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# REVIEW OF CHINESE HERBAL MEDICINE IN THE TREATMENT OF TYPE 2 DIABETES

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HONOURS DEGREE OF BACHELOR HEALTH SCIENCE



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# ABSTRACT

## Background

Diabetes affects 422 million people and directly causes 4.9 million deaths according to global report on diabetes in 2014. By 2030, diabetes will be the 7<sup>th</sup> leading cause of death based on WHO prediction. Type 2 diabetes accounts for 90% of people with diabetes around the world. Diabetes has been recognised since ancient times and Chinese herbal medicine has been used to treat diabetes for more than 2000 years in China. An increasing number of people all over the world are trying to manage type 2 diabetes with Chinese herbal medicine. Many clinical studies have been performed and published inside China that show Chinese herbal medicine can be an effective and safe treatment for type 2 diabetes, but there are very limited clinical studies available outside China in English that report type 2 diabetes treatment with Chinese herbal medicine.

## Objectives

To report the effectiveness and safety and evaluate the quality of the evidence of Chinese herbal medicine for the treatment of patients with type 2 diabetes mellitus.

## Search methods

The following resources were searched for the identification of trials from 2004 to 2015: The Cochrane Library (Wiley Online Library), Web of Science, PubMed, Google Scholar, The University of Adelaide Library Research, China Academic Journals Full-text Database (Basic Search) and Heart & diabetes Institute (Baker IDI). National Resource Centre for Chinese Materia Medica and China Academy of Chinese Medical Sciences have been contacted for relevant studies. Reference lists of relevant trials and reviews were searched for potential eligible studies. Authors of relevant identified studies and experts were contacted to obtain additional references.

## Selection criteria

Randomised controlled clinical trials with full text in English or Chinese and a minimum treatment period of eight weeks, comparing Chinese herbal medicine (alone or combined with other pharmaceuticals or other interventions) with other pharmaceutical, placebo, or other interventions (mainly diet control and exercise therapy) as treatments for type 2 diabetes. Quasi-randomised controlled trials, cluster-randomised trials and other non-randomised controlled trials such as cohort studies, case control studies, case series and case reports were not eligible for inclusion in this review. Pre-diabetes, type 2 diabetes complications, study of herb extracts, study of Chinese herb combined with acupuncture and tuina

treatment, comparison of different forms of Chinese herbs and study duration less than eight weeks were also excluded in this review.

## **Data collection and analysis**

All studies for inclusion were assessed and extracted in Characteristics of included studies by using standard data extraction templates. Risks of bias were evaluated based on the *Cochrane Handbook for Systematic Review of Intervention*. The key criteria of random sequence generation, allocation concealment, blinding of participants, incomplete outcome data, and selection reporting and other bias in the trials were assessed. Any questions were resolved by discussion with two research supervisors and/ or referring back to the original article.

## **Main results**

Fifty-eight randomized clinical trials (involving 6637 type 2 diabetes patients) were included in this review. The trials compared Chinese herbal medicines either in combination with other pharmaceuticals (forty-two trials) or alone (ten trials) versus other pharmaceuticals alone or placebo (four trials). Two studies compared among three groups, one of the studies compared Chinese herbal medicine combined with other pharmaceuticals versus Chinese herbal medicine alone versus other pharmaceuticals alone. Another study compared Chinese herbal medicine alone versus pharmaceutical alone versus other interventions (mainly diet control and exercise therapy).

Most trials tested various Chinese herbal medicines including individual prescriptions modified from classical formulae. Three trials only tested a single Chinese herb Huanglian (*Coptidis Rhizoma*) or Wuweizi (*Fructus Schisandrae*). Pharmaceuticals included commonly used hypoglycemic Western medicines such as metformin, sulfonylurea (glibenclamide, glimepiride, and glipizide), alpha-glucosidase inhibitor (acarbose), thiazolidinediones (rosiglitazone), and insulin etc. Other interventions mainly included diet control, exercise therapy, diabetes health education and other life style changes.

The overall methodological quality in included studies was unsatisfactory. The studies were well-designed, but most studies were not reported correctly, affecting the quality of evidence. Thus, the 'Risk of bias' domains were assessed as unclear risk in about two-thirds of the included trials due to insufficient detail to allow a definite judgement.

The most valuable and important comparison to evaluate the treatment of type 2 diabetes with Chinese herbal medicine is with placebo, and only four trials were available in this review. Three studies were performed in multiple centres (2, 10 and 20) with one study including one centre outside of China. One study were randomised controlled trials with two arms.

Based on available information, Chinese herbal medicines used alone or in combination with other Western hypoglycemic agents or lifestyle changes were associated with a decrease of glycated haemoglobin and blood glucose (FBG & 2h PBG), blood lipid profiles (TC, TG, LDL-C & HDL-C), weight or body mass index (BMI) and TCM clinical symptom score (which is a method of evaluating the symptoms of diabetes including dry throat and mouth, lack of strength, polyphagia, polydipsia, polyuria, shortness of breath, vexing heat in the chest, palms and soles, palpitation, insomnia etc.). A combination of Chinese herbal medicines with either other pharmaceuticals or lifestyle interventions was also associated with enhancing the therapeutic effects of other pharmaceutical by improving insulin sensitivity (HOMA-IR or ISI) in the treatment of type 2 diabetes. However, the overall evidence for effectiveness was insufficient because the studies were not reported correctly and the quality of literature in included studies was unsatisfactory.

Less than half of the studies (22/58) reported adverse effects of the interventions with only one-third of the studies (19/58) providing detailed information of safety assessment, and certainly had no safety assessment comparable with western medicines. So there was very limited safety data to conclude that Chinese herbal medicines were safe for type 2 diabetes treatment based on available information.

### **Author's conclusions**

The evidence to assess the effectiveness of Chinese herbal medicine for treating type 2 diabetes was acceptable in principle (fifty-eight trials with large sample size and forty-two with brief information of randomization), but the risks of bias (uniform bias due to patients selection exclusively from TCM hospitals or patients) in most of the included studies precluded a determination with respect to the effectiveness of Chinese herbal medicine. There was also insufficient data to evaluate safety issues in most of the trials if considering long-term adverse effects of Chinese herbal medicines. (Only less than half of the studies provide information of adverse effects and most of them were performed with short durations of 8 or 12 weeks).

There was limited data (four studies) to compare the effectiveness of Chinese medicine (either alone or in combination with Western medicine) with placebo. From available data, Chinese herbal medicines combined with pharmaceuticals or alone may be more effective than pharmaceutical alone at glycemic control, insulin resistance control and improvement of TCM clinical syndromes. However, the information provided by most of the studies was insufficient with respect to details to allow a definite judgement of risk of bias, which affected the evaluation of overall methodological qualities of included studies.

High quality studies (Long-term well-designed studies with multiple centres and large samples) with sufficient described details about randomisation methods and safety tests are required to compare

Chinese herbal medicine alone with pharmaceutical alone or placebo before any conclusions can be drawn about the effectiveness and safety of type 2 diabetes treatment with Chinese herbal medicines.

## **PLAIN LANGUAGE SUMMARY**

Type 2 diabetes is defined as a progressive disorder of declining insulin secretion and insulin action that lead to abnormal glucose metabolism and related metabolic derangements. 90% of people with diabetes have type 2 diabetes in the world.

Chinese herbal medicines have been used to treat diabetes for the last 2000 years in China. However, there is a lack of evidence to decide if Chinese herbal medicine is effective and safe for the treatment of type 2 diabetes from a western medicine standpoint.

This review identified fifty-eight randomised controlled trials involving 6637 participants with type 2 diabetes and lasting from eight weeks to one year (average 12 weeks). 132 different Chinese herbal medicines were examined. No data for death, diabetes complications and economic outcomes were evaluated. No serious adverse effects were reported. All but one trial did not record research limitations in the trial report.

Chinese herbal medicines appear to be effective at controlling blood sugar, insulin resistance and TCM clinical symptoms based on the available evidence. And many studies reported these evidence as major effectiveness outcomes of type 2 diabetes treatment with Chinese herbal medicine (Ji 2013; Zhang 2010; Lin 2014; Zhu 2016; Kong 2009 etc.). But the overall quality of the evidence is not good. Thus, based on available information, it is impossible to conclude from the included studies that Chinese herbal medicine is effective and safe for patients with type 2 diabetes. Well-designed long-term studies with large samples and multiple centres will be required to determine if Chinese herbal medicine treatment is safe and effective for type 2 diabetes.

## **BACKGROUND**

### **Description of the condition**

As a group of chronic metabolic diseases, diabetes mellitus was identified in 382 million people in 2013 and will affect almost 600 million by 2035 based on the prediction from the International Diabetes Foundation (Zimmet et al. 2014). About 5.8% of the world population were diagnosed with diabetes in 2014 (Krug 2016). Additionally 1.5 million deaths were estimated as a direct result of diabetes in 2012 (Krug 2016) and this number went up to 4.9 million in 2014 (Federation 2015). The World Health Organisation predicts that diabetes will be the 7<sup>th</sup> leading cause of death in 2030 (Mathers & Loncar 2006).

There are 2 main types of diabetes: type 1 diabetes and type 2 diabetes, and gestational diabetes is a third form of diabetes (Assal & Groop 1999). Type 2 diabetes, which is also called non-insulin-dependent or adult-onset diabetes, is described as a progressive condition where the body becomes resistant to insulin and is associated with multiple life style risk factors (Assal & Groop 1999).

Diabetes, predominantly type 2 diabetes, has been recognised as one of the enormous health-care challenges for the 21st century (Zimmet et al. 2014). 90% of the people with diabetes are recognised as type 2 diabetes around the world (Alberti & Zimmet 1998). There is also an increasing prevalence of type 2 diabetes in children, adolescents and young adults (Zimmet et al. 2014).

The economic burden of diabetes is remarkable and estimated as US \$376 billion which was 12% of all global health expenditure in 2010 (Zimmet et al. 2014). It is predicted to rise to between US \$490 to US \$893 billion by 2030 (Zimmet et al. 2014).

China has become the diabetes focus among all nations in the world, there were 98.4 million diabetes patients diagnosed in China in 2013 and this number will increase to 142.7 million in 2035 (Zimmet et al. 2014). 1.3 million Chinese with diabetes died in 2011 (Scully 2012). Direct health care expenditure of type 2 diabetes and its complications in China were estimated at US \$26 billion in 2007 and are expected to increase to US \$47.2 billion by 2030 (Zimmet et al. 2014).

## **Description of intervention**

There is no cure for type 2 diabetes and the management is through the control of blood glucose level by diet and exercise alone or in combination with medications. These include pharmaceuticals which are mainly western hypoglycemic drugs and complementary therapy. Traditional Chinese Medicine (TCM) is becoming more and more popular in western countries as an alternative intervention for type 2 diabetes (Youns, Hoheisel & Efferth 2010).

Diabetes mellitus has been recognized since antiquity and TCM herbs have been used to treat diabetes in China for more than 2000 years (Cheng 2000). Xiaoke (wasting-thirst) is an ancient term for diabetes, which was first recorded in *The Yellow Emperor's Classic of Internal Medicine* (Zhang et al. 2010). The recorded symptoms describe three increases and one decrease (polydipsia, polyphagia, polyuria and weight loss) and probably equates to the term "diabetes" in Western medicine (Zhang et al. 2010).

The treatment of diabetes with Chinese herbs is according to syndrome differentiation based on Qi (vital energy) and blood, Zang-Fu (five viscera and six bowels) and Ying-Yang (representing two opposite principles in the body) theory, which is different from Western medicine (Liu et al. 2002).

The commonly recognised patterns of type 2 diabetes are Qi and Yin (body fluids) deficiency, heat and stasis based on TCM theory. Thus frequently used herbal formulae can be categorised as four groups: Qi invigorating, Yin nourishing, heat clearing and stasis-reducing (improving blood circulation and kidney function) (Xie, Zhao & Zhang 2011). The most frequently prescribed herbs are Huang qi (Membranous milkvetch Root), Di huang (Mongolian Rehmannia Root), Zhi mu (Common Anemarrhena Rhizome) and Fu ling (India Bread) which respectively belong to the above groups (Xie, Zhao & Zhang 2011).

In China, government-owned health care delivery facilities are responsible for the treatment of most of patients and hospital delivery rates averaged 95% in 2011 (Eggleston et al. 2008; Meng et al.). The private sector has grown more quickly than the public sector since the mid-1990s, especially in rural areas (Eggleston et al. 2008). Diabetes in China is mainly managed in public health care sectors as in or out patient (Pan et al. 2008).

