Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review)

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Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

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ABSTRACT

Background

Cordyceps sinensis (Cordyceps, Dong Chong Xia Cao), a herbal medicine also known as Chinese caterpillar fungus, is one of the most commonly used ingredients in traditional Chinese medicine for the treatment of people with chronic kidney disease (CKD).

Objectives

This review aimed to evaluate the therapeutic effects and potential adverse effects of Cordyceps sinensis for the treatment of people with CKD.

Search methods

We searched the Cochrane Renal Group's Specialised Register to 14 April 2014 through contact with the Trials' Search Co-ordinator using search terms relevant to this review. We also searched CINAHL, AMED, Current Controlled Trials, OpenSIGLE, and Chinese databases including CBM, CMCC, TCMLARS, Chinese Dissertation Database, CMAC and Index to Chinese Periodical Literature.

Selection criteria

Randomised and quasi-randomised trials comparing Cordyceps or its products with placebo, no treatment, or conventional treatment were considered for inclusion in the review.

Data collection and analysis

Two authors independently assessed data quality and extracted data. Statistical analyses were performed using the random-effects model and the results expressed as risk ratio (RR) for dichotomous outcomes or mean difference (MD) for continuous data with 95% confidence intervals (CI).

Main results

We included 22 studies that involved 1746 participants. Among people with CKD who were not receiving dialysis, Cordyceps preparations were found to significantly decrease serum creatinine (14 studies, 987 participants): MD -60.76 µmol/L, 95% CI -85.82 to -35.71); increase creatinine clearance (6 studies, 362 participants): MD 9.22 mL/min, 95% CI 3.10 to 15.34) and reduce 24
hour proteinuria (4 studies, 211 participants: MD -0.15 g/24 h, 95% CI -0.24 to -0.05). However, suboptimal reporting and flawed methodological approaches meant that risk of bias was assessed as high in four studies and unclear in 18 studies, and hence, these results need to be interpreted with caution.

Authors’ conclusions

We found that Cordyceps preparation, as an adjuvant therapy to conventional medicine, showed potential promise to decrease serum creatinine, increase creatine clearance, reduce proteinuria and alleviate CKD-associated complications, such as increased haemoglobin and serum albumin. However, definitive conclusions could not be made because of the low quality of evidence.

PLAIN LANGUAGE SUMMARY

Cordyceps sinensis (a Chinese medicinal herb) for treating chronic kidney disease

People with chronic kidney disease (CKD) experience gradual worsening of kidney function. Cordyceps (Cordyceps sinensis), which is sometimes known as Chinese caterpillar fungus, is widely used in traditional Chinese medicine to treat people with CKD. We conducted this review to investigate if Cordyceps was a safe and effective treatment for people with CKD.

We searched the literature published up to April 2014 and assessed evidence from 22 studies conducted in China that involved 1746 people with CKD who received Cordyceps as part of their treatment.

We found some evidence to indicate that Cordyceps preparations given in addition to conventional Western medicine may be beneficial in improving kidney function and addressing some complications. However, evidence quality was poor, and no definitive conclusions could be made about Cordyceps for people with CKD.

BACKGROUND

Description of the condition

Chronic kidney disease (CKD) is a common condition in which kidney function progressively deteriorates, which may be asymptomatic until the disease is advanced. CKD aetiology has been associated with both non-communicable diseases, such as diabetes and hypertension, and infectious diseases including malaria, HIV, and hepatitis B (Nugent 2011). CKD is defined by the Kidney Disease Outcomes Quality Initiative (KDOQI) in terms of either kidney damage (indicated by markers such as abnormalities in urine or blood tests, or on imaging), or decreased glomerular filtration rate (GFR) (< 60 mL/min/1.73 m²) with or without evidence of kidney damage, for three or more months, regardless of cause (Levey 2003; NKF 2008). People with CKD whose kidney function continues to deteriorate may require renal replacement therapy (RRT) (dialysis or kidney transplantation). Adverse effects such as high blood pressure (hypertension), too few red blood cells (anaemia), malnutrition, bone diseases, nerve damage (neuropathy), and decreased quality of life may occur concurrently with gradual loss of kidney function (NKF 2008).

CKD incidence and prevalence is increasing and is associated with escalating rates of hypertension and diabetes mellitus. Together, these diseases pose a major global healthcare challenge (Nugent 2011). In India, where incidence of diabetes and hypertension is high, it has been estimated that between 25% and 40% of the population are at risk of developing CKD (Srinath Reddy 2005). A recent systematic review reported that impaired kidney function prevalence, defined as reduced GFR (< 60 mL/min/1.73 m²), creatinine clearance (CrCl) (< 60 mL/min) or elevated serum creatinine (SCr), ranged from 1.7% in a Chinese study to 8.1% in a US study (McCullough 2012). The high cost of RRT imposes significant economic burden on society, especially in the developing world (Nugent 2011).

Description of the intervention

Laboratory and clinical studies have demonstrated that medicinal herbs traditionally used to treat people with kidney disease may offer potential therapeutic benefits for people with CKD (Wojcikowski 2006). Cordyceps sinensis (Cordyceps) is one of the most commonly used ingredients in traditional Chinese medicine for people with CKD (Deng 2001). Cordyceps, a unique blade-
shaped fungus that grows on caterpillars, is valued as a tonic herb in traditional Chinese medicine to treat a wide range of disorders, including respiratory, kidney, liver and cardiovascular diseases, low libido and impotence, and hyperlipidaemia. Because naturally-occurring *Cordyceps sinensis* is in limited supply, various cultured and fermented mycelial products that have similar pharmacologically active components are now used in clinical practice (Zhu 1998a; Zhu 1998b).

**How the intervention might work**

Clinical studies investigating the use of Cordyceps for treating people with CKD have demonstrated potential beneficial effects in decreasing progression of end-stage kidney disease (ESKD) (Jin 2004), reducing SCr levels (Yu 2003); and increasing CrCl (Wu 2007), serum albumin and haemoglobin (Jin 2004; Yang 1999b); and improving lipid metabolism (Jin 2004; Quan 2004). Studies investigating the active mechanisms of Cordyceps for CKD have found that its observed benefits may be related to its antioxidant and immunostimulation properties (Shin 2001; Yamaguchi 2000), inhibition of mesangial proliferation (Yang 1999a; Yang 2003; Zhao 2000), anti-inflammatory effects (Liu 2005; Shahed 2001; Yin 2007), ability to decrease accumulation of extracellular matrix in the renal cortex (Ma 2008), and in reducing renal interstitial fibrosis (Min 2008).

**Why it is important to do this review**

Previous clinical experience and studies investigating Cordyceps have suggested that it is a promising natural substance for the treatment of people with CKD. Although a previous systematic review that investigated the therapeutic benefits of Cordyceps for people with CKD reported favourable effects, this analysis was methodologically flawed by reliance on a limited literature search, inclusion of inappropriate outcome measures, and poor quality reporting (Xu 2006). Therefore, a systematic review applying appropriate, rigorous scientific methodology will not only provide reliable evidence on the therapeutic effect of Cordyceps for people with CKD, but also identify areas for improvement if future clinical studies are to be undertaken.

**OBJECTIVES**

This review aimed to evaluate the therapeutic effects and potential adverse effects of *Cordyceps sinensis* for the treatment of people with CKD.

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

All randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) evaluating the benefits and potential side effects of *Cordyceps sinensis* for CKD were included in the review.

**Types of participants**

**Inclusion criteria**

We included adults and children with CKD at all stages. Where possible, we applied the KDOQI definition for CKD (NKF 2008). However, we anticipated that most studies were likely to have been conducted in countries where the KDOQI definition was not applied, so we also accepted CKD definitions described by the studies.

**Exclusion criteria**

1. Participants with kidney impairment where baseline GFR or creatinine concentration data could be obtained from the report or through author contact
2. Kidney transplant recipients
3. Participants with diabetic nephropathy and primary nephrotic syndrome. These issues have been investigated in (Feng 2013; Liu 2007)

**Types of interventions**

1. Treatment group participants received Cordyceps or its products as the single treatment drug, regardless of the formulation and route of administration. These could include extracts of Cordyceps (any part of Cordyceps); or any derived, cultured, fermented mycelial products that contain pharmacologically-active components similar to wild Cordyceps
2. Control group participants received placebo, no treatment, or conventional treatment. Other herbal or complementary medicines without validated efficacy were not accepted as the control intervention
3. Studies involving Cordyceps as one of several active components in a compound or as part of a combined treatment regimen were not included in the review
4. Co-interventions were permitted where participants in all randomised arms received the same co-interventions.
Types of outcome measures

Primary outcomes
1. Time to requirement for RRT or initiation of dialysis
2. All-cause mortality
3. CKD progression, defined as increased CrCl or decreased SCr > 20% from baseline (Zheng 2002).

Secondary outcomes
1. Kidney function, measured by GFR, CrCl, or SCr levels
2. Quality of life measured by a validated scale
3. Proteinuria measured by 24 hour urinary protein excretion, protein/creatinine ratio or albumin/creatinine ratio
4. Blood pressure (systolic and diastolic)
5. Anaemia measured by haemoglobin or haematocrit levels
6. Nutritional status assessed by serum albumin, serum total cholesterol, oedema-free actual body weight, per cent standard (NHANES II) body weight, normalised protein nitrogen appearance or dietary interviews and diaries
7. Bone disease measured by serum calcium and phosphorus or bone mineral density
8. Symptoms including skin pruritus, vomiting, measured by visual analogue or other scales
9. Adverse effects.

Primary and secondary outcome measures were collected immediately after treatment and at the end of follow-up.

Search methods for identification of studies

Electronic searches
We searched the Cochrane Renal Group’s Specialised Register to 14 April 2014 through contact with the Trials’ Search Co-ordinator using search terms relevant to this review. The Cochrane Renal Group’s Specialised Register contains studies identified from the following sources.
1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
2. Weekly searches of MEDLINE OVID SP
3. Handsearching of renal-related journals and the proceedings of major renal conferences
4. Searching of the current year of EMBASE OVID SP
5. Weekly current awareness alerts for selected renal journals

Studies contained in the Specialised Register are identified through search strategies for CENTRAL, MEDLINE, and EMBASE based on the scope of the Cochrane Renal Group. Details of these strategies, as well as a list of handsearched journals, conference proceedings and current awareness alerts, are available in the specialised register section of information about the Cochrane Renal Group. See Appendix 1 for search terms used in strategies for this review. We also searched the following electronic databases to July 2012.
1. CINAHL, AMED (Allied and Complementary Medicine Database), and CISCOM (Centralised Information Service for Complementary Medicine). Search strategies were adapted from the approach described for MEDLINE
2. OpenSIGLE (System for Information on Grey Literature in Europe)
3. Chinese language databases were also searched to January 2011:
   i) CBM (Chinese BioMedical Literature Database)
   ii) CMCC (Chinese Medical Current Contents)
   iii) TCMLARS (Traditional Chinese Medical Literature Analysis and Retrieval System)
   iv) Chinese Dissertation Database
   v) CMAC (China Medical Academic Conference)
   vi) Index to Chinese Periodical Literature.

The search strategies for Chinese language databases are also shown in Appendix 1.

Index to Theses and ProQuest Dissertations and Theses were also searched for relevant studies.

Searching other resources
Reference lists of nephrology textbooks, review articles and relevant studies were also checked.

Data collection and analysis

Selection of studies
The search strategies described were used to obtain titles and abstracts of studies possibly relevant to this review. Titles and abstracts were screened independently by two authors who discarded studies that were not applicable; however, studies and reviews thought to potentially include relevant data or information on studies were retained initially. Two authors independently assessed the retrieved abstracts, and if necessary the full text, to determine which satisfied the inclusion criteria.

Data extraction and management
Data extraction was carried out independently by the same authors using a pre-tested data extraction form. Where more than one publication of one study existed, only the publication with the most recent complete data was used. When further information was required, we wrote to the first author of the article concerned.
Disagreements between authors were discussed and resolved by consensus.

**Assessment of risk of bias in included studies**

Two authors independently assessed the risk of bias of the included studies. Any discrepancies were resolved by discussion and conclusions made by consensus.

To detect potential selection bias, performance bias, attrition bias, detection and reporting bias, the following items were assessed using the Cochrane risk of bias assessment tool ([Higgins 2011](#)) (see Appendix 2).

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study (detection bias)?
  - Participants and personnel
  - Outcome assessors
- Were incomplete outcome data adequately addressed (attrition bias)?
- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias?

Baseline comparability was considered as one of the other sources of bias.

We categorised the risk of bias for each outcome within and across the included studies into three levels, i.e. low, unclear and high risk of bias. Based on this, we also used the GRADE system ([Higgins 2011](#)) for evaluating the quality of evidence for each individual outcome, which involved not consideration of risk of bias (methodological quality), and directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias.

