., D. Mavridis, and G. Salanti, A hands-on practical tutorial on performing meta-analysis with Stata. Evid Based Ment Health, 2014. 17(4): p. 111-6.
17) Treatment of chronic allograft nephropathy with mycophenolate mofetil combined with low-dose cyclosporine A and Bailing capsule.
18) Effect of Bailing capsule combined with valsartan on chronic allograft nephropathy.
19) Therapeutic effect of Bailing Capsule on chronic allograft nephropathy.
20) Zhang, Z.H., W.D. Zhang, and K. Yao, [Treatment of chronic allograft nephropathy with combination of enalapril and bailing capsule]. Zhongguo Zhong Xi Yi Jie He Za Zhi, 2008. 28(9): p.806-9.
21) He, X.L., J.H. Chen, and Y.M. Wang, [Clinical observation on treatment of chronic allograft nephropathy with bailing capsule]. Zhongguo Zhong Xi Yi Jie He Za Zhi, 2006. 26(2): p.102-5.
22) Zhang, Z., et al., Effect of Cordyceps sinensis on renal function of patients with chronic allograft nephropathy. Urol Int, 2011. 86(3): p.298-301.
23) Fishman, J.A., Infection in solid-organ transplant recipients. N Engl J Med, 2007. 357(25): p.2601-14.
24) Martin-Gandul, C., et al., The Impact of Infection on Chronic Allograft Dysfunction and Allograft Survival After Solid Organ Transplantation. Am J Transplant, 2015. 15(12): p.3024-40.
25) Modelli de Andrade, L.G., R.M. Viero, and M.F. Carvalho, Role of peritubular capillaries and vascular endothelial growth factor in chronic allograft nephropathy. Transplant Proc, 2009. 41(9): p.3720-5.
26) Bhatti, A.B. and M. Usman, Chronic Renal Transplant Rejection and Possible Anti-Proliferative Drug Targets. Cureus, 2015. 7(11): p.e376.
27. ) Gallagher, M.P., et al., A randomized controlled trial of cyclosporine withdrawal in renal-transplant recipients: 15-year results. Transplantation, 2004. 78(11): p.1653-60.
28) Fletcher, J.T., B.J. Nankivell, and S.I. Alexander, Chronic allograft nephropathy. Pediatr Nephrol, 2009. 24(8): p.1465-71.
29) Zhou, X., et al., Cordyceps fungi: natural products, pharmacological functions and developmental products. J Pharm Pharmacol, 2009. 61(3): p.279-91.
30) Chiu, C.H., et al., Polysaccharide extract of Cordyceps sobolifera attenuates renal injury in endotoxemic rats. Food Chem Toxicol, 2014. 69: p.281-8.
31) Wu, M.F., et al., Cordyceps sobolifera extract ameliorates lipopolysaccharide-induced renal dysfunction in the rat. Am J Chin Med, 2011. 39(3): p.523-35.
32) Sun, M., et al., [Clinical study on application of bailing capsule after renal transplantation]. Zhongguo Zhong Xi Yi Jie He Za Zhi, 2004. 24(9): p.808-10.
33) Shi, J., et al., Differences in Tfh Cell Response Between the Graft and Spleen With Chronic Allograft Nephropathy. Cell Transplant, 2017. 26(1): p.95-102.

*Corresponding Author:*
Shaoqun Chen
Email: 348812926@qq.com
*(China)*