## **How TCM works**

TCM has its own theory for disease mechanism, diagnostic techniques and therapeutic principles. Generally speaking, diseases are considered as interaction between both internal and external causes and result in disturbance of Qi and blood, Zang-fu and imbalance between Yin and Yang (Bing & Hongcai 2010). The diagnostic system in TCM is four examinations which include inspection, listening/smelling, inquiry and palpation (Bing & Hongcai 2010). The tongue inspection and pulse palpation are two unique diagnostic techniques of TCM compared with Western medicine. The discussion of treatment is based on syndrome differentiation. Syndrome differentiation is an approach to make a comprehensive analysis of the data collected from the four examinations and decide the diagnosis based on TCM theory (Bing & Hongcai 2010). The major differentiating methods are developed as follow: eight guiding principles syndrome differentiation, disease-cause syndrome differentiation, syndrome differentiation of qi, blood and body fluids, Zang-fu organ syndrome differentiation, six-channel syndrome differentiation, defence-qi-nutrient-blood syndrome differentiation and triple-burner syndrome differentiation (Bing & Hongcai 2010). The therapeutic philosophy and goals of TCM are focused on the overall functional state of the patient, which can differ from those in Western medicine (Jiang 2005). Acupuncture & moxibustion, Chinese herbal medicine, Chinese dietary therapy, Chinese exercise therapy and manual therapy are the five major branches of TCM treatment methods (Bing & Hongcai 2010).

TCM usually concentrates on holistic treatment of the patient instead of focusing on treating a single disease (Jiang 2005). TCM formulae often contain large numbers of active ingredients which are suitable for regulating several crucial targets based on individualised treatment (Jiang 2005). Thus the action of



Chinese herbal medicine is different due to the therapeutic principles and goals of TCM differing from those in Western medicine. And the measurement of intended effects of TCM herbs is also complicated compared to Western medicine which primarily consists of single chemical compounds (Jiang 2005).

Although many of the anti-hyperglycemic components of TCM herbs are unknown, Chang and his colleagues summarized the chemistry and biological action of 40 extracts and compounds of plant origin (Chang et al. 2013). The mechanism of action of these herbal medicines involves improving insulin sensitivity, stimulating insulin secretion, protecting pancreatic islet cells and inhibiting intake of intestinal carbohydrates (Xie, Zhao & Zhang 2011).

### **Adverse effects of the intervention**

It has been widely acknowledged that medicinal herbs are normally nontoxic, while the consumption of herbs still has risk due to incorrect prescribing, overdose, improper preparation, erroneous substitution, adulteration with Western medicine, and inherent toxicity or contaminants (Youns, Hoheisel & Efferth 2010) (Zhao, Tong & Chan 2006). The toxicity related issues of herbal ingredients have been reported before (Youns, Hoheisel & Efferth 2010). Such as the most commonly seen TCM-dependent clinical complications that are interactions between TCM herbs and conventional drugs taken for diabetes (Youns, Hoheisel & Efferth 2010). Another source of clinical concern is contamination of TCM preparations with impurities, heavy metals or bacteria, and heavy metals have been reported before as a main poison associated with the use of TCM products (Youns, Hoheisel & Efferth 2010). Other causes of toxicity also involve intentional adulteration of TCM with bioactive additives such as corticosteroids, hormones, salicylates or antihistamines (Youns, Hoheisel & Efferth 2010). Improper prescription of herbal formulae and preparation of herbs, which relate to the regulation of herbal medicine and Chinese herbal medicine practitioners, is a cryptic underlying risk factor. For example, if energy invigorating herbs rather than heat clearing herbs are given to a diabetic patient with body heat pattern, the symptoms will get worse in this patient. Also it is both time and financially consuming to identify the active ingredients of herbs and their pharmacological mechanism of actions since one formula is often formed of many single herbs with single herb usually having multiple compounds, and the real efficacy and toxicity of herbal agents are difficult to test using the current evaluation paradigm for single chemical compounds (Jiang 2005).

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

An increasing number of type 2 diabetes patients choose to manage their condition with TCM without consideration of the potential toxic effects of medicinal herbs (Youns, Hoheisel & Efferth 2010). There are limited studies in the English literature discussing both effectiveness and patient safety for Chinese herbs used to treat type 2 diabetes. Finally although TCM herbs are regulated through Australian regulatory guidelines for complementary medicines (Administration 2015), the safety issues for TCM products on the market have actually not been appropriately addressed. TCM herbs are frequently available in grocery stores which are regulated as nutritional goods rather than therapeutic goods. How can safety of prescription and quality control be guaranteed if herbal medicine is not prescribed and distributed by registered TCM practitioner?

This review will evaluate the evidence for effectiveness and safety, explore toxic effects and quality control, and supply an English literature review of type 2 diabetes treatments with Chinese herbal medicines. In practice, it should also provide valuable information of study designs for future research into diabetes treatment with TCM herbal medicines. TGA regulation of TCM herbs are also recommended.

## **OBJECTIVES**

To report the effectiveness and safety of Chinese herbal medicine for the treatment of patients with type 2 diabetes mellitus, evaluate the quality of the evidence, suggest the research limitation and recommend future study direction.

## **METHODS**

### **Criteria for considering studies for this review**

#### **Types of studies**

Randomised controlled clinical trials with a minimum treatment period of eight weeks were included in this review. There were 58 trials which compared Chinese herbal medicines (alone or combined with other intervention or other pharmaceuticals) with other pharmaceuticals (alone or combined with other intervention), placebo or other intervention (including diet control, exercise therapy and diabetes education) as treatments for type 2 diabetes that were eligible for inclusion. 42 trials compared Chinese herbal medicine combined with other pharmaceuticals to other pharmaceuticals alone, 10 trials were

mainly Chinese herbal medicines compared with other pharmaceuticals alone, 4 trials were Chinese herbal medicines (alone or combined with other intervention or other pharmaceuticals) compared with placebo, 2 trials were comparisons among three groups (Chinese herbal medicine combined with other pharmaceuticals compared with Chinese herbal medicine and pharmaceuticals alone; pure Chinese herbal medicine compared with pharmaceuticals and dietary and exercise therapy). Only English and Chinese literature were used in this review.

### **Types of participants**

Adults diagnosed with type 2 diabetes mellitus based on documented diagnostic criteria were included. WHO 1999, WHO 2007, ADA 1999, ADA 2003, China 1994, China 2007 and China 2012 were used as the diagnostic criteria for type 2 diabetes in the inclusion criteria. There was no information regarding if the patients were newly diagnosed or had been given treatment before the entry into the trials. Only type 2 diabetes with Chinese herbal medicine treatment was studied. And only included participants with intervention duration was 8 weeks or over. Trials involving type 2 diabetes treatment with acupuncture or other TCM modalities (alone or combined with Chinese herbal medicine) were excluded.

### **Types of interventions**

Chinese herbal medicines including a compounded herbal formulae or individualized prescriptions by Chinese practitioner(s), patent herbs, single herb, Chinese herbal medicines combined with pharmacological intervention and other intervention including diet control, exercise therapy and diabetes education, regardless of the dose, method of dosing or duration of administration were compared with other treatments (mainly pharmacological intervention). The following comparisons were included:

1. Chinese herbal medicines combined with other pharmaceuticals versus other pharmaceuticals (mainly Western medicines).
2. Chinese herbal medicines alone versus other pharmaceuticals (mainly Western medicines).
3. Chinese herbal medicines (alone or combined with other interventions or other pharmaceuticals) versus placebo
4. Chinese herbal medicines combined with other pharmaceuticals versus Chinese herbal medicines versus pharmaceuticals alone
5. Chinese herbal medicines alone versus pharmaceuticals versus other interventions (including diabetes education, diet control and exercise therapy)

## **Types of outcome measures**

### **Primary outcomes**

Effectiveness of intervention

- Glycemic control: glycated haemoglobin levels (HbA1C) and blood glucose levels (FBG or 2hPBG)
- Blood lipid profiles: TC, TG, LDL-C, HDL-C
- Weight or body mass index (BMI)
- Insulin resistance levels (HOMA-IR or ISI)
- TCM clinical symptom score

Safety of intervention:

- Routine blood and urine test
- Liver and kidney function test
- ECG
- Clinical symptoms of adverse effects

### **Secondary outcomes**

Toxicity & quality control of TCM herbs

TGA regulation

Limitation of research & research findings in English literature

### **Timing of outcome assessment**

Possible effective treatment duration from 8 weeks to 1 year was included for analysis.

## **Search methods for identification of studies**

### **Electronic searches**

The following resources were searched to identify trials:

- The Cochrane Library (Wiley Online Library)
- Web of Science
- PubMed
- Google Scholar
- The University of Adelaide Library Research

- China Academic Journals Full-text Database (Basic Search)
- China Dissertation Database CDDDB
- China Knowledge Resource Integrated Database KNS
- Heart & diabetes Institute (Baker IDI)

Extensive and ongoing searches have been conducted in the above described databases from 2004 until 2015. Search results were screened and the full text of all relevant trials reports were identified by the author and two supervisors. Additional key words of relevance have been detected during any of electronic or other searches by modifying the search strategies to incorporate the search terms. Studies published in English and Chinese were included. For detailed search strategies please see Appendix 2.

### **Searching other resources**

#### **(1) Reference from published studies**

Reference lists of relevant trials and reviews were searched for potential eligible studies.

#### **(2) Personal communication**

National Resource Center for Chinese Materia Medica and China Academy of Chinese Medical Sciences have been contacted for relevant studies. Authors of relevant identified studies and experts were contacted to obtain additional references.

Unpublished literature were not searched.

## **Data collection and analysis**

### **Selection of studies**

The abstract, title or both section of every record retrieved have been scanned by author to determine the studies to be assessed further. All potentially relevant articles were investigated as full text:

- Compare Chinese herbal medicines (alone or combined with other intervention or other pharmaceuticals) with other pharmaceuticals (alone or combined with other intervention), placebo or other intervention (including diet control, exercise therapy and diabetes education) as treatment for type 2 diabetes
- Included patients with type 2 diabetes mellitus; excluded pre-type2 diabetes, diabetes complications.

- Exclude herb extracts, Chinese herbal medicine combined with acupuncture and tuina treatment, comparison of different forms of Chinese herbs
- Assessed more than one relevant outcome
- Used random allocation to the comparison groups
- Study duration no less than 8 weeks

Where information was ambiguous or missing in the article or there was difference of opinion, the decision to include the trial was resolved by consensus with two supervisors. Authors of relevant identified studies and experts in relevant field were contact in order to obtain additional references. Also regulation of reviewed Chinese herbal medicines – National Resource Centre for Chinese Materia Medica and China Academy of Chinese Medical Science were contacted in order to retrieve information on published herb trials.

### **Data extraction and management**

For studies that fulfilled the inclusion criteria, data of relevant population, intervention and outcome characteristics were abstracted by using standard data extraction templates (for details see Characteristics of included studies), any questions were resolved by discussion, referring back to the original article. When necessary, information was sought from the authors of the primary studies.

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

The risk of bias for each study was assessed by the author using the criteria outlined in the Cochrane handbook for Systematic Review of Interventions (Higgins 2008). Any uncertainty was resolved by discussion with two supervisors. The details are listed in *Characteristics of included studies*.

### **Measures of treatment effect**

#### **Unit of analysis issues**

Only one multi-arm trial (Ji 2013 two arms, Chinese herbal medicine combined with pharmaceutical and pharmaceutical alone were assigned to drug naïve group and metformin group separately) was included and is described in the *Characteristics of included studies* table. The comparisons were carried out between each arm and no any subgroup analysis or pair-wise comparisons were undertaken.