**Measures of treatment effect**

For dichotomous outcomes (all-cause mortality, CKD progression), results were expressed as risk ratio (RR) with 95% confidence intervals (CI). Where continuous scales of measurement were used to assess the effects of treatment (kidney function, quality of life, proteinuria, blood pressure, anaemia, nutritional status, bone disease) the mean difference (MD) was calculated.

**Unit of analysis issues**

Analysis of outcomes was based on randomised individuals. In the case of multiple intervention groups within a study, we chose pair-wise comparisons relevant to the study objective. We did not identify any cluster RCTs, cross-over studies, or studies reporting repeated measures on the same participants.

**Dealing with missing data**

Available case analysis was conducted. The potential impact of missing data was considered in the risk of bias assessment and interpretation of results. Because the imbalance of missing data on treatment and control groups is suggestive of high risk of bias, two studies were excluded from our meta-analysis ([Guo 2009; Yu 2003](#)).

**Assessment of heterogeneity**

Heterogeneity was analysed using a \(\chi^2\) test on N-1 degrees of freedom, with an alpha of 0.1 used for statistical significance and with the \(I^2\) test ([Higgins 2003](#)). \(I^2\) values of 25%, 50% and 75% correspond to low, medium and high levels of heterogeneity, respectively.

**Assessment of reporting biases**

Reporting biases were investigated on a funnel plot ([Higgins 2011](#)). Possible reasons other than publication bias, such as poor methodological quality and true heterogeneity, were explored.

**Data synthesis**

Data were pooled using the random-effects model but the fixed-effect model was also analysed to ensure robustness of the model chosen and susceptibility to outliers. Data synthesis was restricted to studies assessed as low or unclear risk of bias. For studies at high risk of bias, results were displayed on a forest plot without pooling. A narrative, qualitative summary is also presented.

**Subgroup analysis and investigation of heterogeneity**

If sufficient evidence was available, we planned to conduct the following subgroup analyses to explore potential sources of heterogeneity.

- CKD stage
- CKD definition (KDOQI or other)
- Risk of bias (low or unclear)
- Cordyceps source (wild or cultivated) and preparation (whole plant or extract)
- Cordyceps use (combined with or without other treatment).

Adverse effects were to be tabulated and assessed using descriptive techniques, because they were likely to be different for the various agents used. Where possible, the risk difference (RD) with 95% CI was to be calculated for each adverse effect, either compared to no treatment or to another agent.

We were able to undertake subgroup analyses on levels of risk of bias only. There were insufficient reported data to define CKD stage; CKD definition; use, source and preparation of Cordyceps, to enable subgroup analyses to be undertaken.

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**Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review)**

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Adverse effects were analysed qualitatively. There were insufficient data in the included studies to calculate risk differences (RD) with 95% CI for adverse effects.

**Sensitivity analysis**
There were insufficient data to conduct sensitivity analyses to explore the influence of risk of bias factors on effect estimates for adequacy of sequence generation and blinding. Likewise, sensitivity analyses were not undertaken to examine if limiting the definition of CKD to the KDOQI standard had an impact on results.

**RESULTS**

**Description of studies**

**Results of the search**
The search of English and Chinese language databases resulted in identification of 1168 citations (Figure 1). Two authors independently screened titles and abstracts and identified 245 studies as potentially relevant. Assessment of full-text articles resulted in identification of 25 potential studies. Three studies are awaiting assessment (Chai 2009; Jin 2006; Lin 2003). As a result, 22 studies were included in this review (Chen 2003; Chen 2006a; Fu 2009; Gao 2007; Guo 2009; Hu 2008; Huang 2008; Jin 2004; Liu 2006a; Liu 2007a; Pan 2007; Shi 2009; Sun 1999; Wang 2005a; Wei 2004; Wu 2007; Xu 2004; Yan 2005a; Yang 1999b; Yu 2002; Yu 2003; Zhang 2009).

**Included studies**
This review included 22 studies, all published in Chinese, that were conducted in hospital settings in China involving 1746 participants (958 males (54.9%); 788 females (45.1%)). Study sample size ranged from 27 to 212 participants.
Participants in 18 studies had reported baseline SCr ranging from 135 to 820 µmol/L. Primary causes of CKD varied, but included chronic glomerulonephritis, diabetic nephropathy, arteriosclerosis of the kidney, chronic pyelonephritis, and hypertension nephropathy. Two studies dealt with aristolochic acid nephropathy (Gao 2007; Zhang 2009), and one investigated participants with hypertension nephropathy (Fu 2009).

Three studies compared Cordyceps plus conventional treatment with Western medicine plus the same conventional treatment (Gao 2007; Huang 2008; Jin 2004), and one compared Cordyceps plus traditional Chinese medicine to the same traditional Chinese medicine (Yan 2005a). The remaining 18 studies compared Cordyceps plus conventional treatment with the same conventional treatment; of these, three studies administered haemodialysis as the co-intervention (Guo 2009; Sun 1999; Yu 2002).

All studies investigated mycelial fermentation products of Cordyceps sinensis. Of the 22 included studies, 13 studied Jin Shui Bao capsules and nine investigated Bai Ling capsules. Jin Shui Bao capsules contain 0.33 g fermented Cordyceps and Bai Ling capsules contain 0.2 g Cordyceps. Both capsules were administered orally, and doses ranged from three to six capsules, taken three times daily. Treatment duration ranged from one to six months.

All studies included co-interventions in all treatment arms. Aside from dietary interventions, the most common co-interventions were symptomatic and supportive treatments including maintaining water, electrolyte and acid-base balance; controlling blood pressure; treating anaemia; and controlling infection when necessary. Yan 2005a reported that the compounded traditional Chinese herbal medicines administered as co-intervention to treat CKD included Cangzhu (Rhizoma Atractylodis), Baizhu (Rhizoma Atractylodis Macrocephalae), Yiyiren (Semen Coicis), Fulingpi (Poria), Zelan (Herba Lycopi), Gouqizi (Fructus Lycii), Sangjisheng (Herba Taxilli), Huainiuxi (Radix Cyathulacae), Dahuang (Radix et Rhizoma Rhei), and Baihuasheshecao (Herba Hedyotidis Diffusae).

See Characteristics of included studies.

Excluded studies
The most common reasons for study exclusion were lack of control arm; no randomisation; Cordyceps was one of many components in the traditional Chinese medicine treatment; and absence of targeted outcomes. See Characteristics of excluded studies.

Studies awaiting classification
See Characteristics of studies awaiting classification

Risk of bias in included studies
Figure 2 and Figure 3 present graphical presentations of assessments of risk of bias in the included studies.
Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding (performance bias and attrition bias)</th>
<th>Incomplete outcome data (attrition bias)</th>
<th>Selective reporting (reporting bias)</th>
<th>Other bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen 2003</td>
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</tr>
</tbody>
</table>
**Allocation**

In most studies, random allocation was briefly mentioned, and detailed methodologies were not provided. One study used a random number table to generate allocation sequence (Wei 2004); and another used entry sequence (Huang 2008). None of the included studies reported allocation concealment.

**Blinding**

Blinding was unclear in three studies (Liu 2006a; Liu 2007a; Yan 2005a) and not reported in the remaining 19 studies.

**Incomplete outcome data**

Two studies reported on missing data. Guo 2009 and Yu 2003 reported attrition rates of 21.9% and 2.5% respectively, but reasons were not provided. Yu 2003 did not report data relating to four control arm participants; and although 34 and 30 participants respectively were enrolled into the intervention and control arms, Guo 2009 included data from 25 participants only from each arm in the analysis.

**Selective reporting**

Because study protocols were not available, and measurement outcomes for assessing the treatment effect were not reported consistently in the included studies, it was not possible to assess for selective reporting.

**Other potential sources of bias**

We considered that blinding may not have substantially influenced objective outcome measures. Our assessment found that risk of bias was unclear in most studies, except for four that were at high risk of bias (Chen 2003; Chen 2006a; Guo 2009; Yu 2003). Participant numbers did not balance after randomisation in Chen 2003 and Chen 2006a; and there were missing data from the treatment phase in Guo 2009 and Yu 2003. These four studies were therefore excluded from our quantitative analysis.

**Effects of interventions**

**Cordyceps + conventional medicine versus conventional medicine**

**Kidney function measures (CKD progression, SCr, CrCl)**

Overall, in studies judged to have unclear risk of bias, Cordyceps preparations did not confer significant benefits for people with CKD (defined as CrCl increase or SCr decrease greater than 20% over baseline) (Analysis 1.1.1 (5 studies, 368 participants): RR 1.09, 95% CI 0.99 to 1.21; I² = 23%). However, effects were significant in studies assessed as being at high risk of bias for this outcome (Analysis 1.1.2 (2 studies, 227 participants): RR 1.36, 95% CI 1.17 to 1.58; I² = 0%). Overall, Cordyceps preparations significantly decreased SCr levels (Analysis 1.2 (15 studies, 1047 participants): MD -53.50 μmol/L, 95% CI -84.17 to -22.83; I² = 93%) in people with CKD. This was seen in both patients not on dialysis (Analysis 1.2.2 and Analysis 1.2.3 (14 studies, 987 participants): MD -60.76 μmol/L, 95% CI -85.82 to -35.71; I² = 82%) and in one study by Sun 1999 in patients on dialysis (Analysis 1.2.1 (1 study, 60 participants): MD -32.88 μmol, 95% CI -44.23 to -21.53). Differences in participants’ CKD stages may explain some heterogeneity in treatment effects on SCr levels. Pooled SCr results also indicated greater effects in studies assessed at high risk of bias for this outcome (Analysis 1.2.3 (3 studies, 273 participants): MD -118.77 μmol, 95% CI -148.81 to -88.74). There were some differences in the pooled result for SCr between the fixed-effect model (MD -39.27 μmol, 95% CI -48.13 to -30.40) and random-effects model. There was no apparent publication bias (Figure 4).
CrCl was significantly increased in participants who received Cordyceps preparations (Analysis 1.3 (6 studies, 362 participants): MD 9.22 mL/min, 95% CI 3.10 to 15.34; I² = 81%). A study in patients with hypertensive nephropathy (Fu 2009), whose kidney function was better than participants in other studies, contributes all of the heterogeneity in this analysis. Removing this study from the analysis did not change the significance of the results (MD 6.16 mL/min, 95% CI 3.78 to 8.54). Chen 2006a, judged to be at high risk of bias for this outcome, also showed a significant increase in CrCl in patients receiving Cordyceps (Analysis 1.3.2 (1 study, 67 participants): MD 5.09 mL/min, 95% CI 0.56 to 9.62), but did not affect the significance of the result when removed (MD 6.57 mL/min, 95% CI 3.77 to 9.37).

### Proteinuria

Cordyceps preparations significantly reduced 24 hour proteinuria (Analysis 1.4 (4 studies, 211 participants): MD -0.15 g/24 h, 95% CI -0.24 to -0.05; I² = 9%).

### Blood pressure

In a study that considered treatment for people with hypertension nephropathy (Fu 2009), no significant effects observed in reducing systolic or diastolic blood pressure in relation to Cordyceps (Analysis 1.5 (systolic, 1 study, 75 participants): -1.40 mm Hg, 95% CI -5.90 to 3.10; (Analysis 1.6 (diastolic, 1 study, 75 participants): 0.80 mm Hg, 95% CI -3.19 to 4.79).

### Anaemia

Cordyceps significantly increased haemoglobin levels in people with CKD regardless of their haemodialysis status (Analysis 1.7 (5 studies, 283 participants): MD 10.40 g/L, 95% CI 6.22, 14.58: I² = 81%). The pooled results of three studies of non-dialysis patients indicated improvement in anaemia (Analysis 1.7.2 (3 studies, 173 participants): MD 8.20 g/L, 95% CI 2.39 to 14.01; I² = 79%). Wei 2004 reported that Cordyceps significantly increased haematocrit levels (Analysis 1.8 (1 study, 60 participants): MD 3.49%, 95% CI 1.42 to 5.56).
Nutritional status (albumin, cholesterol)

Serum albumin levels were increased among Cordyceps recipients (Analysis 1.9: 4 studies, 323 participants): MD 3.52 g/L, 95% CI 2.79 to 4.24; I² = 0%), but there was no significant improvement in total cholesterol (Analysis 1.10: 2 studies, 198 participants): MD 0.41 mmol/L, 95% CI 0 to 0.82; I² = 0%).

Bone disease (calcium, phosphorus)

Liu 2006a reported a significant increase in serum calcium (Analysis 1.11: 1 study, 66 participants): MD 0.15 mmol/L, 95% CI 0.04 to 0.26) and a significant decrease in serum phosphorus (Analysis 1.12: 1 study, 66 participants): MD -0.11 mmol/L, 95% CI -0.18 to -0.04) among Cordyceps recipients.

Cordyceps + conventional medicine versus Western medicine + conventional medicine

Three studies compared Cordyceps preparations with Western medicine interventions. In consideration of the differing Western medicines used the results have not been pooled. In a comparison of prednisone and Cordyceps for treatment of aristolochic acid nephropathy, Gao 2007 (27 participants) reported Cordyceps significantly reduced SCr (Analysis 2.2: MD -116.07 µmol/L, 95% CI -209.13 to -23.01) and significantly increased CrCl (Analysis 2.3: MD 8.07 mL/min, 95% CI 5.22 to 10.92). In comparison to coated aldehyde oxystarch, Jin 2004 (82 participants) reported Cordyceps significantly reduced SCr (Analysis 2.2: MD -41.72 µmol/L, 95% CI -77.99 to -5.45); and increased CrCl (Analysis 2.3: MD 7.25 mL/min, 95% CI 2.29 to 12.21), haemoglobin (Analysis 2.5: MD 21.3 g/L, 95% CI 14.2 to 28.4), haematocrit (Analysis 2.6: MD 3.6%, 95% CI 1.56 to 5.64), and albumin (Analysis 2.7: MD 4.35 g/L, 95% CI 2.89 to 5.81). Huang 2008 (86 participants) reported no significant differences between Lipo PGE1 and Cordyceps preparation on CKD progression (Analysis 2.1: RR 0.92, 95% CI 0.76 to 1.12); SCr (Analysis 2.2: MD 25.14 µmol/L, 95% CI -38.55 to 88.83); CrCl (Analysis 2.3: MD 1.61 mL/min, 95% CI -3.64 to 0.42) or 24 hour proteinuria (Analysis 2.4: MD 0.31 g/24 h, 95% CI -0.06 to 0.68) in CKD patients.

Cordyceps + traditional Chinese medicine versus traditional Chinese medicine alone

Yan 2005a (65 participants) reported no significant differences when Cordyceps was administered as a co-intervention with traditional Chinese herbal medicine for the treatment of CKD for SCr (Analysis 3.1: MD -24.00 µmol/L, 95% CI -49.91 to 1.91), but significantly reduced 24 hour proteinuria (Analysis 3.2: MD -0.59 g/24 h, 95% CI -0.99 to -0.19) and significantly increased haemoglobin levels (Analysis 3.3: MD 24.00 g/L, 95% CI 16.62 to 31.38).

Adverse effects

Four studies reported that no obvious adverse effects were associated with Cordyceps preparations (Chen 2006a; Fu 2009; Sun 1999; Yan 2005a).

Hu 2008 (30 participants) reported that test results for blood chemistry, liver function, cardiographic studies and electrolytes were normal after administration of Jin Shui Bao capsule (Cordyceps 0.33 g) over two months.

Liu 2006a (66 participants) reported that two intervention arm participants (5.9%) had diarrhoea and six (17.6%) experienced constipation; three control arm participants (9.3%) developed nausea, three (9.3%) had abdominal distention, and six (18.8%) became constipated.

Huang 2008 (86 participants) reported that four (4.7%) of 86 participants experienced discomfort after taking Jin Shui Bao capsule. Symptoms were minimised when the capsule was taken after eating.

The remaining 15 included studies did not report adverse events. Therefore definitive associations between adverse effects and Cordyceps could not be derived with certainty.

Other outcomes

Several outcomes were not reported in the included studies.
• Time to requirement for RRT or initiation of dialysis (primary outcome)
• All-cause mortality (primary outcome)
• Quality of life measured by a validated scale (secondary outcome)
• Symptoms including skin pruritus, vomiting, measured by visual analogue or other scales (secondary outcome).

Discussion

Summary of main results

This review included 22 studies that involved 1746 participants with CKD; all studies were undertaken in hospitals in China. Different stages of CKD were represented in the studies; baseline SCr ranged from 135 to 820 µmol/L. All studies investigated mycelial fermentation products of Cordyceps sinensis.

Cordyceps was administered as a co-intervention in all studies: 18/22 studies compared Cordyceps plus conventional treatment with the same conventional treatment, and of these three administered haemodialysis as the co-intervention. Three studies compared Cordyceps plus conventional treatment with Western medicine plus the same conventional treatment; and one study compared Cordyceps plus traditional Chinese medicine to the same traditional Chinese medicine.

As an adjunctive treatment to conventional medicine, Cordyceps preparation had promising effects on decreasing SCr, increasing...
CrCl, reducing proteinuria and alleviating CKD-associated complications such as reduced haemoglobin and serum albumin levels. However, low methodological quality and under-reporting among the included studies meant that definitive conclusions could not be made about the possible effects of Cordyceps preparation for people with CKD.

Overall completeness and applicability of evidence

Although we intended to explore potential benefits of Cordyceps for people with CKD on aspects including CKD progression and complications, none of the included studies reported outcome data on time to requirement for RRT or initiation of dialysis, or all-cause mortality. Data on the effects of Cordyceps preparations on SCr and CrCl were reported. It is noteworthy that CrCl tends to overestimate GFR (Shemesh 1985). Lack of GFR data meant that it was difficult to clearly define degree of kidney function damage and the CKD stage.

Because all included studies were undertaken in China questions about applicability of the evidence to other settings exist. Co-interventions explored in the included studies for CKD management in China are likely to differ from other settings. It is uncertain if this aspect influenced assessment of the effects and safety of Cordyceps for people with CKD.

Quality of the evidence

Evidence quality of included studies in the review was suboptimal. Risk of bias was assessed as high in four and unclear in 18/22 included studies. Methodological flaws related to lack of clear descriptions of randomisation, allocation concealment, and binding. There was marked heterogeneity in the conventional treatment as co-interventions in some included studies. Because of no masking during the study, the possible difference in the multiple co-interventions between treatment and control group would likely introduce bias to the results.

Potential biases in the review process

Four studies were excluded from our quantitative analysis because of the absence of some essential data. However, we believe that exclusion of these studies did not bias review results because they represented similar study populations and results to the body of included studies.

Agreements and disagreements with other studies or reviews

In an earlier review that included six studies, statistically significant treatment effects were reported for Cordyceps compared with control (Xu 2006). Because information about control interventions and definitions of outcome measures were not clearly stated in Xu 2006, we did not compare our results with findings from this review.

AUTHORS’ CONCLUSIONS

Implications for practice

The current evidence indicated that when used with conventional treatment, Cordyceps may offer some benefits for people with CKD by improving kidney function and alleviating complications such as anaemia and malnutrition. However, methodological quality was suboptimal, and further clinical studies are required to ascertain the potential benefits of Cordyceps for people with CKD.

Implications for research

Based on the methodological deficits identified in the available studies, we suggest that future clinical studies investigating Cordyceps for people with CKD consider the following:

1. Randomisation and allocation concealment methodology need to be undertaken and clearly reported.

2. Efforts should be made to develop placebo controls that mimic Cordyceps products to clarify its efficacy for CKD. Blinding intervention assignment to participants, clinicians and outcomes assessors needs to be undertaken and reported. In settings where it is not possible or feasible to blind participants and clinicians, outcomes assessors should be blinded, especially when subjective outcomes are involved.

3. Sample sizes should be calculated to ensure that studies have sufficient power to detect possible differences between groups.

4. Incorporating long-term outcome measures, such as need for RRT, all-cause mortality, or quality of life measures may help to confirm beneficial outcomes associated with Cordyceps for CKD.

5. Record and report all in-study adverse effects. The elaborated CONSORT statement for reporting RCTs of herbal medicines is strongly recommended when designing and reporting clinical studies (Gagnier 2006).

ACKNOWLEDGEMENTS

We would like to thank Fan Cheung and Yi Fong Ho who assisted with study selection, data extraction and data entry.
We would also like to thank the referees for their editorial advice, and Narelle Willis and Gail Higgins of the Cochrane Renal Group for their kind assistance in preparing this review.

References to studies included in this review

Chen 2003 [published data only]

Chen 2006a [published data only]

Fu 2009 [published data only]

Gao 2007 [published data only]

Gao 2009 [published data only]

Hu 2008 [published data only]

Huang 2008 [published data only]

Jin 2004 [published data only]

Liu 2006a [published data only]

Liu 2007 [published data only]

Pan 2007 [published data only]

Shi 2009 [published data only]

Sun 1999 [published data only]

Wang 2005a [published data only]
Wang FL. Clinical observation on the treatment of integrated Chinese and Western medicine on chronic kidney failure [Zhong xi yi jie he zhi liao man xing shen shuai jie de lin chuang guan cha]. Zhongguo Zhongyi Jiehe
Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review)

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Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review)

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Yin 2001 [published data only]

Zhou 2002 [published data only]

Jin 2006 [published data only]

Lin 2003 [published data only]

Additional references

Deng 2001

Feng 2013

Gagnier 2006

Higgins 2003

Higgins 2011

Levey 2003

Liu 2005

Liu 2007

Ma 2008

McCullough 2012

**Min 2008**


**NKF 2008**


**Nugent 2011**


**Shahed 2001**


**Shemesh 1985**


**Shin 2001**

Shin KH, Lim SS, Lee SH, Lee YS, Cho SY. Antioxidant and immunostimulating activities of the fruiting bodies of *Paecilomyces japonica*, a new type of *Cordyceps* sp. and immunostimulating activities of the fruiting bodies of *Cordyceps* sp. *Annals of the New York Academy of Sciences* 2001;928:261–73. MEDLINE: 11795517

**Srinath Reddy 2005**


**Wojcikowski 2006**


**Xu 2006**


**Yang 1999a**


**Yang 2003**


**Yin 2007**


**Zhou 2000**

Zhao LW, Xiao XW, Wei YC. Inhibitory effect of *Cordyceps* sinensis and *Cordyceps* militaris on human glomerular mesangial cell proliferation induced by native LDL. *Cell Biochemistry & Function* 2000;18(2):93–7. MEDLINE: 10814966

**Zheng 2002**


**Zhu 1998a**


**Zhu 1998b**

References to other published versions of this review

Zhang 2010


* Indicates the major publication for the study.
### Characteristics of included studies

#### Chen 2003

| Methods | ● Design: parallel RCT  
<table>
<thead>
<tr>
<th></th>
<th>● Power calculation: no</th>
</tr>
</thead>
</table>
| Participants | ● Country: China  
|         | ● Setting: Hospital  
|         | ● CKD patients; SCr < 442 µmol/L  
|         |   ○ Baseline mean SCr (µmol/L): treatment group (252.4); control group (249.72)  
|         | ● Number: treatment group (164); control group (48)  
|         | ● Mean age: 42.57 years  
|         | ● Sex (M/F): 130/82  
|         | ● Exclusion criteria: NR |
| Interventions | Treatment group  
| Control group | ● Conventional treatment  
| Conventional treatment | ● High quality, low phosphate, calorie, and protein diet  
|         | ● Symptomatic treatment, including maintaining water, electrolyte and acid-base balance, controlling BP, anticoagulation treatment and infection control as needed |
| Outcomes | ● SCr  
|         | ● 24 h proteinuria  
|         | ● Hb  
|         | ● Albumin |
| Notes | ● Further information about allocation methodology was requested from the author, but no response was received at the time of drafting this review |

#### Risk of bias

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<th>Authors’ judgement</th>
<th>Support for judgement</th>
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<td>Randomisation claimed, but there were 164 participants in treatment group and 48 in the control group</td>
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<tr>
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<td>High risk</td>
<td>No placebo control and no description of blinding</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>No losses to follow-up. All participants included in the analysis</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Limited outcome measures were reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Imbalance in the patient numbers in the treatment and control group</td>
</tr>
</tbody>
</table>

### Chen 2006a

#### Methods
- **Design:** parallel RCT
- **Power calculation:** no

#### Participants
- **Country:** China
- **Setting:** hospital
- **CKD patients; Scr 178 to 707 µmol/L**
  - Baseline mean Scr (µmol/L): treatment group (371.85); control group (389.84)
- **Number:** treatment group (36); control group (31)
- **Mean age (range):** 63.87 years (29 to 83)
- **Sex (M/F):** 32/35
- **Exclusion criteria:** NR

#### Interventions
- **Treatment group**
  - Cordyceps
    - Oral Jin Shui Bao: 6 capsules, 3 times/d
    - Treatment duration: 1 month
  - Conventional treatment
- **Control group**
  - Conventional treatment
  - Treatment of primary disease
  - High quality, low salt, lipid and protein diet
  - Symptomatic treatment, including maintaining water, electrolyte and acid-base balance, BP and infection control, anaemia resolution as needed
  - Oral medicinal charcoal: 5 tablets, 3 times/d

#### Outcomes
- **CKD progression**
- **Scr**
- **CrCl**

#### Notes
- **No drop-outs or withdrawals**
<table>
<thead>
<tr>
<th>Bias</th>
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<tr>
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<td>High risk</td>
<td>Imbalance in participant numbers in treatment and control groups</td>
</tr>
</tbody>
</table>

**Fu 2009**

**Methods**
- Design: parallel RCT
- Power calculation: no

**Participants**
- Country: China
- Setting: hospital
- Diagnosis of hypertension nephrology
- Number: treatment group (35); control group (30)
- Mean age (range): 52.78 years (29 to 64)
- Sex (M/F): 39/26
- Exclusion criteria: primary glomerular diseases; diabetes mellitus; other causes of kidney injury