## RESULTS

### Description of studies

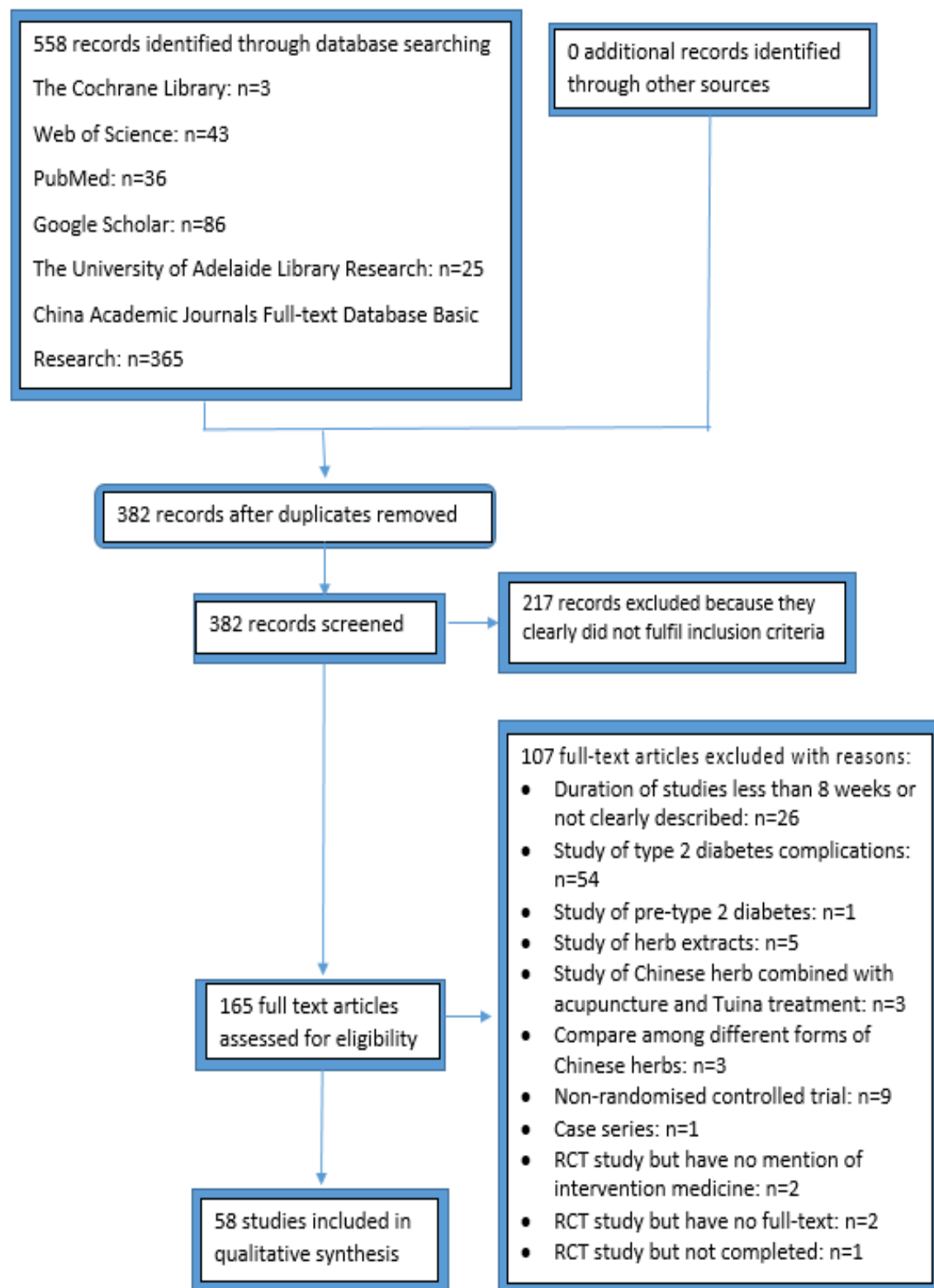
Five hundred fifty-eight clinical trials of type 2 diabetes with Chinese herbal medicine treatment were identified and one hundred sixty-five full text articles were eligible for detailed review. Fifty-eight studies were included and one hundred and seven studies were excluded.

See “Characteristics of included studies” and “Characteristics of excluded studies” for more information.

### Results of the search

558 references were identified by initial database searching up to 8<sup>th</sup> of April 2016. 382 potentially eligible studies were kept for further assessed after duplicates removed. 217 studies were excluded because they clearly didn't fulfil inclusion criteria. Full-text articles were explored for clarification if the title and abstract haven't given clear information. 165 full-text articles were assessed for eligibility. 58 full-text articles were included in qualitative synthesis and 107 full-text articles were excluded. The reasons for exclusion were listed under the following flow-chart and “Characteristics of excluded studies”. Further investigation of the full articles retrieved five included studies which were excluded before, and nine studies were excluded which were included before. An adapted PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) flow-chart of study selections is attached (Liberati 2009). (Figure 1)

Figure 1. .PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of study selection





## **Included studies**

Fifty-eight trials were included for effectiveness and safety assessment and risk of bias analysis. For more information see *Characteristics of included studies*.

## **Study design**

All of the included studies stated as randomised controlled clinical trials, but only thirteen trials reported the details of randomisation methods and three trials (Ji 2013; Chao 2009; Tong 2013) described very detailed information of randomisation methods. One trial (Ji 2013) had two arms.

## **Participants**

All the study participants were hospital patients diagnosed with type 2 diabetes mellitus and receiving or not receiving treatment before the study commenced. 55 studies were carried out in a single study centre, mainly different provincial and municipal hospitals of main cities in mainland China. Three trials (Chao 2009; Tong 2013; Ji 2013) were carried out in multiple study centres with two studies using two and ten centres respectively in China and the other study using 20 centres (19 participant centres in China and one participant centre in Queensland, Australia).

## **Diagnosis**

The diagnostic criteria for type 2 diabetes mellitus were mainly based on WHO criteria (43 trials by criteria in 1999, 1 trial by 2007, 2 trials without specification), and three trials used the criteria of ADA (1 trial by 1999, 1 trial by 2003 and 1 trial without specification). Four trials used their diagnostic criteria based on textbook criteria, and five trials had no specification.

## **Interventions and comparisons**

Forty-two trials compared combined Chinese herbal medicines and other pharmaceuticals with other pharmaceutical alone; ten trials compared Chinese herbal medicines alone with other pharmaceuticals alone; four trials compared Chinese herbal medicines with placebo; two trials compared three groups' (one was comparisons of Chinese herbal medicines combined with pharmaceuticals to other pharmaceuticals alone or to Chinese herbal medicines alone; the other was comparisons of Chinese herbal medicines alone to pharmaceuticals alone or to other interventions); only one trial was a two armed study comparing Chinese herbal medicines combined with pharmaceuticals to other pharmaceutical alone between a drug naïve group and drug group. Most trials tested various Chinese herbal medicines including individual prescriptions modified from classical formulae. Three trials only tested a single Chinese herb Huanglian (*Coptidis Rhizoma*) or Wuweizi (*Fructus Schisandrae*).

The formulae of Chinese herbal medicines were different in each study. All recorded formulae, individual formulae and patent herbal formulae were included in the studies and the basic composition consisted of the 132 common Chinese herbal medicines, for more details please see Appendix 1 *List of Chinese herbal medicine used as treatment for type 2 diabetes*. Pharmaceuticals included commonly used hypoglycemic Western medicines such as: metformin, sulfonylureas (glibenclamide, glimepiride, and glipizide), alpha-glucosidase inhibitor (acarbose), thiazolidinediones (rosiglitazone), and insulin etc. Other interventions mainly included diet control, exercise therapy, diabetes health education and other life style changes.

### **Follow-up**

All of the fifty-eight included trials followed up the participants until the end of the treatments. Twenty-four trials studied and/or reported the adverse effects of the intervention.

### **Publication details**

See “Characteristics of included studies” for detailed information

### **Excluded studies**

One hundred and seven trials were excluded because they did not satisfy the inclusion criteria for selection of studies. See *Characteristics of excluded studies* for more information.

### **Risk of bias in included studies**

Most participants in included studies were mainly Chinese recruited from TCM hospitals, which led to selection bias because the results might not be applicable to the general population. A general conclusion cannot be drawn because the sample might not be representative of the whole population.

Also there was insufficient information to make a formal assessment, most included studies were at an unclear risk of bias for nearly all of the “Risk of bias” domains apart from attrition bias. See *Characteristics of included studies* for more information.

### **Allocation**

Forty-two included studies reported that the participants were randomly divided into two groups for respective treatments without giving further details. Eleven included studies reported a further randomization method: “by using random number table method”. And two trials mention by “random file number method”. Only three trials reported a detailed randomization method “Statistics Analysis System software was used to randomly divide the subjects” (Ji et al. 2013) or “randomization was performed

centrally and was concealed and stratified in blocks of four” (Chao et al. 2009) or “randomization and blinding were conducted by personnel who did not participate in data acquisition and evaluation; a computer program was used to generate the subject assignment; each subject was given a unique number and this number was used throughout the trial” (Tong et al. 2013). And all of these sixteen trials were assessed as having a low risk of selection bias.

### **Blinding**

Fifty-three studies were assessed as unclear for performance bias and detection bias because no information on blinding of participants and personnel or outcome assessors was provided in the trial reports. Only five studies reported detailed information of blinding methods “double-blinded and placebo-controlled” or “All investigators were blinded from the study drug assignment, in which only a randomization code was disclosed. Unblinding was conducted only after all study data were collected”. And all of these five trials were assessed as having a low risk of performance bias and detection bias.

### **Incomplete outcome data**

All fifty-eight studies were assessed as having a low risk of attrition bias. After checking the total number of participants and the patients included in each intervention group, there were no missing data in fifty-three studies. There were exclusions or losses to follow-up reported in five included studies. One trial lost follow-up in both groups before the start of the study. Two trials had missing outcome data balanced in numbers and with similar reasons for missing data across groups. Another trial had missing outcome data balanced in numbers across groups for no reported reason (s). The last one had missing outcome data balanced in numbers across intervention groups, and the proportion of missing data compared with observed event risk was not enough to have a clinically relevant impact on the intervention effect estimate (Higgins & Green 2008).

### **Selective reporting**

Fifty-four studies were assessed as having an unclear risk of reporting bias since their protocols were not available. Four trials had clear protocols and were assessed as having a low risk of reporting bias.

### **Other potential sources of bias**

All fifty-eight studies were assessed as unclear risk of other potential bias. All included studies followed up the participants until the end of treatment. Most of studies reported that there was no significant difference amongst the groups before the interventions, and were considered to have good baseline similarity. But other aspects of bias were still unclear, such as most studies did not clearly report how diabetes had been controlled, and for how long, before the studies.

## **Effects of interventions**

Fifty-eight studies with 6637 patients diagnosed of type 2 diabetes were included in the review. All included studies compared Chinese herbal medicine with other interventions (pharmaceuticals, diet control, and exercise therapy and health education). Five comparisons were available for the summary of findings.

### **Chinese herbal medicines combined with other pharmaceuticals versus other pharmaceuticals alone**

#### **Primary outcomes**

##### **Effectiveness of the intervention**

Forty-two trials with 4462 patients compared Chinese herbal medicines combined with pharmaceuticals versus other pharmaceuticals reported better outcomes in the treatment group (Chinese herbal medicines combined with pharmaceuticals) than in the control group (hypoglycemic Western medicines) with all or some of the following outcomes: glycated haemoglobin, glycemic level, blood lipid profiles, BMI, insulin resistance level and TCM clinical symptoms score. The outcomes were summarized in *Characteristics of included studies*.

##### **Safety of intervention**

Only seventeen studies reported adverse effects and /or safety issues with fourteen of them reporting the results of examinations for testing adverse effects, such as routine blood test, liver and kidney function test or ECG. Another three trials only reported no observed clinical symptoms indicating adverse effects without mention of what kind of examinations had been performed for identifying adverse effects. The outcomes were also summarized in *Characteristics of included studies*.

##### **Secondary outcomes**

Except one study (Ji 2013) mentioned the limitation of research in English literature, there were no data available in relation to any of secondary outcomes in the rest of these included studies.

## **Chinese herbal medicines alone versus other pharmaceuticals alone**

### **Primary outcomes**

#### **Effectiveness of the intervention**

Ten trials with 1201 patients compared Chinese herbal medicines with pharmaceuticals which were mainly hypoglycemic western medicines. Eight studies reported better outcomes in treatment group (Chinese herbal medicines) than that in control group (hypoglycemic western medicines) with all or some of the following outcomes: glycated haemoglobin, glycemic level, blood lipid profiles, BMI, insulin resistance level and TCM clinical symptoms score. The outcomes are especially significant at blood sugar control (FBG, 2hPBG) in Chinese herbal medicine group in above eight trials. Two studies only reported fasting insulin Fins and leptin etc. but not blood glucose outcomes. One study reported there was no statistical difference of blood sugar control between two groups. All ten trials reported statistical significant improvement of TCM clinical symptom score. The outcomes were also summarized in *Characteristics of included studies*.