**Interventions**
- Treatment group
  - Cordyceps
    - Oral Jin Shui Bao: 3 capsules, 3 times/d
    - Treatment duration: 3 months
  - Conventional treatment
- Control group
  - Conventional treatment
  - Oral captopril and nifedipine controlled release tablet
  - Oral hydrochlorothiazide or metoprolol tartrate tablets were administered to obtain target BP as needed

**Outcomes**
- SCr
- CrCl
- 24 h proteinuria
### Risk of bias

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<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Conventional treatment may differ between arms</td>
</tr>
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</table>

### Gao 2007

**Methods**
- Design: parallel RCT
- Power calculation: no

**Participants**
- Country: China
- Setting: hospital
- History of taking Chinese medicines containing aristolochic acid; normal or slightly abnormal routine urine test; increased nocturnal urine volume, high BP; kidney function impairment that could not be explained by primary disease, or acellular interstitial fibrosis confirmed by kidney puncture biopsy; SCr ranging from 133 to 707 \( \mu \)mol/L.
  - Number: treatment group (15); control group (12)
  - Mean age (range): 49.86 years (31 to 65)
  - Sex (M/F): 11/16
  - Exclusion criteria: CKD caused by other primary or secondary diseases; noncompliance with dietary and treatment interventions; ESKD; cancer or other severe disease; peritoneal dialysis and haemodialysis

**Interventions**
- Treatment group
  - Cordyceps
    - Oral Bai Ling: 2 g capsule, 3 times/d
    - Treatment duration: 6 months
  - Conventional treatment
Control group
- Oral prednisone: 0.75 mg/d/kg initially, then reduced to 0.5 mg/d/kg after one month
- Treatment duration: 6 months
- Conventional treatment
  - Dietary protein restricted to 0.6 g/kg/d, low salt, low lipid
  - Control BP
  - Correct anaemia
  - Control infection

Outcomes
- SCr
- CrCl

Notes
- No drop-outs or withdrawals

### Risk of bias

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</tr>
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</table>

**Guo 2009**

**Methods**
- Design: parallel RCT
- Power calculation: no

**Participants**
- Country: China
- Setting: hospital
- CKD patients who need dialysis treatment
  - Baseline mean SCr (µmol/L): treatment group (821.7); control group (817.6)
Guo 2009  (Continued)

- Number: treatment group (34); control group (30)
- Age range: 16 to 78 years
- Sex (M/F): 33/31
- Exclusion criteria: NR

### Interventions

#### Treatment group
- Cordyceps
  - Oral Jin Shui Bao: 6 capsules, 3 times/d
  - Treatment duration: 3 months
- Haemodialysis
- Conventional treatment

#### Control group
- Haemodialysis
- Conventional treatment

#### Conventional treatment
- Low protein and phosphorous diet
- BP control
- Anaemia correction
- Maintain water, electrolyte and acid-base balance

### Outcomes

- CKD progression
- SCr
- Hb

### Notes

- Drop-outs/withdrawals: Data from 9 participants in the treatment group and 5 in the control group missing

### Risk of bias

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### Methods
- Design: parallel RCT
- Power calculation: no

### Participants
- Country: China
- Setting: hospital
- Patients with CKD
  - Baseline mean SCr ($\mu$mol/L): treatment group (303.22); control group (304.88)
  - Number: treatment group (15); control group (15)
  - Mean age (range): 31.8 years (8 to 52)
  - Sex (M/F): 12/18
  - Exclusion criteria: NR

### Interventions
#### Treatment group
- Cordyceps
  - Oral Jin Shui Bao: 5 capsules, 3 times/d
  - Treatment duration: 2 months
- Conventional treatment

#### Control group
- Conventional treatment
- High quality, low protein diet
- Control BP, blood lipids, and blood glucose
- Correct water and electrolyte imbalance
- Treat complications, such as infection

### Outcomes
- SCr
- 24 h proteinuria

### Notes
- No drop-outs or withdrawals

### Risk of bias

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### Other bias

**Unclear risk**  
Conventional treatment may differ between arms

### Huang 2008

#### Methods
- **Design**: parallel quasi-RCT
- **Power calculation**: no

#### Participants
- **Country**: China
- **Setting**: hospital
- **CKD patients**
  - Baseline mean SCr (μmol/L); treatment group (398.76); control group 1 (386.15); control group 2 (390.56)
- **Number**: treatment group (43); control group 1 (43); control group 2 (43)
- **Age range**: 31 to 81 years
- **Sex (M/F)**: 90/39
- **Exclusion criteria**: NR

#### Interventions

**Treatment group**
- **Cordyceps**
  - Oral Jin Shui Bao: 6 capsules, 3 times/d
  - Treatment duration: 1 month
- **Conventional treatment**

**Control group 1**
- **Western medicine**
  - IV Lipo PGE1: 10 μg + 0.9% normal saline, 4 times/d
  - Treatment duration: 1 month
- **Conventional treatment**

**Control group 2**
- **Cordyceps**
  - Oral Jin Shui Bao: 6 capsules, 3 times/d
  - Treatment duration: 1 month
- **Western medicine**
  - IV Lipo PGE1: 10 μg + 0.9% normal saline, 4 times/d
  - Treatment duration: 1 month
- **Conventional treatment**

**Conventional treatment**
- **Low protein diet**
- **Treatment of primary diseases**

#### Outcomes
- **CKD progression**
- **SCr**
- **CrCl**
- **UPE**
- **24 hour proteinuria**

#### Notes
- **No drop-outs or withdrawals**
## Huang 2008 (Continued)

### Risk of bias

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</table>

### Jin 2004

#### Methods

- **Design:** parallel RCT
- **Setting:** 2 hospitals in China
- **Power calculation:** no

#### Participants

- **Country:** China
- **Setting:** 2 hospitals
- **CKD patients, baseline SCr ranging from 177 to 707 µmol/L or baseline CrCl from 10 to 50 mL/min**
  - Mean SCr (µmol/L): treatment group (317.76); control group 1 (318.68); control group 2 (316.78)
- **Number:** treatment group (41); control group 1 (41); control group 2 (41)
- **Mean age:** 50.2 years
- **Sex (M/F):** 64/59
- **ESKD (SCr > 707 µmol/L or CrCl < 10 mL/min); AKI**

#### Interventions

- **Treatment group**
  - Cordyceps
    - Oral Jin Shui Bao: 6 capsules, 3 times/d
    - Treatment duration: 6 months
  - Conventional treatment
- **Control group 1**
  - TCM
    - Individualised traditional Chinese herbal medicine orally, twice/d
    - Treatment duration: 6 months
  - Conventional treatment
Jin 2004  (Continued)

Control group 2
- Oral coated aldehyde oxystarch: 5 g, 4 times/d
  - Treatment duration: 6 months
- Conventional treatment

Conventional treatment
- Symptomatic therapy for high BP, high blood glucose, gout or acidosis

Outcomes
- SCr
- CrCl
- Hb
- HCT
- Albumin
- Total cholesterol

Notes
- No drop-outs or withdrawals

Risk of bias

<table>
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<th>Support for judgement</th>
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Liu 2006a

Methods
- Design: parallel RCT
- Power calculation: no

Participants
- Country: China
- Setting: hospital
- CKD patients
  - Baseline mean SCr (µmol/L): treatment group (372.6); control group (369.2)
4)  
- Number: treatment group (34); control group (32)
- Mean age (range): 42.06 years (24 to 69)
- Sex (M/F): 39/27
- Exclusion criteria: NR

### Interventions

#### Treatment group
- Cordyceps
  - Oral Bai Ling: 5 capsules, 3 times/d
  - Treatment duration: 2 months
- Conventional treatment

#### Control group
- Conventional treatment

### Conventional treatment

#### Primary disease treatment
- High quality, low salt and lipid diet
- Symptomatic treatment, including maintaining water, electrolyte and acid-base balance, BP and infection control, treating anaemia as needed
- Oral charcoal: 5 tablets, 3 times/d

### Outcomes

- CKD progression
- SCr
- Albumin
- Total cholesterol
- Calcium
- Phosphorous

### Notes
- No drop-outs or withdrawals

### Risk of bias

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### Liu 2006a

**Other bias**

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### Liu 2007a

#### Methods

- **Design:** parallel RCT
- **Power calculation:** no

#### Participants

- **Country:** China
- **Setting:** hospital
- **CKD patients**
  - Baseline mean SCr (µmol/L): treatment group (246.58); control group (248.35)
  - Number: treatment group (68); control group (64)
  - Mean age: 56.78 years
  - Sex (M/F): 42/26
  - Exclusion criteria: NR

#### Interventions

**Treatment group**
- Cordyceps
  - Oral Bai Ling: 5 capsules, 3 times/d
  - Treatment duration: 1.5 months
- Conventional treatment

**Control group**
- Conventional treatment

**Conventional treatment**
- General and symptomatic treatment
- Dietary treatment
- Oral Shen Shuai Ning*: 6 capsules, 3 times/d

#### Outcomes

- Progress of CKD
- SCr
- Albumin
- Total cholesterol

#### Notes

- No drop-outs or withdrawals
- * Shen Shuai Ning capsule is a patent Chinese herbal formula for the treatment of CKD, mainly composed of Taizishen (Radix Pseudostellariae), Dahuang (Radix et Rhizoma Rhei), Honghua (Flos Carthami), Danshen (Radix Rhizoma Salviae Miltiorrhizae), Niuxi (Radix Cyathulae), Dongchongxiacao (Cordyceps), and Gancao (Radix et Rhizoma Glycyrrhiza)

### Risk of bias

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- **Unclear risk**: Not reported

### Blinding (performance bias and detection bias)
- **Unclear risk**: No placebo control and no description of blinding

### Incomplete outcome data (attrition bias)
- **Unclear risk**: No losses to follow-up. All participants included in the analysis

### Selective reporting (reporting bias)
- **Unclear risk**: Limited outcome measures were reported

### Other bias
- **Unclear risk**: Conventional treatment may differ between arms

---

### Pan 2007

#### Methods
- **Design**: parallel RCT
- **Power calculation**: no

#### Participants
- **Country**: China
- **Setting**: hospital
- **CKD patients**
  - Baseline mean SCr ($\mu$mol/L): treatment group (546); control group (561.9)
  - Number: treatment group (32); control group (32)
  - Mean age (range): 43.35 years (21 to 75)
  - Sex (M/F): 39/25
  - Exclusion criteria: NR

#### Interventions
- **Treatment group**
  - **Cordyceps**
    - Oral Bai Ling: 5 capsules, 3 times/d
    - Treatment duration: 2 months
  - Conventional treatment
- **Control group**
  - Conventional treatment
  - Adequate high quality protein diet
  - BP control
  - Maintain water, electrolyte and acid-base balance
  - Oral Niaoduqing granules*
  - Participants with diabetes mellitus received insulin
  - Participants with anaemia received erythropoietin 2000 U SC injection 2 to 3/wk, Shengxuening** tablet 0.5 g, and folic acid 10 mg, 3/d

#### Outcomes
- **CKD progression**
- **SCr**
- **CrCl**
Notes

- No drop-outs or withdrawals
- * Oral Niaoduqing granules* (a patent Chinese herbal formula for the treatment of uraemia, mainly composed of Huangqi (Radix Astragali), Dangshen (Radix Codonopsis), Heshouwu (Radix Polygoni Multiflori), Dahuang (Radix et Rhizoma Rhei), Baizhu (Rhizoma Atractylodis Macrocephalae), Fuling (Poria), Cheqiancao (Hegba Plantaginis Asiaticae), Banxia (Rhizoma Pinelliae Ternatae), Chuanshong (Rhizoma Chuanxiong) and Danshen (Radix Rhizoma Salviae Miltiorrhizae)
- ** Shengxuening tablet is extract of Cansha (Feculae Bombycis)

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Shi 2009

Methods

- Design: parallel RCT
- Power calculation: no

Participants

- Country: China
- Setting: hospital
- Patients with 24 h proteinuria 0.8 to 3 g
- Number: treatment group (32); control group (28)
- Mean age (range): 40.93 years (19 to 76)
- Sex (M/F): 36/24
- Exclusion criteria: Henoch-Schönlein purpura nephritis, lupus nephritis, or hepatitis B virus associated-glomerulonephritis; secondary glomerular diseases, such as diabetic retinopathy

Interventions

- Treatment group
  - Cordyceps
    - Oral Bai Ling: 1 g capsule, 3 times/d
Shi 2009  (Continued)

- Treatment duration: 6 months
  - Conventional treatment
  - Control group
    - Conventional treatment
- Conventional treatment
  - High quality low protein, low salt diet
  - Individualised symptomatic treatment, e.g. antihypertensives
  - Control infection control, diuretics, calcium or Vitamin D as needed
  - Valsartan 160 mg/d

Outcomes
- 24 h proteinuria

Notes
- No drop-outs or withdrawals

Risk of bias

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Sun 1999

Methods
- Design: parallel RCT
- Power calculation: no

Participants
- Country: China
- Setting: hospital
- CKD patients requiring dialysis
  - Baseline mean SCr (µmol/L): treatment group (876.60); control group (843.63)
- Number: treatment group (30); control group (30)
- Age range: 21 to 76 years
- Sex (M/F): 36/24
### Interventions

**Treatment group**
- Cordyceps
  - Oral Jin Shui Bao: 4 capsules, 3 times/d
  - Treatment duration: 3 months
- Conventional treatment

**Control group**
- Conventional treatment
- Haemodialysis
- Conventional symptomatic treatment

### Outcomes

- SCr
- Hb

### Notes

- No drop-outs or withdrawals

### Risk of bias

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### Wang 2005a

**Methods**
- Design: parallel RCT
- Power calculation: no

**Participants**
- Country: China
- Setting: hospital
- CKD patients; SCr 178 to 442 µmol/L; 24 h proteinuria < 3 g/L; SCr value constant in past 3 months
- Number: treatment group (30); control group (30)
**Interventions**

**Treatment group**
- Cordyceps
  - Oral Jin Shui Bao: 3 capsules, 3 times/d
  - Treatment duration: 2 months

**Control group**
- Conventional treatment

**Conventional treatment**
- Low salt and phosphorus, high quality protein diet
- BP control
- Maintenance of water, electrolyte and acid-base balance
- Oral coated aldehyde oxystarch: 12 capsules

**Outcomes**

- CKD progression
- SCr
- CrCl
- Hb

**Notes**

- No drop-outs or withdrawals

**Risk of bias**

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Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review)
Methods

- Design: parallel RCT
- Power calculation: no

Participants

- Country: China
- Setting: hospital
- CKD patients
  - Baseline mean SCr (µmol/L): treatment group (250.36); control group (252.52)
- Number: treatment group (30); control group (30)
- Mean age (range): 45.5 years (39 to 70)
- Sex (M/F): 28/32
- Exclusion criteria: ESKD; severe complicated primary diseases including heart, brain, liver and hematopoietic system diseases; psychoses

Interventions

Treatment group

- Cordyceps
  - Oral Bai Ling: 8 capsules, 3 times/d
  - Treatment duration: 2 months
- Conventional treatment

Control group

- Conventional treatment

Conventional treatment

- Low protein diet
- BP control
- Acidosis correction

Outcomes

- SCr
- CrCl
- Albumin
- Hb
- HCT

Notes

- No drop-outs or withdrawals

Risk of bias

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### Wei 2004 (Continued)

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### Wu 2007

#### Methods
- Design: parallel RCT
- Power calculation: no

#### Participants
- Country: China
- Setting: hospital
- CKD patients
  - Baseline mean SCr ($\mu$mol/L): treatment group (542.04); control group (429.35)
  - Number: treatment group (24); control group (22)
  - Mean age (range): 47.60 years (34 to 69)
  - Sex (M/F): 24/22
  - Exclusion criteria: NR

#### Interventions
- **Treatment group**
  - Cordyceps
    - Oral Jin Shui Bao: 6 capsules, 3 times/d
    - Treatment duration: 1 month
  - Conventional treatment
- **Control group**
  - Conventional treatment
  - Baseline treatment, including low salt and phosphorus, high quality protein diet

#### Outcomes
- CKD progression
- SCr
- CrCl

#### Notes
- No drop-outs or withdrawals

### Risk of bias

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*Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review) Copyright © 2014 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.*
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<td>SCr</td>
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### Xu 2004

**Methods**
- Design: parallel RCT
- Power calculation: no

**Participants**
- Country: China
- Setting: hospital
- CKD patients requiring dialysis
  - Baseline mean SCr (µmol/L): treatment group (742); control group (725)
  - Number: treatment group (42); control group (40)
  - Mean age (range): 41.8 years (17 to 75)
  - Sex (M/F): 52/30
  - Exclusion criteria: NR

**Interventions**
- Treatment group
  - Cordyceps
    - Oral Bai Ling: 5 capsules, 3 times/d
    - Treatment duration: 2 months
  - Conventional treatment
- Control group
  - Conventional treatment

Conventional treatment
- Low protein, high calorie, and adequate vitamin diet
- BP control
- Maintain water, electrolyte and acid-base balance
- Oral coated aldehyde oxystarch: 8 to 10 tablets, 3 times/d
- IM Testosterone propionate: 25 mg, once every 2 days
- 20 and 18 participants respectively in the treatment and control arms received erythropoietin 2000 U SC injection 2 to 3 times/wk and were administered oral ferrous succinate 0.2 g and folic acid 10 mg, 3 times/d

**Outcomes**
- SCr

**Notes**
- No drop-outs or withdrawals
### Xu 2004 (Continued)

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### Yan 2005a

**Methods**
- Design: parallel RCT
- Power calculation: no

**Participants**
- Country: China
- Setting: hospital
- CKD patients
  - Baseline mean SCr (µmol/L): treatment group (135); control group (131)
- Number: treatment group (33); control group (32)
- Mean age (range): 48.27 years (34 to 69)
- Sex (M/F): 33/32
- Exclusion criteria: NR

**Interventions**
- **Treatment group**
  - Cordyceps
    - Oral Jin Shui Bao: 4 capsules, 3 times/d
    - Treatment duration: 6 months
  - TCM treatment
- **Control group**
  - TCM treatment
  - TCM treatment
- Traditional Chinese herbal medicine for CKD

**Outcomes**
- SCr
- Hb
- 24 h proteinuria

**Notes**
- No drop-outs or withdrawals
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**Yang 1999b**

**Methods**
- Design: parallel RCT
- Power calculation: no

**Participants**
- Country: China
- Setting: hospital
- CKD patients
  - Baseline mean SCr ($\mu$mol/L): treatment group (478.5); control group (456.7)
- Number: treatment group (29); control group (24)
- Mean age (range): 38.2 years (18.7 to 57.7)
- Sex (M/F): 29/24
- Exclusion criteria: NR

**Interventions**
- Treatment group
  - Cordyceps
    - Oral Jin Shui Bao: 2 capsules, 3 times/d
    - Treatment duration: 3 months
  - Conventional treatment
- Control group
  - Conventional treatment
- Conventional treatment
  - Conventional symptomatic treatment, such as captopril and furosemide

**Outcomes**
- SCr
- Hb
### Notes
- No drop-outs or withdrawals

### Risk of bias

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### Yu 2002

#### Methods
- Design: parallel RCT
- Power calculation: no

#### Participants
- Country: China
- Setting: hospital
- Participants with uraemia at haemodialysis commencement
  - Baseline mean SCr (µmol/L): treatment group (810.34); control group (793.57)
  - Number: treatment group (35); control group (30)
- Age: NR
- Sex (M/F): 36/29
- Exclusion criteria: diseases that may cause malnutrition, such as chronic nephritis, diabetic nephropathy, hypertensive kidney disease, gout nephropathy and polycystic kidney disease

#### Interventions
- Treatment group
  - Cordyceps
    - Oral Bai Ling: 5 capsules, 3 times/d
    - Treatment duration: 6 months
  - Conventional haemodialysis with sodium bicarbonate dialysate
- Control group
  - Conventional haemodialysis with sodium bicarbonate dialysate
### Outcomes
- Albumin

### Notes
- No drop-outs or withdrawals

---

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomisation method not reported</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not reported</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias)</td>
<td>High risk</td>
<td>No placebo control and no description of blinding</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>No losses to follow-up. All participants included in the analysis</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Limited outcome measures were reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Conventional treatment may differ between arms</td>
</tr>
</tbody>
</table>

---

### Yu 2003

#### Methods
- Design: parallel RCT
- Power calculation: no

#### Participants
- Country: China
- Setting: hospital
- CKD patients
  - Baseline mean SCr (µmol/L): treatment group (451.16); control group (475.25)
  - Number: treatment group (78); control group (82)
- Mean age (range): 46.5 years (30 to 68)
- Sex (M/F): 100/60
- Exclusion criteria: NR

#### Interventions
- **Treatment group**
  - Cordyceps
    - Oral Bai Ling: 5 capsules, 3 times/d
    - Treatment duration: 3 months
  - Conventional treatment
- **Control group**
  - Conventional treatment
  - Conventional treatment
Yu 2003

- Low protein and phosphorus diet
- Close observation on the BP and keep it in the normal range
- Maintain water, electrolyte and acid-base balance

Outcomes
- CKD progression
- SCr

Notes
- Data from 4 control arm participants were not reported

<table>
<thead>
<tr>
<th>Risk of bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomisation method not reported</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not reported</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias) All outcomes</td>
<td>High risk</td>
<td>No placebo control and no description of blinding</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
<td>Data from 4 control arm participants were not reported; no reason for data omission provided</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Limited outcome measures were reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Conventional treatment administered not identical in both arms</td>
</tr>
</tbody>
</table>

Zhang 2009

- Design: parallel RCT
- Power calculation: no

Participants
- Country: China
- Setting: 2 hospitals
- CKD patients with a history of taking medicine containing aristolochic acid; no history of taking other related medicine; normal or slightly abnormal urine routine test; anaemia not related to kidney dysfunction; acellular interstitial fibrosis; no other related diseases
- Number: treatment group (28); control group (28)
- Mean age: 64.2 years
- Sex (M/F): 26/30
- Exclusion criteria: CKD caused by other primary or secondary diseases; non-compliance with dietary and treatment interventions; ESKD; cancer or other severe disease; peritoneal dialysis or haemodialysis patients
Interventions

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cordyceps</td>
<td></td>
</tr>
<tr>
<td>◦ Oral Jin Shui Bao: 1.98 g capsule, 3 times/d</td>
<td></td>
</tr>
<tr>
<td>◦ Treatment duration: 6 months</td>
<td></td>
</tr>
<tr>
<td>• Conventional treatment</td>
<td></td>
</tr>
</tbody>
</table>

Control group

• Conventional treatment

Conventional treatment

• Oral prednisone 1 mg/d/kg for one month, reduced by 0.1 mg/kg/d every two months, then maintained at 0.15 mg/d/kg for the study duration
• High quality, low protein (0.6 g/d/kg) diet
• BP control
• Erythropoietin 3000 U SC, 3 times/wk for anaemia

Outcomes

• SCr
• 24 h proteinuria

Notes

• No drop-outs or withdrawals

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomisation method not reported</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not reported</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias)</td>
<td>High risk</td>
<td>No placebo control and no description of blinding</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>No losses to follow-up. All participants included in the analysis</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Limited outcome measures were reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Conventional treatment may differ between arms</td>
</tr>
</tbody>
</table>

AKD - acute kidney injury; BP - blood pressure; CKD - chronic kidney disease; CrCl - creatinine clearance; ESKD - end-stage kidney disease; Hb - haemoglobin; HCT - haematocrit; NR - not reported; SCr - serum creatinine; TCM - traditional Chinese medicine; UPE - urinary protein electrophoresis
### Characteristics of excluded studies  
[ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bao 1994</td>
<td>Information about the duration of aminoglycoside nephrotoxicity was not available</td>
</tr>
<tr>
<td>Huang 2008b</td>
<td>Ginkgo leaf tablet was used with Cordyceps preparation in the treatment group</td>
</tr>
<tr>
<td>Jiang 2008</td>
<td>Did not include outcomes relevant to the review</td>
</tr>
<tr>
<td>Li 1992</td>
<td>Wrong population: participants had respiratory infection or febrile diseases, normal kidney function, and absence of history of kidney disease</td>
</tr>
<tr>
<td>Quan 2004</td>
<td>Follow up periods differed for individual participants</td>
</tr>
<tr>
<td>Wu 2005</td>
<td>Participant allocation was not randomised</td>
</tr>
<tr>
<td>Xu 2009</td>
<td>Did not include outcomes relevant to the review</td>
</tr>
<tr>
<td>Yan 2005b</td>
<td>Participant allocation was not randomised</td>
</tr>
<tr>
<td>Yan 2007</td>
<td>The wording and data were similar to those in Liu 2007a to some degree, possibly duplicate report</td>
</tr>
<tr>
<td>Yang 2001</td>
<td>Did not include outcomes relevant to the review</td>
</tr>
<tr>
<td>Yin 2001</td>
<td>Did not include outcomes relevant to the review</td>
</tr>
<tr>
<td>Zhou 2002</td>
<td>Did not include outcomes relevant to the review</td>
</tr>
</tbody>
</table>

### Characteristics of studies awaiting assessment  
[ordered by study ID]

**Chai 2009**

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>CKD patients</td>
</tr>
<tr>
<td>Interventions</td>
<td>Cordyceps + conventional treatment versus conventional treatment</td>
</tr>
<tr>
<td>Outcomes</td>
<td>SCr</td>
</tr>
<tr>
<td></td>
<td>CrCl</td>
</tr>
<tr>
<td></td>
<td>ECT 20 minER</td>
</tr>
<tr>
<td>Notes</td>
<td>Request was made to the authors to elicit information about the treatment information of Cordyceps and control group. No response received at the time of drafting the review.</td>
</tr>
<tr>
<td><strong>Jin 2006</strong></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>● RCT</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>● CKD patients</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>● Chinese herb + conventional treatment versus Cordyceps + conventional medicine versus Western medicine + conventional treatment</td>
</tr>
</tbody>
</table>
| **Outcomes** | ● SCr  
● CrCl  
● Hb  
● Albumin  
● Total cholesterol  
● HCT |
| **Notes** | ● Information on the evaluated number was not provided although mortality was reported. Additional information was not available upon written correspondence at the time of drafting the review |