#### **Safety of intervention**

Only two studies reported adverse effects with detailed information of what kind of examinations had been performed for identifying adverse effects. The remaining studies had no information reported in terms of adverse effects. The outcomes were also summarized in *Characteristics of included studies*.

#### **Secondary outcomes**

There were no data available in relation to any of secondary outcomes in all of these included studies.

## **Chinese herbal medicines alone or combined with other interventions or other pharmaceuticals versus placebo**

### **Primary outcomes**

#### **Effectiveness of the intervention**

Four trials with 794 patients compared Chinese herbal medicines alone or combined with other interventions to placebo. Other interventions were diet control and programmed daily exercise alone or in combination with hypoglycemic agents and lipid treatment. All four studies reported significant outcomes in treatment group (Chinese herbal medicines) than that in control group (placebo) with glycated haemoglobin and glycemic level control. TCM symptoms score were improved significantly in

treatment groups in two studies. The outcomes were also summarized in *Characteristics of included studies*.

### **Safety of intervention**

All four trials reported adverse effects and safety issues with detailed information of what kinds of examinations had been performed for identifying adverse effects, such as routine blood test, liver and kidney function test or ECG as well as clinical symptoms. The outcomes were also summarized in *Characteristics of included studies*.

### **Secondary outcomes**

There were no data available in relation to any of secondary outcomes in all of these included studies.

## **Combined Chinese herbal medicines with other pharmaceuticals versus Chinese herbal medicines alone versus other pharmaceuticals alone**

### **Primary outcomes**

#### **Effectiveness of the intervention**

One study with 90 patients performed three groups comparison of Chinese herbal medicines combined with other pharmaceuticals versus Chinese herbal medicine alone versus pharmaceuticals alone, reported that combining TCM and western medicine was more effective at controlling glycated haemoglobin and glycemic level than other two groups. The outcomes were also summarized in *Characteristics of included studies*.

### **Safety of intervention**

There was no information in terms of adverse effects and safety issues.

### **Secondary outcomes**

There were no data available in relation to any of secondary outcomes in this study.

## **Chinese herbal medicines alone versus other pharmaceuticals alone versus other interventions**

### **Primary outcomes**

#### **Effectiveness of the intervention**

One study with 90 patients performed three groups comparison of Chinese herbal medicines alone versus pharmaceuticals alone versus other interventions (including diabetes education, diet control and exercise therapy), reported that Chinese herbal medicine group and western medicine group were more effective at controlling glycated haemoglobin and glycemic level than other intervention group. The outcomes were also summarized in *Characteristics of included studies*.

#### **Safety of intervention**

There was no information was reported in terms to adverse effect and safety issues.

#### **Secondary outcomes**

There were no data available in relation to any of secondary outcomes in this study.

## **DISCUSSION**

Type 2 diabetes is recognised as an enormous global health-care challenge in the twenty-first century (Zimmet 2014). Chinese herbal medicine has been used to treat diabetes for more than two thousand years in China (Cheng 2000). More and more people in the west are now accepting Chinese herbal medicine as an effective and safe complementary treatment for type 2 diabetes (Youns 2010). The therapeutic effects of Chinese herbal medicine on the control of glycated haemoglobin and glycemic level, insulin resistant level and TCM clinical symptoms score have been studied and reported mostly inside China and very few English language studies have been found outside of China. This research included fifty-five studies from the Chinese literature and three studies from the English literature (fifty-eight studies involving 6637 type 2 diabetes patients together). All included studies from the Chinese literature have been translated into English and incorporated into “Characteristics of included studies”. There were five different comparisons with 132 herbal medicines involved in the fifty-eight trials lasting from eight weeks to one year. This review aimed to evaluate the effectiveness and safety of Chinese herbal medicine as a treatment of type 2 diabetes mellitus. Meta-analysis was not performed in this review because there was a mix of comparisons of different treatments, the outcomes were too diverse in most of the included studies, and bias was present in most of the individual studies (Higgins & Green 2008). There was also no picture of general statistics for average change rate of primary outcomes in this review because insufficient information was available to allow this summary in many included studies, plus the same reason as no meta-analysis.

### **Summary of main results**

#### **Effectiveness**

The general results suggested that Chinese herbal medicines used alone or in combination with other Western hypoglycemic agents or lifestyle changes was associated with a decrease of glycated haemoglobin and blood glycemic level, blood lipid profiles, BMI and TCM clinical symptom score. Scoring of TCM symptoms is a method of evaluating the symptoms of diabetes including dry throat and mouth, lack of strength, polyphagia, polydipsia, polyuria, shortness of breath, vexing heat in the chest, palms and soles, palpitation, insomnia etc. In terms of insulin resistance, a combination of Chinese herbal medicines with either other pharmaceuticals or lifestyle interventions was also associated with enhancing the therapeutic effects of other pharmaceuticals by improving insulin sensitivity in the treatment of type 2 diabetes (fourteen trials were performed to test this outcome by recruiting type 2 diabetes patients with insulin resistance).



All of forty-two trials showed statistically significant improvement of blood glucose control by Chinese herbal medicines combined with Western hypoglycemic agents compared to Western medicine alone for type 2 diabetes. Thirty-four of the forty-two trials indicated improvement with statistical significance at both glycosylated haemoglobin and glycemic control. Except for one case of asymptomatic type 2 diabetes, forty-one of the forty-two trials showed better improvement of TCM clinical symptoms with twenty-one trials measuring TCM symptoms scores of diabetes indicating statistically significant improvement.

All of ten trials claimed more improvement of glycemic control by Chinese herbal medicines alone or in combination with lifestyle interventions than Western medicine for type 2 diabetes. Eight of the ten trials indicated effectiveness with statistical significance. Seven of ten trials showed both glycated haemoglobin and glycemic control improvement. All ten trials showed better improvement of TCM clinical symptoms with seven trials indicating statistically significant improvement of TCM clinical symptom score.

Four trials showed better improvement at glycemic control of Chinese herbal medicines alone or in combination with other lifestyle interventions than placebo for type 2 diabetes, with two of four trials had statistical significance. All four trials showed TCM symptom improvement with only two had statistical significance.

For the two trials with comparisons of three groups, effectiveness was not able to be evaluated based on the available data (one study only reported effectiveness in the combination group compared to single Chinese herbal medicine group and western medicine group; another study reported the effectiveness in two treatment groups compared to no treatment group).

Most studies had average study durations of 8 to 12 weeks, which was too short to assess the effectiveness in related to glycated haemoglobin and glycemic level control of Chinese herbal medicines treatment for type 2 diabetes.

### **Safety**

Naturopathy including Chinese herbal medicine is generally believed to be safe. Chinese herbal medicines are regarded as safe to treat type 2 diabetes if used properly, and this is supported by its long history of clinical practice. However, all medicines are associated with some risks and there is no exception for Chinese herbal medicine. The safety issues related to type 2 diabetes treatment with Chinese herbal medicines may associated with many aspects including incorrect prescription, over dosage, improper preparation, erroneous substitution, adulteration with Western medicine and inherent toxicity or contaminants (Zhao, Tong & Chan 2006). But there was lack of universal criteria for scientific evidence to assess the safety of this intervention and the data related to the safety of Chinese herbal

medicine is also insufficient. This might be because of the time and money needed to perform the clinical trials to study toxicity and adverse effects of Chinese herbal medicine, because the chemical components of Chinese herbal medicines are more complex than that in Western medicine and each formula usually contain several herbs with each single herb usually having multiple active ingredients.

Twenty-two clinical trials out of fifty-eight included studies reported adverse effects such as nausea, vomiting, bloating, diarrhoea or other stomach discomfort along with hypoglycemic episodes. Nineteen trials out of twenty-two reported the examination details for identifying adverse effects and certainly had no safety assessment comparable with Western medicines. Three trials out of twenty-two reported no adverse effects observed and they did not mention if and what kinds of examinations had been performed for identifying the adverse effects. There was no information reported in terms of adverse effects in the other thirty-six included studies. There was no information reported safety issues in relation to any of secondary outcomes in all of the fifty-eight included studies.

### **Secondary outcomes**

It was impossible to carry out the analysis on toxicity and quality control of Chinese herbs, TGA regulation and limitation of research & research findings in English literature due to the lack of information in most of these studies. There were no available data in relation to any of above secondary outcomes in all of the fifty-eight included studies.

### **Overall completeness and applicability of evidence**

There are three main approaches of intervention for type 2 diabetes in all included studies: pharmaceutical treatment, Chinese herbal medicine and lifestyle (diet and exercise) control. In this review, all these three major treatments were included for analysis. The most valuable and important comparison to evaluate the treatment of type 2 diabetes is with placebo and both Western medicine and Chinese herbal medicine were effective, although only four studies were included in the review. The results also suggests that Chinese herbal medicines combined with other interventions (diet control, exercise therapy and pharmaceuticals) were more effective than pharmaceuticals alone but with a major limitation (selection bias of patients recruitment). Most clinical trials were well-designed but the overall quality of the studies was hard to determine because of the limited information reported in the studies. The quality of evidence was unsatisfactory and the risk of bias was unclear due to insufficient available information from most included studies. Most participants were from the Chinese population and were recruited from TCM hospitals, and this could impact the applicability of the interventions to other populations. This is a major source of bias.

## **Quality of the evidence**

All included studies in this review have many limitations in terms to quality of methodology, study design, results reported & analysis and conclusions.

### **1. Quality of methodology**

The general methodological quality of all selected trials was unsatisfactory based on international standards for a well-conducted RCT. All selected trials reported important demographic information and mentioned that no significant difference was found between intervention groups on baseline data at recruitment. Most studies provided detailed information with baseline data before the recruitment of the study. In terms of randomisation, allocation and concealment methods, only three studies provided sufficient details. Thirteen trials reported limited details of randomisation and allocation concealment method. The remaining forty-two trials only generally mentioned that randomisation was applied in their studies without details of the randomisation, allocation and concealment methods. Only five studies reported detailed information of blinding methods. Most studies that did not mention blinding may be due to the fact that blinding is difficult with respect to Chinese medicine studies, as the patients expected to receive only Chinese herbal treatment rather than Western medicines or placebo if they decided to see a traditional Chinese medicine practitioner.

### **2. Study design**

In general, all included studies were well-designed. Most of included studies provided the information of hypothesis, the baseline information of participants, the recruitment criteria, WHO diagnosis criteria of T2DM and diagnosis criteria by Chinese medicine theory, clear information on study and control groups, the details of intervention medicines and treatment methods, the duration of intervention and the proper outcome measurements. However, only twenty-two clinical trials out of fifty-eight reported adverse effects, with nineteen trials reporting the examination details for adverse effects. Most trials did not report potential side-effects as a study outcome. Safety issues of Chinese herbal medicines may have been neglected in most clinical studies due to various reasons mentioned above. Except one trial, none of the secondary outcomes were reported in the most included studies as pre-listed in the protocol. Meta-analysis could not be performed due to the limited information with respect to study medicines and varied Chinese herbs in each study. Furthermore there were only four placebo-controlled trials, which were insufficient for drawing any conclusion with respect to the effectiveness and safety of Chinese herbal medicine for treating type 2 diabetes mellitus.

### **3. Result report and analysis**

No exclusion or losses were reported in most of included trials, but the number of participants remained the same at the beginning and the endpoint of studies. So apart from five trials which reported lost follow-up data, all remaining fifty-three trials can be assumed to have had no drop-outs by checking the numbers of participants from the beginning and the end of the study. The five studies which reported the incomplete data were assessed as low risk based on the Cochrane Collaboration's tool for assessing risk of bias (Higgins & Green 2008). The protocol of most included studies were not described in sufficient details, so it is not possible to carry out a meta-analysis.

### **4. Conclusions of the included studies**

All studies reported the therapeutic effects of the interventions, but only two studies which published outside of China recorded their limitations in the discussion section of the trial report. The formulae for treating type 2 diabetes may differ according to TCM syndrome differentiation. Many herbal formulae are slightly modified compared to the classical prescription depending on individual clinical presentation. Most studies described formulae with multiple herbs and only three studies reported single herb usage. Therefore, the conclusion on effectiveness in this review is only in general terms but not for specific formulae or individual Chinese herbal medicines.

In conclusion, all selected studies were eligible for this review but the overall quality of the methodology was inconclusive and unsatisfactory. The evidence of included studies is insufficient, so the risk of bias of included studies are unclear. Thus, one cannot decide if it is effective to use Chinese herbal medicine to treat type 2 diabetes. Also the evidence of safety of Chinese herbal medicines as treatment for type 2 diabetes was inadequate due to the variation in studies and methodology. Well-designed clinical trials with standard criteria are required for the study of safety of Chinese herbal medicines.

#### **Potential biases in the review process**

We tried to include all relevant studies on type 2 diabetes treatment with Chinese herbal medicine by searching with very general terms with all types of possible entries during the review process. Most full-texts were in Chinese with only English abstracts. The author's native language is Chinese, so there is no likelihood of potential selection bias. All data were extracted under the strict supervision of research specialist. Comprehensive searches were conducted to try to avoid potential dissemination bias due to language and location. However, not all literature are in all database. Some database may not be

accessed due to location and language limitation, such as some Chinese database are not access from Australia. It is also impossible to avoid publication bias as negative studies are not reported. Or there is something published but not in peer review. Meta-analysis cannot be conducted due to the reason mentioned before.

Systematic bias could be possible since most of the included studies did not provide detailed protocol of administration of treatment and assessment of outcomes but only simply reported that randomisation was performed for allocation of intervention groups. Selection bias could not be avoided since most study participants were Chinese recruited from TCM hospital. Blinding of participants and personnel processes were also not described with detailed information in most included studies.

In terms of duration of intervention, only two studies lasted 4 months, five studies lasted 6 months, one study 48 weeks and one study 1 year. Most trials reported end-of treatment outcomes ranging from 8 to 12 weeks, which was too short to address long-term effectiveness and toxicity of the herbs. In particular for Chinese herbal medicine, there is a lack of information about the half-life of active ingredients in herbs to test long-term effectiveness and adverse effects, making it problematic to determine if Chinese herbal medicine could be an effective and safety treatment for type 2 diabetes. Effectiveness and safety issues should be a future research emphasis for Chinese herbal medicine used to treat chronic disease like type 2 diabetes.

### **Agreements and disagreements with other studies or reviews**

The findings in this review related to effectiveness of Chinese herbal medicines to treat type 2 diabetes are similar to the conclusion of previous systematic reviews. So far the last and the only Cochrane systematic review on Chinese herbal medicine to treat type 2 diabetes was in 2004 by Liu JP and others. No other Cochrane review with English literature has been found on the application of Chinese herbal medicine for type 2 diabetes in the past ten years. Liu JP and his colleagues analysed the effects of 66 randomized trials of 69 herbs involving 8302 patients with type 2 diabetes. And the conclusion was some herbal medicine were effective on blood glucose control in people with type 2 diabetes mellitus. But there was no mention of any safety issues or adverse effects related to type 2 diabetes with Chinese herbal medicine treatment.

As far as we know, no other Cochrane systematic review has been undertaken to provide an overview of both effectiveness and safety of Chinese herbal medicine for type 2 diabetes mellitus. This review provides a comparison between Chinese herbal medicines and other interventions for type 2 diabetes. And the general quality of the clinical trials have been previously documented and evaluated as unsatisfactory.

## **AUTHORS' CONCLUSIONS**

### **Implications for practice**

A combination of Chinese herbal medicine and other pharmaceuticals (mainly western hypoglycemic agents) proved to be more effective than pharmaceutical alone in terms of glycated haemoglobin, glycemia and insulin resistance level control in type 2 diabetes mellitus. But there was limited evidence to assess the effectiveness of Chinese herbal medicine alone for treating type 2 diabetes (only 10 trials with small sample size). Also the evidence for both effectiveness and safety was limited because most studies have unclear risk of bias in major domains due to insufficient information. There was no sufficient evidence (data of study duration and outcome) to fully evaluate the adverse effects and toxicity rate of the intervention.

Also, no further recommendation can be drawn that Chinese herbal medicines are effective and safe to treat type 2 diabetes mellitus due to the insufficient information available to evaluate the overall methodological quality of included studies.

In summary, there is insufficient data on both acute and long-term potential side effects with respect to Chinese herbal medicines treatment of type 2 diabetes. High-quality and long-term studies with sufficient information are needed to fully evaluate the effectiveness and safety of Chinese herbal medicine for treating type 2 diabetes mellitus.

### **Implications for research**

Long-term well-designed studies are required to compare Chinese herbal medicines alone with pharmaceutical alone or placebo before any conclusion can be drawn about the effectiveness and safety of type 2 diabetes treatment with Chinese herbal medicine. We suggest that high quality clinical trials with two arms and multiple centres (large samples) be published in English. Adequate randomization methods need to be applied and clearly reported. There should be clear information about the management methods and duration before the study along with other baseline characteristics for the recruitment of patients. Evaluation of effectiveness should be more clearly specified and focused on glycated haemoglobin and glycemic control.

Standardisation and quality controls are recommended for assessing effectiveness and safety of Chinese herbal medicine for type 2 diabetes treatment. Future studies should address safety issues by not only

reporting adverse effects but also supplying details of toxicity tests for type 2 diabetes patients. Concerning TCM assessment and treatment variation based on syndrome differentiation, we suggest recruiting same category of type 2 diabetes patients and treat with similar Chinese herbal medicines in future study in order to reduce the information bias of study as more as possible. We recommend multiple centre with type 2 diabetes patients recruiting from different resources (such as patients outside hospitals, patients outside China and so on) in order to avoid selection bias. We also suggest regulation of TCM herbs in a more stringent fashion.

Word count: 9291

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## CHARACTERISTICS OF STUDIES

### Characteristics of included studies [ordered by study ID]

Zhu LQ 2009

Clinical research on improving insulin resistance in type 2 diabetes mellitus with Chinese medicine

Tangmaikang

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=138 Inclusion criteria: T2DM WHO 1999; insulin resistance (HOMA-IR); TCM differentiation China 1993: Qi and Yin deficiency, Qi and blood deficiency; informed consent Exclusion criteria: have diabetes ketosis, ketoacidosis and infections, pregnancy diabetes, hyperthyroidism or hepatitis and other diseases which can lead to hyperglycemia within one month; psychotic and senile dementia cannot cooperate; severe heart, brain, liver, kidney complications or severe primary complications; pregnancy or breastfeeding; long-term or current use insulin treatment
Interventions	Number of study centres: 1 Location: China Setting: outpatients and inpatients in TCM hospital Intervention: Basic treatment: diet control, exercise therapy and oral intake of hypoglycemic medicine: metformin sustained-release tablet, sulfonylurea and acarbose. Treatment group: basic treatment plus TCM medicine: Tangmaikang (TMK) including Huangqi, Shengdihuang, Shudihuang, Danshen, Niuxi, Chishao, Huanglian, Huangjing, Gegen, Yinyanghuo Control group: use basic treatment to control FBG 4.5-6.5mmol/L and 2hPBG 4.5-8.0mmol/L
Outcomes	FBG, 2hBG, Fins, HbA1c, HOMA-IR, blood fat and blood coagulation had obvious improvement in varied level after treatment and treated group had better improvement than control group.

	<p>Safety index was measured by general physique examination (BMI, BP, and Pulse etc.), blood routine examination, urine routine examination, liver function and kidney function examination etc.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“A Research on the effect of Chinese medicine TMK on improving IR in T2DM”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into 2 groups” , no described information in sufficient detail to allow a definite judgement
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into 2 groups” , no described information in sufficient detail to allow a definite judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Two cases lost follow up in treated group and eight cases lost in control group before the interventions. No exclusion or losses were reported after the interventions, and the number of participants remained the same at the endpoint of study

Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Wu JJ 2015

Curative effect of therapy with Chinese medicine on type 2 diabetes of damp-heat type and life quality

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=120 Inclusion criteria: T2DM WHO 1999; TCM differentiation: damp-heat type Exclusion criteria: patients used insulin before were selected in study, psychotic, dementia, anemia, severe infection, myocardial infarction, heart failure, severe renal dysfunction, active hepatitis, tumour, pregnancy, breastfeeding, diabetes ketosis acidosis, hypertonicity coma
Interventions	Number of study centres: 1 Location: China Setting: inpatients in TCM hospital Intervention: diet control, diabetes health education and exercise instruction Treatment group was treated with differential therapy with Chinese medicine jia wei gan lu xiao du dan (include: Hua Shi Fen, Yinchen, Huangqin, Shichangpu, Huoxiang, Chuanbeimu and Lianqiao) on the basis of treatment in control group Control group use oral hypoglycemic western medicine alone: metformin, acarbose, glipizide, sulfonyleurea, rosiglitazone and so on.
Outcomes	The life quality score (QLICD-DM, SF-36FBG) of the patients in both group after treatment were improved significantly, and the improvement in treatment group was

	<p>better than that in the control group. The improvement of blood sugar (FBG, 2hPG), blood fat and HbA1c were better in treatment group than that in the control group.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“to observe the curative effect of differential therapy with Chinese medicine on type 2 diabetes of damp-heat type and life quality of the patients”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into 2 groups”
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into 2 groups”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

## Jiangtangjing Granule Treatment of Type 2 Diabetes Clinical Observation and Mechanism Research

Methods	<p>Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone</p> <p>Randomisation ratio: 1:1</p>
Participants	<p>Ethnic: Chinese n=40</p> <p>Inclusion criteria: T2DM WHO 1999: FPG<math>\geq</math>7.0mmol/L, or 2hPG<math>\geq</math>11.1mmol/L; TCM differentiation: qi and yin deficiency</p> <p>Exclusion criteria: <math>\leq</math>18 y or <math>\geq</math>65y; pre-diabetes; pregnancy or breastfeeding, patients combine with other severe primary diseases or psychotic, patients with diabetic ketoacidosis and other acute metabolism disorders as well as associated infections within one month</p>
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients in TCM hospital</p> <p>Intervention:</p> <p>Basic treatment: exercise intervention and diet intervention</p> <p>Treatment group: basic treatment + Chinese medicine Jiangtangjing granule (mainly include: Huangqi, Huangjing, Yiyiren, Gegen, Shanyao, shanzha, Shuizhi, baijiezi etc.) on the basis of treatment in control group</p> <p>Control group use western medicine alone: Saxagliptin</p>
Outcomes	<p>Both groups show significant difference in fasting blood sugar (FBG), blood sugar (2hPG), 2h postprandial glycosylated haemoglobin (HbA1c) compared with before, but the TCM symptoms integral change of Jiangtangjing granule group patients significantly reduced compared with the control group.</p> <p>Liver and kidney metabolism related indexes were measured after the treatment and no abnormal was observed.</p> <p>Outcomes were assessed at baseline and trial completion</p>
Study details	<p>Duration of intervention: 8 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>



Stated aim of study	"To observe the Jiangtangjing granule in effect of treatment for type 2 diabetes and its hypoglycemic mechanism of the initial study"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into Jiangtangjing group and control group"
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into Jiangtangjing group and control group"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Zhou JG 2012

Influence on insulin Resistance of Type 2 diabetes mellitus with Lijian Decoction

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1	
Participants	Ethnic: Chinese n=96 Inclusion criteria: T2DM WHO 1999; HOMA-IR (FPGx FINS/22.5) ≥28; Exclusion criteria: liver and renal dysfunction, type 1 diabetes, tumour, hematopoiesis system disease as well as psychotic, acute myocardial infarction, severe heart rhythm abnormal, acute heart failure or chronic heart dysfunction over level 3	
Interventions	Number of study centres: 1 Location: China Setting: patients in TCM college hospital Intervention: two groups used sulphonylureas, metformin, and alpha glucosidase inhibitor conventional therapy for 4 weeks. When fasting glucose < 7.0 mmol/L, the treatment group combined with Lijian Decoction (Lizhihe, Huoxiang, Peilan, Cangzhu, Jixuecao, Guijianyu) Control group maintained the original conventional treatment	
Outcomes	Compare to control group, blood cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL-C), high density lipoprotein (HDL-C), fasting plasma glucose (FBG), fasting insulin (FINS) and insulin sensitivity index (ISI) were significantly decreased in treatment group after treatment. Adverse effect was measured by blood, urine, stool routine examination and liver, kidney function examination. No adverse effect was observed during the intervention. Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 8 weeks Duration of Follow-up: not reported Run-in period: 4 weeks	
Stated aim of study	"To observe the effect of treatment of eliminating dampness with aromatics for type 2 diabetes mellitus"	
Risk of bias		
Bias	Authors judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, medical condition and disease course Other aspects of bias were unclear.