<table>
<thead>
<tr>
<th><strong>Lin 2003</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>● RCT</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>● CKD patients</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>● Cordyceps + conventional treatment versus Western medicine + conventional treatment</td>
</tr>
</tbody>
</table>
| **Outcomes** | ● SCr  
● Hb |
| **Notes** | ● Request was made to the authors to elicit information about numbers of participants recruited which was not available from the published report. No response received at the time of drafting the review |

CKD - chronic kidney disease; CrCl - creatinine clearance; Hb - haemoglobin; HCT - haematocrit; RCT - randomised controlled trial; SCr - serum creatinine
### Analysis of Outcomes

#### Comparison 1. Cordyceps + conventional treatment versus conventional treatment

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 CKD progression (%)</td>
<td>8</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>1.1 Unclear risk of bias subgroup</td>
<td>6</td>
<td>418</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.09 [0.99, 1.21]</td>
</tr>
<tr>
<td>1.2 High risk of bias subgroup</td>
<td>2</td>
<td>227</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.36 [1.17, 1.58]</td>
</tr>
<tr>
<td>2 Serum creatinine</td>
<td>15</td>
<td>1047</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td></td>
</tr>
<tr>
<td>2.1 Dialysis</td>
<td>1</td>
<td>60</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>32.88 [21.53, 44.23]</td>
</tr>
<tr>
<td>2.2 Non-dialysis (unclear risk of bias)</td>
<td>11</td>
<td>714</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-44.43 [-69.04, -19.83]</td>
</tr>
<tr>
<td>2.3 Non-dialysis (high risk of bias group)</td>
<td>3</td>
<td>273</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-118.77 [-148.81, -88.74]</td>
</tr>
<tr>
<td>3 Creatinine clearance</td>
<td>6</td>
<td>362</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>9.22 [3.10, 15.34]</td>
</tr>
<tr>
<td>3.1 Unclear risk of bias subgroup</td>
<td>5</td>
<td>295</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>10.78 [2.54, 19.02]</td>
</tr>
<tr>
<td>3.2 High risk of bias subgroup</td>
<td>1</td>
<td>67</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>5.09 [0.56, 9.62]</td>
</tr>
<tr>
<td>4 Proteinuria</td>
<td>4</td>
<td>211</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-0.15 [-0.24, -0.05]</td>
</tr>
<tr>
<td>5 Systolic BP</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>6 Diastolic BP</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>7 Haemoglobin</td>
<td>5</td>
<td>283</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>10.40 [6.22, 14.58]</td>
</tr>
<tr>
<td>7.1 Dialysis</td>
<td>1</td>
<td>60</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>19.0 [14.44, 23.56]</td>
</tr>
<tr>
<td>7.2 Non-dialysis (unclear risk of bias)</td>
<td>3</td>
<td>173</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>8.20 [2.39, 14.01]</td>
</tr>
<tr>
<td>7.3 Non-dialysis (high risk of bias)</td>
<td>1</td>
<td>50</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>7.70 [2.61, 12.79]</td>
</tr>
<tr>
<td>8 Haematocrit</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>9 Serum albumin</td>
<td>4</td>
<td>323</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>3.52 [2.79, 4.24]</td>
</tr>
<tr>
<td>9.1 Dialysis</td>
<td>1</td>
<td>65</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>3.08 [1.44, 4.72]</td>
</tr>
<tr>
<td>9.2 Non-dialysis</td>
<td>3</td>
<td>258</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>3.62 [2.81, 4.43]</td>
</tr>
<tr>
<td>10 Total cholesterol</td>
<td>2</td>
<td>198</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-0.41 [-0.82, 0.00]</td>
</tr>
<tr>
<td>11 Calcium</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>12 Phosphorus</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>
## Comparison 2. Cordyceps + conventional treatment versus Western medicine + conventional treatment

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 CKD progression (%)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>2 Serum creatinine</td>
<td>3</td>
<td>195</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-37.49 [-101.43, 26.44]</td>
</tr>
<tr>
<td>3 Creatinine clearance</td>
<td>3</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>4 Proteinuria</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>5 Haemoglobin</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>6 Haematocrit</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>7 Serum albumin</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>8 Total cholesterol</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>

## Comparison 3. Cordyceps + TCM versus TCM

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Serum creatinine</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>2 Proteinuria</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>3 Haemoglobin</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>
Analysis 1.1. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 1 CKD progression (%).

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 1 Cordyceps + conventional treatment versus conventional treatment

Outcome: 1 CKD progression (%)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Risk Ratio MHC, Random 95% CI</th>
<th>Weight</th>
<th>Risk Ratio MHC, Random 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Unclear risk of bias subgroup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang 2005a</td>
<td>26/30</td>
<td>22/30</td>
<td>13.2 % 1.18 [0.91, 1.53]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liu 2006a</td>
<td>30/34</td>
<td>22/32</td>
<td>12.7 % 1.28 [0.99, 1.67]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pan 2007</td>
<td>28/32</td>
<td>25/32</td>
<td>16.4 % 1.12 [0.89, 1.40]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liu 2007a</td>
<td>60/68</td>
<td>58/64</td>
<td>37.5 % 0.97 [0.87, 1.09]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu 2007</td>
<td>20/24</td>
<td>17/22</td>
<td>10.9 % 1.08 [0.81, 1.44]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guo 2009</td>
<td>21/25</td>
<td>17/25</td>
<td>9.2 % 1.24 [0.90, 1.70]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>213</td>
<td>205</td>
<td>100.0 % 1.09 [0.99, 1.21]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events: 185 (Cordyceps), 161 (Conventional medicine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.00; Chi^2 = 6.49, df = 5 (P = 0.26); I^2 = 23%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.70 (P = 0.088)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 High risk of bias subgroup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu 2003</td>
<td>69/78</td>
<td>54/82</td>
<td>75.7 % 1.34 [1.13, 1.60]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chen 2006a</td>
<td>31/36</td>
<td>19/31</td>
<td>24.3 % 1.40 [1.03, 1.91]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>114</td>
<td>113</td>
<td>100.0 % 1.36 [1.17, 1.58]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events: 100 (Cordyceps), 73 (Conventional medicine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0; Chi^2 = 3.93, df = 1 (P = 0.80); I^2 = 0.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.93 (P = 0.000083)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi^2 = 5.27, df = 1 (P = 0.02), I^2 = 81%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5 0.7 1 1.5 2</td>
<td>Favours control</td>
<td>Favours Cordyceps</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Analysis 1.2. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 2 Serum creatinine.

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 1 Cordyceps + conventional treatment versus conventional treatment

Outcome: 2 Serum creatinine

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD) [mol/L]</td>
<td>N</td>
<td>Mean(SD) [mol/L]</td>
<td>IV/Random,95% CI</td>
</tr>
<tr>
<td>1 Dialysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sun 1999</td>
<td>30</td>
<td>397.13 (26.53)</td>
<td>30</td>
<td>364.25 (17.39)</td>
<td>9.0 %</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>30</td>
<td></td>
<td>30</td>
<td>-9.0 %</td>
<td>32.88 [ 21.53, 44.23 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 5.68 (P < 0.00001)

2 Non-dialysis (unclear risk of bias)

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang 1999b</td>
<td>29</td>
<td>351.7 (137.3)</td>
<td>24</td>
<td>376.9 (159.4)</td>
<td>5.6 %</td>
</tr>
<tr>
<td>Wei 2004</td>
<td>30</td>
<td>180.02 (125.36)</td>
<td>30</td>
<td>248.38 (141.01)</td>
<td>6.3 %</td>
</tr>
<tr>
<td>Xu 2004</td>
<td>42</td>
<td>608.3 (402.1)</td>
<td>40</td>
<td>735.8 (498.3)</td>
<td>1.9 %</td>
</tr>
<tr>
<td>Wang 2005a</td>
<td>30</td>
<td>201.08 (38.99)</td>
<td>30</td>
<td>285.11 (44.21)</td>
<td>8.7 %</td>
</tr>
<tr>
<td>Liu 2006a</td>
<td>34</td>
<td>268.7 (103.6)</td>
<td>32</td>
<td>345.2 (109.5)</td>
<td>7.3 %</td>
</tr>
<tr>
<td>Pan 2007</td>
<td>32</td>
<td>408.2 (238.1)</td>
<td>32</td>
<td>508.7 (251.4)</td>
<td>3.8 %</td>
</tr>
<tr>
<td>Wu 2007</td>
<td>24</td>
<td>419.67 (241.21)</td>
<td>22</td>
<td>401.43 (158.77)</td>
<td>3.9 %</td>
</tr>
<tr>
<td>Liu 2007a</td>
<td>68</td>
<td>200.36 (95.78)</td>
<td>64</td>
<td>203.45 (96.43)</td>
<td>8.3 %</td>
</tr>
<tr>
<td>Hu 2008</td>
<td>15</td>
<td>254.65 (78.32)</td>
<td>15</td>
<td>306.84 (84.22)</td>
<td>6.9 %</td>
</tr>
<tr>
<td>Zhang 2009</td>
<td>28</td>
<td>198.62 (33.03)</td>
<td>28</td>
<td>204.59 (30.4)</td>
<td>8.9 %</td>
</tr>
<tr>
<td>Fu 2009</td>
<td>35</td>
<td>95.2 (29.5)</td>
<td>30</td>
<td>140.6 (30.1)</td>
<td>8.9 %</td>
</tr>
</tbody>
</table>

Subtotal (95% CI) 367 347 500 44.43 [-69.04, -19.83 ]

Heterogeneity: Tau² = 929.54; Chi² = 43.79, df = 10 (P<0.00001); I² =77%

Test for overall effect: Z = 3.54 (P = 0.00040)

3 Non-dialysis (high risk of bias group)

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yu 2003</td>
<td>78</td>
<td>321.15 (98.06)</td>
<td>78</td>
<td>455.32 (154.15)</td>
<td>7.9 %</td>
</tr>
<tr>
<td>Chen 2006a</td>
<td>36</td>
<td>290.68 (90.37)</td>
<td>31</td>
<td>379.85 (126.79)</td>
<td>7.1 %</td>
</tr>
<tr>
<td>Guo 2009</td>
<td>25</td>
<td>614.4 (109.7)</td>
<td>25</td>
<td>739.6 (176.2)</td>
<td>5.6 %</td>
</tr>
</tbody>
</table>

Subtotal (95% CI) 139 134 500 20.6 % -118.77 [-148.81, -88.74 ]

Heterogeneity: Tau² = 0.0; Chi² = 1.75, df = 2 (P = 0.42); I² =0.0%

Test for overall effect: Z = 7.75 (P < 0.00001)

---

Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review) 49

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## Analysis 1.3. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 3 Creatinine clearance.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 1 Cordyceps + conventional treatment versus conventional treatment

**Outcome:** 3 Creatinine clearance

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)[mL/min]</td>
<td>N Mean(SD)[mL/min]</td>
<td>IV,Random,95% CI</td>
<td></td>
<td>IV,Random,95% CI</td>
</tr>
<tr>
<td></td>
<td>N [mol/L]</td>
<td>N [mol/L]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FU 2009</td>
<td>35 90.4 (26.4)</td>
<td>30 50 (28.6)</td>
<td>10.9 %</td>
<td>40.40 [26.94, 53.86]</td>
<td></td>
</tr>
<tr>
<td>Pan 2007</td>
<td>32 31.26 (7.5)</td>
<td>32 23.51 (7.3)</td>
<td>21.5 %</td>
<td>7.75 [4.12, 11.38]</td>
<td></td>
</tr>
<tr>
<td>Wang 2005a</td>
<td>30 32.18 (16.94)</td>
<td>30 30.18 (18.94)</td>
<td>15.4 %</td>
<td>2.00 [-7.09, 11.09]</td>
<td></td>
</tr>
<tr>
<td>Wei 2004</td>
<td>30 34 (12.37)</td>
<td>30 28.25 (9.27)</td>
<td>19.5 %</td>
<td>5.75 [0.22, 11.28]</td>
<td></td>
</tr>
<tr>
<td>Wu 2007</td>
<td>24 18.52 (15.94)</td>
<td>22 13.12 (25.12)</td>
<td>12.0 %</td>
<td>5.40 [-6.88, 17.68]</td>
<td></td>
</tr>
</tbody>
</table>

**Subtotal (95% CI)** 151 144

- Heterogeneity: Tau² = 67.70, Chi² = 24.75, df = 4 (P = 0.00006); I² =84%
- Test for overall effect: Z = 2.56 (P = 0.010)

<table>
<thead>
<tr>
<th>2 High risk of bias subgroup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen 2006a</td>
</tr>
</tbody>
</table>

**Subtotal (95% CI)** 36 31

- Heterogeneity: not applicable

---

Continued...
### Analysis 1.4. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 4 Proteinuria.