Nie JT 2010

Effects of combing traditional Chinese medicine with Western medicine on life quality and carbohydrate metabolism in patients with type 2 diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=118 Inclusion criteria: T2DM TCM differentiation: qi and yin deficiency with blood stasis

	Exclusion criteria: not described	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: inpatients in TCM hospital</p> <p>Intervention:</p> <p>Basic treatment: controlling blood pressure, adjusting blood lipid and having diabetic diet</p> <p>Combining TCM and western medicine group: added TCM herbs according to syndrome differentiation (Huangqi, Huaishangyao, Fuling plus Gegen, Tianhuafen or Shengshigao, Huanglian, Zhimu, Shengdihuang, Maidong and Gegeng or Fuzi, Rougui, Lurong and Fupengzi or Taoren, Honghua or Shenqu, Maiya and Yiyiren or Yanhuoshuo, Jiangchan, Quangxie and Yujin) on the basis of western medicine group</p> <p>Western medicine (WM) group: insulin or oral blood sugar control medicine only in addition to basic treatment (no details information about the medicine)</p>	
Outcomes	<p>After treatment, physiological and psychological/ spiritual functions of QOL in both groups were improved markedly, variation of physiological and treatment functions in combing TCM with WM group in pre and post treatment had significant difference comparing with those in WM group. FPG, 2hPG, HbA1c obviously decreased and variation of observation indexes in combining TCM with WM in pre and post treatment had a significant decrease comparing with those in WM group.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To study the effects of combing traditional Chinese medicine with Western medicine on life quality (QOL) and carbohydrate metabolism in patients with type 2 diabetes”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into combining TCM with WM group and WM group”
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into combining TCM with WM group and WM group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Hu YT 2014

Effect observation of integrated Chinese and western medicine in the treatment of obesity and type 2 diabetes mellitus

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=150

	<p>Inclusion criteria: T2DM ADA 2003, TCM diagnostic criteria, obesity diagnostic criteria China 2003; age: 40-75 years old; stable condition and complications under ideal control; clear consciousness; informed consent;</p> <p>Exclusion criteria: type 1 diabetes; tumour, combine with ketoacidosis or hypertonicity coma or severe infections, combine with severe disturbance of consciousness, severe heart, liver and renal failure; cannot take medicine according prescription; take other TCM; outcome is not clear; cannot cooperate</p>	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: inpatients in TCM hospital</p> <p>Intervention:</p> <p>Treated group added TCM treatment (Dangshen, Shashen, Taizishen, Huangbai, Shengdi, Huangqi, Chuangxiong, Dilong, Maidong, Zhimu, Tianhuafen) based on treatment in control group</p> <p>Control group: conventional western medicine treatment: diabetic diet, rational exercise, emotional and psychological therapy, oral taking metformin</p>	
Outcomes	<p>The curative effect (FPG, 2hPG) and the total effective rate of the decrease of body weight (waistline, BMI) in treatment group were better than that in control group, and the difference was statistically significant.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To observe the clinical curative effect of integrated traditional Chinese and western medicine in the treatment of obese type 2 diabetes”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”

Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Fu NY 2012

Insulin Resistance of Type 2 Diabetes Mellitus Diagnosis and Treatment of Traditional Chinese Medicine Clinical Observation

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:6
Participants	Ethnic: Chinese n=140 (20 in control group, 120 in treatment group) Inclusion criteria: T2DM WHO 1999, IR, TCM differentiation: yin deficiency with dryness-heat, damp-heat restrain spleen, qi and yin deficiency, blood stasis resistance of meridians

	Exclusion criteria: type 2 diabetes with severe damage of heart, brain, kidney and other vital organs; life signs unstable, cannot cooperate with examination	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: inpatients in TCM hospital</p> <p>Intervention:</p> <p>Treatment group added TCM formula according to TCM differential patterns on the basis of treatment in control group (Yin deficiency with dry heat: Shengdi, Shashen, Shihu, Tianhuafen, Gegen, Tiandong, Maidong, Zhimu, Huangqin, Huanglian; Damp-heat restrict spleen: Chenpi, Banxia, Fuling, Juemingzi, Zhexie, Ganchao, Zhuru, Dangnanxing; Qi and yin deficiency: Shenghuangqi, Shanyao, Dangshen, Shengdi, Xuanshen, Maidong, Digupi, Shanzhuyu, Changzhu, Wuweizi, Wumei; Phlegm stagnation: Dangshen, Shengdi, Xuanshen, Danggui, Baishao, Chuanxiong, Jixueteng, Danshen, Tianhuafen, Gegen, Rendongteng, Honghua)</p> <p>Control group: metformin</p>	
Outcomes	<p>Significant change with index (FPG, IAI, FINS, TG, HDL-C, TNF-<math>\alpha</math>) was observed after treatment and treatment group has larger indexes variations than the control group.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
In Study details	<p>Duration of intervention: 8 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	"To explore the pathogenesis of insulin resistance of traditional Chinese medicine and TCM treatment effect characteristics of insulin resistance type 2 diabetes cases by differentiation of TCM clinical observation"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"



Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Zhang Y 2010

Influence on insulin resistance of Type 2 Diabetes Mellitus by the Treatment of Yangyin Qingre method

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=80 Inclusion criteria: T2DM WHO 1999, TCM diagnostic criteria: Xiaoke yin deficiency with heat, FPG $\geq$ 5.8mmol/L $\leq$ 13.8mmol/L, BMI:21-35kg/m <sup>2</sup> , HOMA-IR $\geq$ 2.8; age: 35-85; T2DM over 6 months since diagnose, no insulin and other medicine affecting glycolipid metabolism; TCM pattern: yin deficiency with excess heat

	Exclusion criteria: type 1 diabetes; severe cardio diseases, myocardial infarction, unstable stenocardia, chronic heart dysfunction; severe diabetic complications and liver, kidney disease, other endocrine disease; recent acute infectious disease and acute diabetic complications; systolic pressure $\geq$ 160mmHg and /or diastolic pressure $\geq$ 100mmHg; current with insulin treatment	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients and inpatients in TCM hospital</p> <p>Intervention: two groups' patients were by diet control, lipid-lowering drugs, hypoglycemic drug sulfonylurea and metformin for two weeks as observation platform period.</p> <p>Treatment group were added nourishing Yin and clear heat Chinese herbal decoction (Shengdi, Shanzhuyu, Huaishanyao, Mudanpi, Fuling, Zelan, Zhimu, Huangbai, Huanglian, Huangqin, Zhizi, Banxia, Chenpi, Yiyiren, Danshen, Taoren, Dangshen, Baizhu, Yujin, Chaihu)</p> <p>Control group remain the original treatment.</p>	
Outcomes	<p>Treatment group was observed better results in efficiency and FPG, 2hPG, HbA1C, TC, TG, Fins, HOM-IR and the difference was significant.</p> <p>Safety was measured by ECG, urine routine examination, liver and kidney function examination, ALT, SCR, BUN and UA. No adverse effect was observed during the intervention.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 8 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: 2 weeks</p>	
Stated aim of study	"To observe the law YangyinQingre Chinese medicine for the effects of insulin resistance type 2 diabetes mellitus"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"

Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Exclusion or losses were reported before the study and the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Xu Q 2007

A Clinical observation on Treatment of Integrated Chinese and Western Medicine for 35 cases of type 2 Diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=69 Inclusion criteria: T2DM WHO 1999; have typical diabetes symptoms with once FPG $\geq$ 7.0mmol/L or 2hPG $\geq$ 11.1mmol/L or blood sugar $\geq$ 11.1mmol/L; have no typical diabetes symptoms with twice FPG $\geq$ 7.0mmol/L; or twice blood sugar $\geq$ 11.1mmol/L after OGTT, or once FPG $\geq$ 7.0mmol/L and blood sugar $\geq$ 11.1mmol/L after OGTT;

	<p>TCM diagnostic criteria (China 1993): TCM differentiation: qi and yin deficiency; blood sugar&lt;20mmol/L, age:40-75, voluntary to study and can take medicine according to prescription</p> <p>Exclusion criteria: FPG≤7mmol/L or 2hPG≤11.1mmol after diet control and exercise therapy; combine with severe heart, liver, kidney complications or other severe primary diseases, or psychotic; have diabetic ketoacidosis and other acute metabolism disorders as well as with associated infections within one month; pregnancy, breastfeeding and drug allergy; type 2 diabetes with insulin treatment</p>	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients in TCM hospital</p> <p>Intervention:</p> <p>Treatment group added TCM decoction of lower blood sugar and nourishing yin decoction (Sheng Huangqi, Xuanshen, Shanyao, Dangshen, Maidong, Sheng Dihuang, Shu Dihuang, Wuweizi, Tianhuafen, Gegen, Danshen, Chishao, Chuanxiong) on the basis of treatment in control group</p> <p>Control group: oral intake of hypoglycemic drug sulfonylurea (metformin)</p>	
Outcomes	<p>FPG, 2hPG and GHbA1c decreases significantly in both groups especially in treatment group; blood lipid (TC, TG, LDL-C, and HDL-C) and score of Chinese medical pattern and therapeutic effect improved significantly in treatment group.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 8 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To observe the therapeutic effect of integrated therapy of Chinese and western medicine for type 2 diabetes”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”

Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Wang YG 2013

Clinical Observation on Si-huang Hypoglycemic Granule (SHHG) improving Patients Symptoms of TCM with T2DM

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals and placebo Randomisation ratio: 2:1
Participants	Ethnic: Chinese n=126 (82 in treatment group, 44 in control group) Inclusion criteria: T2DM WHO 1999; TCM diagnostic criteria; T2DM patients with long-term hyperglycosemia with HbA1c $\geq$ 7.5%; patients not include in exclusion cases

	Exclusion criteria: pregnancy or breastfeeding; severe heart, liver, kidney and brain complications, or combine other severe primary diseases; have diabetes ketosis or hypertonicity coma or infections within 1 month; not satisfy with TCM diagnostic criteria	
Interventions	Number of study centres: 1 Location: China Setting: inpatients and outpatients in TCM university hospital Intervention: Treated group added Sihuang hypoglycemic granule (SHHG) (Huangqi, Sheng Dihuang, Dahuang, Huanglian, Guijianyu) on the basis of conventional western medicine hypoglycemic therapy Control group: conventional western medicine hypoglycemic therapy (glipizide and metformin oral intake) with placebo	
Outcomes	Two groups had good curative effect in reducing blood glucose and glycosylated haemoglobin (FPG, 1hPG, 2hPG, HbA1C), the treatment group is better than the control group in improving the TCM clinical symptoms (TCM symptom score). No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 6 months Duration of Follow-up: not reported Run-in period: none	
Stated aim of study	"To observe the effect of Dangua prescription on type 2 diabetes patients with long-term hyperglycosemia"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It only motioned when allocating patients in two groups, no report in intervention.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Luo YY 2010

Clinical Effect of Prescription for Invigorating spleen to reduce Sugar on the Insulin Resistance of Type 2 Diabetes Patients

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=80 Inclusion criteria: T2DM WHO 1999; T2DM patients with insulin resistance, FPG>7mmol/L, FINS>15IU/L after basic treatment Exclusion criteria: type 1 diabetes; pregnancy or breastfeeding or plan pregnancy; over sensitive to the treatment drug or the ingredients; have surgery or other emergency circumstance; have diabetic ketoacidosis or hypertonicity coma; severe liver, kidney diseases, severe coronary heart disease; over 70 years old

Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: inpatients and outpatients in TCM hospital</p> <p>Intervention: conventional diet and exercise therapy</p> <p>Treatment group added TCM prescription for invigorating spleen to reduce blood sugar (Huangqi, Guijinyu, Shouwu, Huaishanyao, Chaihu, Yujin, Zexie, Huangjing, Gegen; and Dangshen, Baizhu for Qi deficiency; Sheng Dihuang, Tianhuafeng for Yin deficiency; Huanglian for heat; Danggui for blood deficiency; Tusizi for Yang deficiency; Changzhu, Fuling and Yiyiren for Phlegm dampness) on the basis of control group</p> <p>Control group: oral intake of metformin hydrochloride</p>	
Outcomes	<p>More significant difference was observed in indicators (FPG, 2hBG, FINS, HbA1C, TC, TG, HDL-C, LDL-C and HOMA-IR) before and after treatment in treatment group</p> <p>No adverse effect was observed through liver, kidney, heart function examination and blood, urine and stool routine examination.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To observe the clinical effect of prescription for invigorating spleen to reduce sugar on the insulin resistance of type 2 diabetes patients”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias)	Unclear risk	The information was not reported in this study



All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, and disease course BMI, laboratory text indexes, insulin resistant index etc. Other aspects of bias were unclear

Xu CX 2006

Clinical observation of Qi-Enriching and Yin-Nourishing, Heat-clearing and Blood-activating Therapy for 30 Cases of Type 2 Diabetes Insulin Resistance

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=60 Inclusion criteria: T2DM WHO 1999; FPG $\geq$ 7mmol/L; blood sugar $\geq$ 11.1mmol/L; random blood sugar $\geq$ 11.1mmol/L ; OGTT 2hPG $\geq$ 11.1mmol/L; blood sugar cannot be controlled to ideal level after diet control, exercise therapy and western medicine treatment for over two weeks Exclusion criteria: type 1 diabetes; pregnancy diabetes; other type diabetes and diabetes with acute or severe complications within one month; over 75 years old
Interventions	Number of study centres: 1 Location: China

	<p>Setting: inpatients and outpatients in hospital</p> <p>Intervention:</p> <p>Treated group added TCM prescription for qi-enriching, yin-nourishing, heat-clearing and blood-activating (Taizishen, Huangqi, Guijijanyu, Cangzhu, Xuanshen, Dihuang, Gegen, Shanyao, Tianhuafen, Zhimu, Shanzhuyu, Huanglian; add Maidong for severe Yin deficiency; add Yinyanghuo for cold aversion) on the basis of control group</p> <p>Control group: diet control and exercise therapy with oral intake berberine tablet</p>	
Outcomes	<p>The total clinical effect and insulin resistance improving were significant higher in treatment group than in control group. 2hPG, FINS, HbA1C, TG, and ISI improved more obviously in treatment group than in control group.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 2 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To observe the clinical efficacy of qi-enriching, yin-nourishing, heat-clearing and blood-activating therapy in treating type 2 diabetes insulin resistance”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study

Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general background. Other aspects of bias were unclear

Li HM 2011

Effect of a prescription for tonifying kidney and spleen combination with conventional western medicine on blood sugar and hemorheology of patients with type 2 diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 3:4
Participants	Ethnic: Chinese n=160 (60 in control group, 80 in treatment group) Inclusion criteria: T2DM WHO 1999; TCM differentiation: spleen and kidney deficiency type Exclusion criteria: ≤18 y or ≥75y; critical medical history within 6 months: myocardial infarction, cerebrovascular accident, diabetes ketoacidosis; pregnancy or breastfeeding; diabetic ketoacidosis.
Interventions	Number of study centres: 1 Location: China Setting: inpatients and outpatients in TCM hospital Intervention: Treated group added TCM decoction for tonifying kidney and spleen (Bajitian, Yinyanghuo, Duzhong, Taizishen, Biandou, Shanyao, Heshouwu, Mohanlian, Dangshen, Baizhu, Fuling, Danshen, Shen Dahuang) on the basis of control group Control group: diabetes conventional treatment (diet control, exercise therapy, diabetes education and mental adjustment plus no more than two kinds of

	hypoglycemic western medicine: insulin inhibitor, alpha glucosidase inhibitor, metformin and glimepiride etc.	
Outcomes	<p>The total effective rate in treatment group was higher than that in control group. The levels of FPG and 2hPG after treatment were decreased in comparison with those before treatment in two groups but was superior in treatment group. Whole blood viscosity, plasma viscosity, haematocrit and fibrinogen in treatment group were significantly decreased in comparison with those in control group after treatment.</p> <p>Blood, urine and stool routine examination have been measured before and after treatment and no adverse effect has been observed. 7 cases in control group used to have hypoglycemic symptom and it was relieved by having food.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 2 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	"To observe the effect of a prescription for tonifying kidney and spleen combination with conventional western medicine on blood sugar and hemorheology of type 2 diabetes patients with spleen and kidney deficiency type"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into two groups"
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into two groups"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study

Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general background. Other aspects of bias were unclear

Lin JJ 2014

Effect of Compound Hypoglycemic Yuye Oral Liquor combined with Metformin and glimepiride on Type 2 diabetes Mellitus

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=80 Inclusion criteria: T2DM WHO 1999; T2DM blood sugar $\geq$ 11.1mmol/L or FPG $\geq$ 7.0mmol/L or 2hPG $\geq$ 11.1mmol/L; TCM diagnostic criteria, China 2002. TCM differentiation: qi and yin deficiency; have never used blood sugar controlled medicine before, age:20-65 years old, informed consent, voluntary to examination and treatment Exclusion criteria: not cooperated and psychotic; pregnancy or breastfeeding; combine other severe primary diseases; have diabetes ketoacidosis and other acute metabolism disorder as well as combine with infections within one month; need insulin treatment; sensitive to treatment drug
Interventions	Number of study centres: 1 Location: China Setting: outpatients in TCM hospital Intervention: both groups have diet control, exercise therapy, diabetes education and other lifestyle adjustment.

	<p>Treatment group added TCM compound hypoglycemic Yuye oral liquor (Huangqi, Sheng Dihuang, Zhi Heshouwu, Huangjing, Taizishen, Zhimu, Yuzhu) on the basis of control group</p> <p>Control group: metformin hydrochloride tablets and glimepiride tablets</p>	
Outcomes	<p>FPG, 2hPG, and HbA1C were decreased after treatment and the decrease was more notable in treatment group than that in control group with statistically significant; TCM syndrome score was lower and clinical efficiency was higher in treatment group compared to control group with statistically significant.</p> <p>One case had mild hypoglycemic symptom and two cases had mild nausea symptom in control group, one case had mild nausea in treatment group. The symptoms were disappeared after heteropathy. No difference was observed between two groups about the adverse effect. Liver and kidney function examination were all normal. No severe adverse effect was observed.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To observe the clinical efficacy and safety of compound hypoglycemic Yuye oral liquor combined with metformin hydrochloride and glimepiride in the treatment of type 2 diabetes mellitus (deficiency of both Qi and Yin).”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Zhu LY 2015

Clinical Curative Effect of Self-made herbal Medicine Combined with Western Medicine on Diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=70 Inclusion criteria: T2DM internal medicine 7 <sup>th</sup> edition 2007, FPG $\geq$ 7.0mmol/L or 2hPG $\geq$ 11.1mmol/L; voluntary to study and informed consent; take medicine according to prescription; TCM diagnostic criteria 2002, TCM differentiation: yin deficiency with excess heat; can stick to take drug according to the prescription Exclusion criteria: liver and kidney dysfunction; pregnancy and breastfeeding; psychotic; severe diabetes complications; cannot cooperate; drop off due to no effect with the study drug
Interventions	Number of study centres: 1 Location: China Setting: outpatients in TCM hospital Intervention: both groups have lifestyle improvement, health education, proper exercise, quit smoking, limit alcohol and other non-drug therapy

	<p>Integrated group: self-made TCM prescription (Shanyao, Sheng Shigao, Huangqi, Tianhuafen, Sheng Dihuang, Zhimu, Xuanshen, Maidong, Huainiuxi, Fuling, Zexie, Tusizi, Taizishen, Biazhu, Cangzhu, Tiandong, Chishao, Danshen, Shanzhizi) on the basis of western group</p> <p>Western medicine group: oral intake metformin hydrochloride enteric coated tablets and gliclazide tablets</p>	
Outcomes	<p>The combination group was significantly better than the control group in TCM syndromes score. FPG, 2hPG, FINS, 2hINS levels in integrated group were significantly lower than those in the western medicine group</p> <p>The adverse reactions occurred lower in integrated group than that in the western group.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To investigate the clinical efficacy of self-made prescription of traditional Chinese medicine combined with western medicine in the treatment of patients with diabetes mellitus”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into combination group and western medicine group by using random number table”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into combination group and western medicine group by using random number table”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study



Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on sex, age distribution, medical condition and other general backgrounds. Other aspects of bias were unclear

Kong M 2009

Qi-invigorating, Yin-nourishing and Blood circulation activating prescription Improving Insulin Resistance in patients with Type 2 Diabetes Mellitus

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=70 Inclusion criteria: T2DM WHO 1999; Homa-IR $\geq$ 2.8 with insulin resistance; TCM diagnostic criteria 1993: qi and yin deficiency, qi and blood stagnation; informed consent; run-in period with lifestyle therapy and stop other medicine for one month with stable blood sugar but above normal Exclusion criteria: have diabetes ketosis, ketoacidosis and infections, pregnancy diabetes, hyperthyroidism or hepatitis and other diseases which can lead to hyperglycemia within 1 month; psychotic and senile dementia cannot cooperate; severe heart, brain, liver, kidney complications or severe primary complications; pregnancy or breastfeeding; long-term or current use insulin
Interventions	Number of study centres: 1

	<p>Location: China</p> <p>Setting: outpatients and inpatients in TCM hospital</p> <p>Intervention:</p> <p>Treatment group: TCM prescription of qi-invigorating, yin-nourishing and blood circulation-activating (Huangqin, Sangbaipi, Sangye, Sangzhi, Sheng Dihuang, Shanyao, Danggui, Chishao) on the basis of control group</p> <p>Control group: basic treatment: diet control, exercise therapy, health education and oral intake one of hypoglycemic drug: metformin, glipizide or diamicron</p>	
Outcomes	<p>FPG, 2hPG, FINS, HbA1c, Homa-IR, blood fat and blood coagulation (PT, Fib, APTT, TC, TG) were all significantly improved and the improvement degree of treatment group was better than that of control group. The hypoglycemic and therapeutic effects on TCM syndrome in treatment group were superior to those in control group.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: one month</p>	
Stated aim of study	<p>“To explore the mechanism of recipe of qi-invigorating, yin-nourishing and blood circulation-activating in the improvement of insulin resistance in patients with type 2 diabetes mellitus”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on sex, age, medical condition and disease course. Other aspects of bias were unclear

Yu ZM 2015

Therapeutic Effect of Xiaoke Jiangtang Fang Combined with Pioglitazone Hydrochloride and Metformin Hydrochloride tablets on Patients with type 2 Diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=96 Inclusion criteria: T2DM WHO 1999; TCM diagnostic criteria: yin and yang deficiency, blood stasis with fluid stagnation; HbA1c 7%-11%; have never used other medicine before the study Exclusion criteria: type 1 diabetes; comply with cardiovascular, cerebrovascular and nervous system disease; severe heart dysfunction, liver and kidney primary disease; have medical history of surgery and severe trauma; psychotic
Interventions	Number of study centres: 1 Location: China Setting: inpatients and outpatients in hospital

	<p>Intervention: both groups have diet control and oral intake of pioglitazone hydrochloride and metformin hydrochloride tablets</p> <p>Observation group: TCM prescription Xiaoke Jiangtang Fang (Tianhuafen, Zhimu, Huanglian, Shichangpu, Shihu, Chuanxiong, Guijiayu; add Ouzhi, Maidong, Tiandong, Dihuang, Gegen for Lung heat; add Huangqin, Zhizi, Xuanshen, Maidong, Sheng Dihuang, Huainiuxi for stomach heat; add Huangqi, Fuling, Baizhu, Huaishanyao, Dangshen, Ganchao for Qi and Yin deficiency; add Shanyurou, Gouqizi, Shu Dihuang, Huaishanyao for liver kidney Yin deficiency) plus pioglitazone hydrochloride and metformin hydrochloride tablets</p>	
Outcomes	<p>The effective rate of observation group was significantly higher than control group. BMI, FBG, 2hPG, HbA1c, TG, high/midst/low shear rate of blood viscosity, plasma viscosity, fibrinogen in two groups were significant decreased after treatment, and the decrease in observation group were significant lower than those of control group. The score of TCM symptom in observation group was also significant lower than that of control group after treatment.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To evaluate the therapeutic effect of Xiaoke Jiangtang Fang combined with pioglitazone hydrochloride and metformin hydrochloride tablets on patients with type 2 diabetes”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into observation group and control group by using random number table”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into observation group and control group by using random number table”

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on sex, age, disease course and medical history of hypertension. Other aspects of bias were unclear

Zheng HX 2014

An observation of the clinical effect of Taohong Siwu decoction in the treatment of T2DM