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 1 Cordyceps + conventional treatment versus conventional treatment

Outcome: 4 Proteinuria

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Mean(SD)[g/24 h]</td>
<td>N</td>
<td>Mean(SD)[g/24 h]</td>
<td>IV,Random,95% CI</td>
<td>IV,Random,95% CI</td>
</tr>
<tr>
<td>Fu 2009</td>
<td>35 0.4256 (0.0028)</td>
<td>30 0.56 (0.1908)</td>
<td>-0.13 [-0.20, -0.07]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hu 2008</td>
<td>15 1.84 (0.77)</td>
<td>15 2.04 (0.9)</td>
<td>2.5 % -0.20 [-0.80, 0.40]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shi 2009</td>
<td>32 1.1 (0.8)</td>
<td>28 1.6 (0.8)</td>
<td>5.3 % -0.50 [-0.91, -0.09]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang 2009</td>
<td>28 1.52 (0.54)</td>
<td>28 1.6 (0.47)</td>
<td>11.8 % -0.08 [-0.35, 0.19]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>110</strong></td>
<td><strong>101</strong></td>
<td><strong>100.0 % -0.15 [-0.24, -0.05]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 3.28, df = 3 (P = 0.35); I² =9%
Test for overall effect: Z = 3.07 (P = 0.0021)
Test for subgroup differences: Not applicable
Analysis 1.5. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 5 Systolic BP.

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 1 Cordyceps + conventional treatment versus conventional treatment

Outcome: 5 Systolic BP

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[mm Hg]</td>
<td>N</td>
<td>Mean(SD)[mm Hg]</td>
</tr>
<tr>
<td>Fu 2009</td>
<td>35</td>
<td>128.3 (9.9)</td>
<td>30</td>
<td>129.7 (8.6)</td>
</tr>
</tbody>
</table>

Favours Cordyceps Favours control

Analysis 1.6. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 6 Diastolic BP.

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 1 Cordyceps + conventional treatment versus conventional treatment

Outcome: 6 Diastolic BP

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[mm Hg]</td>
<td>N</td>
<td>Mean(SD)[mm Hg]</td>
</tr>
<tr>
<td>Fu 2009</td>
<td>35</td>
<td>78.2 (8.5)</td>
<td>30</td>
<td>77.4 (7.9)</td>
</tr>
</tbody>
</table>

Favours Cordyceps Favours control
### Analysis 1.7. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 7 Haemoglobin.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 1 Cordyceps + conventional treatment versus conventional treatment

**Outcome:** 7 Haemoglobin

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Random,95% CI</td>
<td>IV,Random,95% CI</td>
<td></td>
</tr>
<tr>
<td><strong>1 Dialysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sun 1999</td>
<td>30 97.8 (9.2)</td>
<td>30 78.8 (8.8)</td>
<td>20.6 % 19.00 [ 14.44, 23.56 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>30</strong></td>
<td><strong>30</strong></td>
<td><strong>20.6 % 19.00 [ 14.44, 23.56 ]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 8.17 (P &lt; 0.00001)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>2 Non-dialysis (unclear risk of bias)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang 1999b</td>
<td>29 87.2 (0.44)</td>
<td>24 75.2 (0.37)</td>
<td>27.3 % 12.00 [ 11.78, 12.22 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wei 2004</td>
<td>30 107.35 (12.19)</td>
<td>30 103.63 (11.22)</td>
<td>17.6 % 3.72 [-2.21, 9.65 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang 2005a</td>
<td>30 87.69 (17.36)</td>
<td>30 80.69 (10.36)</td>
<td>15.0 % 7.00 [-0.23, 14.23 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>89</strong></td>
<td><strong>84</strong></td>
<td><strong>59.9 % 8.20 [ 2.39, 14.01 ]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 20.04; Chi² = 9.31, df = 2 (P = 0.0056); I² = 79%</td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 2.77 (P = 0.0056)</td>
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<td></td>
</tr>
<tr>
<td><strong>3 Non-dialysis (high risk of bias)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guo 2009 (1)</td>
<td>25 94.3 (9.8)</td>
<td>25 86.6 (8.5)</td>
<td>19.4 % 7.70 [ 2.61, 12.79 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>25</strong></td>
<td><strong>25</strong></td>
<td><strong>19.4 % 7.70 [ 2.61, 12.79 ]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 2.97 (P = 0.0030)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>144</strong></td>
<td><strong>139</strong></td>
<td><strong>100.0 % 10.40 [ 6.22, 14.58 ]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 16.66; Chi² = 21.14, df = 4 (P = 0.00030); I² = 81%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 4.87 (P &lt; 0.00001)</td>
<td></td>
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</tr>
<tr>
<td>Test for subgroup differences: Chi² = 13.34, df = 2 (P = 0.00), I² = 85%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Why is this study excluded?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Analysis 1.8. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 8 Haematocrit.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 1 Cordyceps + conventional treatment versus conventional treatment

**Outcome:** 8 Haematocrit

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)[%]</td>
<td>N Mean(SD)[%]</td>
<td>IV,Random,95% CI</td>
<td>IV,Random,95% CI</td>
</tr>
<tr>
<td>Wei 2004</td>
<td>30 34.28 (4.68)</td>
<td>30 30.79 (3.38)</td>
<td>3.49 [ 1.42, 5.56 ]</td>
<td>-10 -5 0 5 10</td>
</tr>
</tbody>
</table>

-10 -5 0 5 10
Favours control Favours Cordyceps

### Analysis 1.9. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 9 Serum albumin.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 1 Cordyceps + conventional treatment versus conventional treatment

**Outcome:** 9 Serum albumin

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)[g/L]</td>
<td>N Mean(SD)[g/L]</td>
<td>IV,Random,95% CI</td>
<td>IV,Random,95% CI</td>
</tr>
<tr>
<td>1 Dialysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu 2002</td>
<td>35 38.31 (3.47)</td>
<td>30 35.23 (3.27)</td>
<td>19.5 % 3.08 [ 1.44, 4.72 ]</td>
<td>-10 -5 0 5 10</td>
</tr>
<tr>
<td>Liu 2006a</td>
<td>34 35.26 (2.44)</td>
<td>32 31.32 (3.97)</td>
<td>20.5 % 3.94 [ 2.34, 5.54 ]</td>
<td></td>
</tr>
<tr>
<td>Liu 2007a</td>
<td>68 35.1 (3.03)</td>
<td>64 31.28 (3.85)</td>
<td>37.3 % 3.82 [ 2.63, 5.01 ]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>132 35</td>
<td>126</td>
<td>80.5 % 3.62 [ 2.81, 4.43 ]</td>
<td></td>
</tr>
</tbody>
</table>

(Continued...)
### Study or subgroup Cordyceps Conventional medicine

<table>
<thead>
<tr>
<th>N</th>
<th>Mean(SD)[g/L]</th>
<th>N</th>
<th>Mean(SD)[g/L]</th>
<th>IV, Random, 95% CI</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Heterogeneity: $\tau^2 = 0.0$, $\chi^2 = 0.88$, $df = 2$ ($P = 0.64$); $I^2 = 0.0$
- Test for overall effect: $Z = 8.79$ ($P < 0.00001$)

**Total (95% CI)**: 156

- Heterogeneity: $\tau^2 = 0.0$, $\chi^2 = 0.88$, $df = 2$ ($P = 0.64$); $I^2 = 0.0$
- Test for overall effect: $Z = 8.79$ ($P < 0.00001$)

Test for subgroup differences: $\chi^2 = 0.34$, $df = 1$ ($P = 0.56$); $I^2 = 0.0$

#### Analysis 1.10. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 10 Total cholesterol.

**Review**: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison**: 1 Cordyceps + conventional treatment versus conventional treatment

**Outcome**: 10 Total cholesterol

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)[mmol/L]</td>
<td>N Mean(SD)[mmol/L]</td>
<td>IV, Random, 95% CI</td>
<td>IV, Random, 95% CI</td>
<td></td>
</tr>
<tr>
<td>Liu 2006a</td>
<td>34 5.13 (1.42)</td>
<td>32 5.48 (1.53)</td>
<td>33.3 %</td>
<td>-0.35 [ -1.06, 0.36 ]</td>
<td></td>
</tr>
<tr>
<td>Liu 2007a</td>
<td>68 5.52 (1.42)</td>
<td>64 5.96 (1.53)</td>
<td>66.7 %</td>
<td>-0.44 [ -0.94, 0.06 ]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>102 96</td>
<td></td>
<td>100.0 %</td>
<td>-0.41 [ -0.82, 0.00 ]</td>
<td></td>
</tr>
</tbody>
</table>

- Heterogeneity: $\tau^2 = 0.0$, $\chi^2 = 0.04$, $df = 1$ ($P = 0.84$); $I^2 = 0.0$
- Test for overall effect: $Z = 1.95$ ($P = 0.051$)
- Test for subgroup differences: Not applicable
### Analysis 1.11. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 11 Calcium.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 1 Cordyceps + conventional treatment versus conventional treatment

**Outcome:** 11 Calcium

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Conventional medicine</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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<td></td>
<td>N</td>
<td>Mean(SD)[mmol/L]</td>
<td>IV, Random, 95% CI</td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>Liu 2006a</td>
<td>34</td>
<td>2.21 (0.23)</td>
<td>-0.15 [ 0.04, 0.26 ]</td>
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</tr>
</tbody>
</table>

-0.5 -0.25 0 0.25 0.5
Favours control Favours Cordyceps

### Analysis 1.12. Comparison 1 Cordyceps + conventional treatment versus conventional treatment, Outcome 12 Phosphorus.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 1 Cordyceps + conventional treatment versus conventional treatment

**Outcome:** 12 Phosphorus

<table>
<thead>
<tr>
<th>Study or subgroup</th>
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<th>Mean Difference</th>
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<td>N</td>
<td>Mean(SD)[mmol/L]</td>
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<td>IV, Random, 95% CI</td>
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<tr>
<td>Liu 2006a</td>
<td>34</td>
<td>1.52 (0.12)</td>
<td>-0.11 [-0.18, -0.04]</td>
<td></td>
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</table>

-0.2 -0.1 0 0.1 0.2
Favours Cordyceps Favours control
**Analysis 2.1. Comparison 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment, Outcome 1 CKD progression (%).**

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment

Outcome: 1 CKD progression (%)

<table>
<thead>
<tr>
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<th>Cordyceps</th>
<th>Control</th>
<th>Risk Ratio M, Random, 95% CI</th>
<th>Risk Ratio M, Random, 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Huang 2008</td>
<td>34/43</td>
<td>37/43</td>
<td>0.92 [0.76, 1.12]</td>
<td></td>
</tr>
</tbody>
</table>

Analysis 2.2. Comparison 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment, Outcome 2 Serum creatinine.

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment

Outcome: 2 Serum creatinine

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Control</th>
<th>Mean Difference, Weight</th>
<th>Mean Difference, Weight</th>
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</thead>
<tbody>
<tr>
<td>Gao 2007</td>
<td>15 390.65 (108.91)</td>
<td>12 506.72 (132.53)</td>
<td>24.2 % -116.07 [ -209.13, -23.01 ]</td>
<td></td>
</tr>
<tr>
<td>Huang 2008</td>
<td>43 335.79 (153.76)</td>
<td>43 310.65 (147.52)</td>
<td>33.2 % 25.14 [ -38.55, 88.83 ]</td>
<td></td>
</tr>
<tr>
<td>Jin 2004</td>
<td>41 251.31 (94.9)</td>
<td>41 293.03 (70.93)</td>
<td>42.7 % -41.72 [ -77.99, -5.45 ]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>99 96</td>
<td>100.0 % -37.49 [ -101.43, 26.44 ]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 2151.02; Chi² = 6.47, df = 2 (P = 0.04); I² = 69%

Test for overall effect: Z = 1.15 (P = 0.25)

Test for subgroup differences: Not applicable
### Analysis 2.3. Comparison 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment, Outcome 3 Creatinine clearance.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment

**Outcome:** 3 Creatinine clearance

<table>
<thead>
<tr>
<th>Study or subgroup</th>
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<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[mL/min]</td>
<td>N</td>
<td>Mean(SD)[mL/min]</td>
</tr>
<tr>
<td>Gao 2007</td>
<td>15</td>
<td>21.62 (5.02)</td>
<td>12</td>
<td>13.55 (2.28)</td>
</tr>
<tr>
<td>Huang 2008</td>
<td>43</td>
<td>17.25 (5.11)</td>
<td>43</td>
<td>18.86 (4.47)</td>
</tr>
<tr>
<td>Jin 2004</td>
<td>41</td>
<td>30.78 (13.51)</td>
<td>41</td>
<td>23.53 (8.92)</td>
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### Analysis 2.4. Comparison 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment, Outcome 4 Proteinuria.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment

**Outcome:** 4 Proteinuria

<table>
<thead>
<tr>
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<th>Mean Difference</th>
<th>Mean Difference</th>
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<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[g/24 h]</td>
<td>N</td>
<td>Mean(SD)[g/24 h]</td>
</tr>
<tr>
<td>Huang 2008</td>
<td>43</td>
<td>1.63 (0.86)</td>
<td>43</td>
<td>1.32 (0.88)</td>
</tr>
</tbody>
</table>

---

Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review)  
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### Analysis 2.5. Comparison 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment, Outcome 5 Haemoglobin.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment

**Outcome:** 5 Haemoglobin

<table>
<thead>
<tr>
<th>Study or subgroup</th>
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<th>Mean (SD) [g/L]</th>
<th>Control</th>
<th>Mean (SD) [g/L]</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td></td>
<td>N</td>
<td></td>
<td>IV, Random, 95% CI</td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>Jin 2004</td>
<td>41</td>
<td>122.33 (14.79)</td>
<td>41</td>
<td>101.03 (17.88)</td>
<td>-21.30 [14.20, 28.40]</td>
<td></td>
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</tbody>
</table>

-50 -25 0 25 50
Favours control Favours Cordyceps

---

### Analysis 2.6. Comparison 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment, Outcome 6 Haematocrit.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment

**Outcome:** 6 Haematocrit

<table>
<thead>
<tr>
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<th>Cordyceps</th>
<th>Mean (SD) [%]</th>
<th>Control</th>
<th>Mean (SD) [%]</th>
<th>Mean Difference</th>
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<td></td>
<td>N</td>
<td></td>
<td>IV, Random, 95% CI</td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>Jin 2004</td>
<td>41</td>
<td>33.92 (3.86)</td>
<td>41</td>
<td>30.32 (5.45)</td>
<td>3.60 [1.56, 5.64]</td>
<td></td>
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</table>

-10 -5 0 5 10
Favours control Favours Cordyceps
**Analysis 2.7. Comparison 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment, Outcome 7 Serum albumin.**

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment

Outcome: 7 Serum albumin

<table>
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<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)[g/L]</td>
<td>N Mean(SD)[g/L]</td>
<td>IV,Random,95% CI</td>
<td>IV,Random,95% CI</td>
</tr>
<tr>
<td>Jin 2004</td>
<td>41 33.13 (2.45)</td>
<td>41 28.78 (4.08)</td>
<td>4.35 [2.89, 5.81]</td>
<td></td>
</tr>
</tbody>
</table>

Favours control

Favours Cordyceps

**Analysis 2.8. Comparison 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment, Outcome 8 Total cholesterol.**

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 2 Cordyceps + conventional treatment versus Western medicine + conventional treatment

Outcome: 8 Total cholesterol

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)[mmol/L]</td>
<td>N Mean(SD)[mmol/L]</td>
<td>IV,Random,95% CI</td>
<td>IV,Random,95% CI</td>
</tr>
<tr>
<td>Jin 2004</td>
<td>41 6 (0.78)</td>
<td>41 6.1 (0.74)</td>
<td>-0.10 [-0.43, 0.23]</td>
<td></td>
</tr>
</tbody>
</table>

Favours Cordyceps

Favours control
Analysis 3.1. Comparison 3 Cordyceps + TCM versus TCM, Outcome 1 Serum creatinine.

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 3 Cordyceps + TCM versus TCM

Outcome: 1 Serum creatinine

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>TCM</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[mol/L]</td>
<td>N</td>
<td>Mean(SD)[mol/L]</td>
</tr>
<tr>
<td>Yan 2005a</td>
<td>33</td>
<td>104 (21.2)</td>
<td>32</td>
<td>128 (71.8)</td>
</tr>
</tbody>
</table>

Favours Cordyceps

Analysis 3.2. Comparison 3 Cordyceps + TCM versus TCM, Outcome 2 Proteinuria.

Review: Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

Comparison: 3 Cordyceps + TCM versus TCM

Outcome: 2 Proteinuria

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>TCM</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[g/24 h]</td>
<td>N</td>
<td>Mean(SD)[g/24 h]</td>
</tr>
<tr>
<td>Yan 2005a</td>
<td>33</td>
<td>0.62 (0.38)</td>
<td>32</td>
<td>1.21 (1.08)</td>
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</tbody>
</table>

Favours Cordyceps
### Analysis 3.3. Comparison 3 Cordyceps + TCM versus TCM, Outcome 3 Haemoglobin.

**Review:** Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease

**Comparison:** 3 Cordyceps + TCM versus TCM

**Outcome:** 3 Haemoglobin

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Cordyceps</th>
<th>TCM</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[g/L]</td>
<td>N</td>
<td>Mean(SD)[g/L]</td>
</tr>
<tr>
<td>Yan 2005a</td>
<td>33</td>
<td>140 (17.8)</td>
<td>32</td>
<td>116 (12.1)</td>
</tr>
</tbody>
</table>

![Favours Cordyceps vs TCM for Haemoglobin](image)

### APPENDICES

#### Appendix 1. Electronic search strategies

<table>
<thead>
<tr>
<th>Database</th>
<th>Search terms</th>
</tr>
</thead>
</table>
| CENTRAL  | 1. MeSH descriptor Cordyceps, this term only  
2. (cordyceps sinensis*) in Clinical Trials  
3. (cordyceps*) in Clinical Trials  
4. (dongchongxiacao) or (dong chong xia cao) or (dongchong xiacao) in Clinical Trials  
5. (chongcao*) or chong cao* in Clinical Trials  
6. (1 OR 2 OR 3 OR 4 OR 5)  
7. MeSH descriptor Renal Dialysis explode all trees  
8. (hemodialysis) or (haemodialysis) in Clinical Trials  
9. (hemofiltration) or (haemofiltration) in Clinical Trials  
10. (hemodiafiltration) or (haemodiafiltration) in Clinical Trials  
11. (dialysis) in Clinical Trials  
12. (PD or CAPD or CCPD or APD) in Clinical Trials  
13. MeSH descriptor Renal Insufficiency, this term only  
14. MeSH descriptor Kidney Failure, this term only  
15. MeSH descriptor Renal Insufficiency, Chronic explode all trees  
16. MeSH descriptor Kidney Diseases, this term only  
17. MeSH descriptor Uremia, this term only  
18. “end-stage renal” or “end-stage kidney” or “endstage renal” or “endstage kidney” in Clinical Trials |
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<tr>
<td>19.</td>
<td>(ESRF or ESKF or ESRD or ESKD) in Clinical Trials</td>
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<td>“chronic kidney” or “chronic renal” in Clinical Trials</td>
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<td>21.</td>
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<td>22.</td>
<td>(ur?emi*) in Clinical Trials</td>
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**MEDLINE**

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<td>4.</td>
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<td>or/1-5</td>
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<td>Kidney Failure/</td>
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<td>exp Renal Insufficiency, Chronic/</td>
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**EMBASE**

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</tr>
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<td>5.</td>
<td>(Chongcao or chong cao).tw.</td>
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<tr>
<td>6.</td>
<td>or/1-5</td>
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<tr>
<td>7.</td>
<td>exp Renal Replacement Therapy/</td>
</tr>
<tr>
<td>8.</td>
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<td>9.</td>
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<td>Kidney Failure/</td>
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17. Uremia/
18. (chronic kidney or chronic renal).tw.
19. (CKF or CKD or CRF or CRD).tw.
20. (end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw.
21. (ESRF or ESKF or ESRD or ESKD).tw.
23. or/7-22
24. and/6,23

<table>
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| CBM               | 1. dong chong xia cao (Cordyceps) or chong cao (Cordycep in abbreviation)  
                    2. jin shui bao or bai he or zhi ling or ning xin bao or xin gan bao  
                    3. 1 or 2  
                    4. shen bing (Kidney disease) or shen shuai (kidney failure) or shen gong neng shuai jie  
                       (kidney function failure) or shen gong neng bu quan (kidney function insufficiency) or  
                       niao du zheng (uremia) or dan zhi xue zheng (azotemia)  
                    5. 3 and 4  
                    6. limit 5 to human                                         |
| CMCC              | 1. dong chong xia cao (Cordyceps) or chong cao (Cordycep in abbreviation)  
                    2. jin shui bao or bai he or zhi ling or ning xin bao or xin gan bao  
                    3. 1 or 2 |
| TCMLARS           | 1. dong chong xia cao (Cordyceps) or chong cao (Cordycep in abbreviation)  
                    2. jin shui bao or bai he or zhi ling or ning xin bao or xin gan bao  
                    3. 1 or 2  
                    4. shen bing (Kidney disease) or shen shuai (kidney failure) or shen gong neng shuai jie  
                       (kidney function failure) or shen gong neng bu quan (kidney function insufficiency) or  
                       niao du zheng (uremia) or dan zhi xue zheng (azotemia)  
                    5. 3 and 4  
                    6. limit 5 to human                                         |
| Chinese Dissertation Database | 1. dong chong xia cao (Cordyceps) or chong cao (Cordycep in abbreviation).abstract  
                               2. (jin shui bao or bai he or zhi ling or ning xin bao or xin gan bao).abstract  
                               3. 1 or 2  
                               4. (shen bing (Kidney disease) or shen shuai (kidney failure) or shen gong neng shuai jie  
                                  (kidney function failure) or shen gong neng bu quan (kidney function insufficiency) or  
                                  niao du zheng (uremia) or dan zhi xue zheng (azotemia)).abstract  
                               5. 3 and 4  
                               6. limit 5 to human                                         |
| CMAC              | 1. dong chong xia cao (Cordyceps) or chong cao (Cordycep in abbreviation)  
                    2. jin shui bao or bai he or zhi ling or ning xin bao or xin gan bao  
                    3. 1 or 2 |
| Index to Chinese Periodical Literature | 1. dong chong xia cao (Cordyceps) or chong cao (Cordycep in abbreviation)  
                                              2. shen gong neng (kidney function)  
                                              3. 1 and 2 |
### Appendix 2. Risk of bias assessment tool

<table>
<thead>
<tr>
<th>Potential source of bias</th>
<th>Assessment criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Random sequence generation</strong>&lt;br&gt;Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence</td>
<td><em>Low risk of bias:</em> Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random)&lt;br&gt;<em>High risk of bias:</em> Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention&lt;br&gt;<em>Unclear:</em> Insufficient information about the sequence generation process to permit judgement</td>
</tr>
<tr>
<td><strong>Allocation concealment</strong>&lt;br&gt;Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment</td>
<td><em>Low risk of bias:</em> Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes)&lt;br&gt;<em>High risk of bias:</em> Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly un concealed procedure&lt;br&gt;<em>Unclear:</em> Randomisation stated but no information on method used is available</td>
</tr>
<tr>
<td><strong>Blinding of participants and personnel</strong>&lt;br&gt;Performance bias due to knowledge of the allocated interventions by participants and personnel during the study</td>
<td><em>Low risk of bias:</em> No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken&lt;br&gt;<em>High risk of bias:</em> No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding&lt;br&gt;<em>Unclear:</em> Insufficient information to permit judgement</td>
</tr>
<tr>
<td><strong>Blinding of outcome assessment</strong></td>
<td>Low risk of bias: No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>High risk of bias: No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.</td>
<td></td>
</tr>
<tr>
<td>Unclear: Insufficient information to permit judgement.</td>
<td></td>
</tr>
</tbody>
</table>

| **Incomplete outcome data** | Low risk of bias: No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods. |
| High risk of bias: Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; ‘as-treated’ analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation. |
| Unclear: Insufficient information to permit judgement. |

| **Selective reporting** | Low risk of bias: The study protocol is available and all of the study’s pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon). |
**C O N T R I B U T I O N S O F A U T H O R S**

1. Draft protocol: HWZ, ZXL
2. Study selection: HWZ, FC, YFH
3. Extract data from studies: HWZ, FC, YFH
4. Enter data into RevMan/check data entry: HWZ, FC
5. Carry out the analysis: HWZ
6. Interpret the analysis: HWZ, ZXL, CL, LSC
7. Draft the final review: HWZ, ZXL
8. Disagreement resolution: ZXL,
9. Update the review: HWZ, ZXL
DECLARATIONS OF INTEREST
None known.

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- Yan Oi Tong, Hong Kong, China.

External sources
- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW
Diabetic nephropathy and primary nephrotic syndrome, which will be covered in other reviews (Feng 2013; Liu 2007), were excluded from this review after discussion with the Cochrane Renal Group.

INDEX TERMS

Medical Subject Headings (MeSH)
*Cordyceps; Creatine [metabolism]; Creatinine [blood]; Phytotherapy [*methods]; Proteinuria [prevention & control]; Randomized Controlled Trials as Topic; Renal Insufficiency, Chronic [*drug therapy; metabolism]

MeSH check words
Humans