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=54 Inclusion criteria: T2DM ADA; age>18 years old; first diagnosis of diabetes; no other vital organs damage; no recent acute diabetes complications; patients are agree with treatment and can stick with long-term treatment, also with informed consent Exclusion criteria: type 1 diabetes; have diabetes ketoacidosis or hyperglycemia hypertonicity syndrome and other acute complications; combine with acute cardiovascular and cerebrovascular disease; combine tumour, infection, active infection, immune system disease, hemopoietic system disease; T2DM with severe heart, liver and kidney dysfunction; pregnancy or breastfeeding; allegory or intolerant

	to all drugs; combine clinical proteinuria, dominance proteinuria or persistent proteinuria; psychotic cannot cooperate; age<18 years; medical history not completed	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients in hospital</p> <p>Intervention: both two groups have diabetes dietary therapy and oral intake metformin hydrochloride sustained-release tablets</p> <p>Observation group: TCM prescription Taohong Siwu decoction modified (Zhimu, Huangqi, Shanyao, Shu Dihuang, Rougui, Duzhong for Ying and Yang Deficiency; Xiyangshen, Huangqi, Gegen, Shu Dihuang, Maidong for Qi and Yin deficiency; Shanyao, Niuxi, Sheng Dihuang, Gouqi, Fuling for Liver and Kidney Yin deficiency; Sheng Dihuang, Huangbai, Baizhu, Zhimu, Huanglian, Danggui, Maidong for Yin deficiency with heat; Yiyiren, Xingren, Baikouren, Huanglian, Banxia, Tongcao for Damp-heat) plus metformin hydrochloride sustained-release tablets</p>	
Outcomes	<p>FBG, 2hPG and HbA1c significantly decreased after treatment in both two groups. The decrease of 2hPG in observation group was significantly lower than the control group. The occurrence of clinical symptoms in observation group was significantly lower than the control group</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To explore and observe the clinical curative of Taohong Siwu decoction using by TCM in the treatment of type 2 diabetes mellitus on the basis of taking metformin hydrochloride sustained-release tablets ”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into observation group and control group”

Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into observation group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on age, FBG, 2hPBG, HbA1C. Other aspects of bias were unclear

Liu YH 2008

Clinical research on effect of YiqiYangyinHuoxue (supplementing Qi, nourishing Yin and activating Blood circulation decoction) in improving insulin resistance in patients with type 2 diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=110 Inclusion criteria: T2DM WHO 1999; insulin resistance HOMA-IR criteria; TCM diagnosis criteria China 2006, TCM differentiation: qi and yin deficiency, qi and blood stagnation Exclusion criteria: have diabetes ketosis, ketoacidosis and infections, pregnancy diabetes, hyperthyroidism or hepatitis and other diseases which can lead to

	hyperglycemia within 1 month; psychotic and senile dementia cannot cooperate; severe heart, brain, liver, kidney complications or severe primary complications; pregnancy or breastfeeding; long-term or current use insulin	
Interventions	Number of study centres: 1 Location: China Setting: outpatients and inpatients in TCM hospital Intervention: basic treatment: diet control and exercise therapy and oral intake of hypoglycemic western medicine: metformin, sulfonylurea , acarbose or glipizide Observation group: TCM prescription of supplement qi, nourish yin and active blood circulation (Huangqi, Danggui, Shanyao, Sangbaipi, Snagye, Sangzhi, Chishao, Dilong) on the base of basic treatment Control group: basic treatment	
Outcomes	FBG, 2hBG, FINS, HOMA-IR, blood fat and blood coagulation (PT, APTT, Fib, TC, TG) of treatment group was distinctly improved compared with that of control group No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 3 months Duration of Follow-up: not reported Run-in period: stop other TCM medicine over 2 weeks	
Stated aim of study	“To study the therapeutic effect of integrated use of Chinese and Western medicine on the improvement of insulin resistance in patients with both deficiency of vital energy and yin and blood stasis in patients of type 2 diabetes”	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study



Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on sex, age, disease course, medical condition. Other aspects of bias were unclear

Deng HL 2012

Clinical observation of Tangwei capsule combined with Metformin in treatment of patients with Type 2 Diabetes Mellitus

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 5:6
Participants	Ethnic: Chinese n=110 (50 in control group, 60 in treatment group) Inclusion criteria: T2DM WHO 1999; TCM diagnosis criteria China 1993 Exclusion criteria: severe kidney dysfunction, diabetes combine with ketoacidosis, insulin resistance patients and pregnancy or breastfeeding
Interventions	Number of study centres: 1 Location: China Setting: outpatients in TCM hospital Intervention: both two groups have diet control and diabetes education and other secondary treatment Control group: metformin hydrochloride tablets orally intake

	Observation group: TCM prescription Tangwei capsule (Huangqi, Xiyangshen, Huangjing, Tianhuafen, Gegen, Huanglian, Danshen) on the basis of control group	
Outcomes	<p>The total effective rate in treatment group was higher than that in control group.</p> <p>FPG, 2hPG, HbA1c, TG, BMI, hemorheology index: whole blood viscosity, plasma viscosity, platelet adhesion rate and LDL-C were all more significantly decreased after treatment and the treatment group has better clinical effect compared to control group</p> <p>3 cases have nausea in treatment group, 4 cases have stomach discomfort and all relieve without intervention. No kidney function damage after the treatment have been observed in both groups</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	"To observe the clinical effect of Tangwei capsule combined with metformin in treatment of patients with type 2 diabetes mellitus "	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into two groups"
Allocation concealment (selection bias)	Unclear risk	It only mentioned in the trial that "patients were randomly divided into two groups"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study

Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Zhang YL 2012

Pei Ruixia’s Modified Er Dong Tang Combined with Western Medicine Therapy to treat Type 2 Diabetes of Lung and Kidney Qi Yin Deficiency Randomized Controlled Study

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=80 Inclusion criteria: T2DM WHO 1999; DM clinical symptoms + random blood sugar $\geq 11.1$ mmol/L or FPG $\geq 7.0$ mmol/L or OGTT 2hPG $\geq 11.1$ mmol/L; age:30-70 years old; informed and signed consent Exclusion criteria: age < 30 years or > 70 years old; cannot take medicine according to prescription and hard to judge treatment effect; allergic constitution or allergy to ingredients of study drugs; no enough data to support therapeutic effects and safety; use others drug which influence the treatment
Interventions	Number of study centres: 1 Location: China Setting: inpatients in TCM hospital Intervention: both groups have conventional therapy: diabetic die, exercise and lifestyle, blood pressure, blood glucose, expansion of the crown etc. Control group: pioglitazone capsule, metformin enteric coated tablets Observation group: TCM prescription modified Er Dong Tang (Tiandong, Maidong, Tianhuafen, Huangqin, Zhimu, Gancao, Beishashen, Heye) on the basis of control group

Outcomes	Treatment group is more effective than the control group in clinical effects. FPG, 2hPG and HbA1c were significantly lower but no significant difference between two groups No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 3 months Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	“Observe the efficacy of Pei Ruixia’s Modified Er Dong Tang combined with western medicine therapy to treat lung and kidney qi yin deficiency pattern type 2 diabetes”	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “randomized parallel controlled is used and patients were randomly divided into two groups by random number table”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “randomized parallel controlled is used and patients were randomly divided into two groups by random number table”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference

		was found between groups on demography data and clinical features (sex, age, and disease course). Other aspects of bias were unclear
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Lu PY 2013

Clinical Research of combined Traditional Chinese and Western Medicine in the Treatment of Type 2 Diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=128 Inclusion criteria: T2DM, age:31-77 years old; others not described Exclusion criteria: not described
Interventions	Number of study centres: 1 Location: China Setting: inpatients in hospital Intervention: control group: oral intake metformin and glipizide Observation group: TCM hypoglycemic 1 (no mention of detailed herbs) based on control group
Outcomes	FPG, 2hPG, and HbA1c are all significantly decreased after treatment and much lower in treatment group. hospitalization days and cost are also lower in treatment group 4 cases in control group and 3 cases in experimental group had hypoglycemic symptom in the early stage of treatment and it had disappeared after had some food. No information was reported about liver and kidney function. Outcomes were assessed at baseline and trial completion
Study details	Duration of intervention: 12 weeks Duration of Follow-up: not reported Run-in period: not described
Stated aim of study	"To explore the clinical curative effect of combined traditional Chinese and western medicine in the treatment of type 2 diabetes"

Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that "patients were randomly divided into control group and experimental group by using random number table method"
Allocation concealment (selection bias)	low risk	It mentioned in the trial that "patients were randomly divided into control group and experimental group by using random number table method"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Xie PF 2009

The clinical research on treatment of type 2 diabetes mellitus by western medicine combining with traditional Chinese medicine

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
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Participants	<p>Ethnic: Chinese n=60</p> <p>Inclusion criteria: T2DM WHO 1999; therapeutic effects are not ideal with western medicine of sulfonylurea, metformin or alpha glucosidase inhibitor; TCM differentiation: qi and yin deficiency with abundance heat</p> <p>Exclusion criteria: combined with severe acute diabetes complication</p>	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients or inpatients in TCM hospital</p> <p>Intervention:</p> <p>Treatment group: TCM prescription Jinqijiangtangpian (Huangqi, Huanglian, Jinyinhua) on the basis of control group</p> <p>Control group: dietary and exercise therapy + western medicine: sulfonylurea, metformin or alpha glucosidase inhibitor</p>	
Outcomes	<p>FBG, 2hPBG, HbA1C, TC and TG in treatment group were significantly lower than that in the control group. No difference found in fasting insulin, C peptide. 2h postprandial insulin and C peptide rose. HOM A-<math>\beta</math> rose, HOMA-R declined.</p> <p>Liver, kidney function, blood and urine routine examination were measured for adverse effect. No abnormal was observed from above test</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To investigate the effect of western medicine combining with traditional Chinese medicine on patients with T2DM and function of islet <math>\beta</math> cell”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Blinding of participants and personnel (performance bias)	Unclear risk	The information was not reported in this study

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on disease course, age, sex, blood sugar, HbA1C and insulin. Other aspects of bias were unclear

Gao ZT 2015

Clinical Efficacy of Yupujiangtang Decoction in treatment of 50 Patients with T2DM

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 2:3
Participants	Ethnic: Chinese n=50 (20 in control group, 30 in treatment group) Inclusion criteria: T2DM WHO 1999: DM clinical symptoms plus random blood sugar $\geq 11.1$ mmol/L or FPG $\geq 7.0$ mmol/L or OGTT2hPG $\geq 11.1$ mmol/L; TCM differentiation China 2002 : qi and yin deficiency; 31-72 years old; informed and signed consent Exclusion criteria: type 1 diabetes; diabetes with severe heart, brain, kidney and retinal diseases; tumour and cancer patients; pregnant and breastfeeding diabetes; allergy to the study drugs.
Interventions	Number of study centres: 1 Location: China Setting: outpatients or inpatients in TCM hospital Intervention: diet control and rational exercise



	<p>Treatment group: TCM prescription Yupujiangtang decoction (Renshen, Huangqi, Huanglian, Qumai, Gualougen, Shanyao, Fangji, Fuling, Gouqizi, Zexie, Cijili, Yuzhu, Wubeizi, Nvzhenzi, Yvmixv) on the basis of control group</p> <p>Control group: Novolin 50 R Penfill injection and take metformin tablets</p>	
Outcomes	<p>Blood glucose level (FPG, OGTT2h, GHbA1c) had significant difference and the total effective rate of TCM syndrome was 95%</p> <p>No detail information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 8 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To observe the clinical efficacy and safety of Yupujiangtang decoction in treatment of patients with type 2 diabetes mellitus”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were divided into treatment group and control group by random number method”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were divided into two treatment group and control group by random number method”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study

Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Shu Q 2013

Dan Melon Decoction in Treating phlegm and Blood Stasis Type of Type 2 Diabetes: clinical Analysis of 50 Cases

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=100 Inclusion criteria: T2DM ,TCM differentiation: phlegm stagnation; age:43-75 y, disease course 1-17 year Exclusion criteria: not described
Interventions	Number of study centres: 1 Location: China Setting: patients in hospital Intervention: Observation group: TCM prescription Dan melon decoction (Danshen, Gualou, Xiebai, Chuanxiong, Danggui, Chishao, Banxia) on the basis of control group Control group: conventional treatment of western medicine: metformin sustained-release tablets and /or rosiglitazone with insulin
Outcomes	FBG, 2hPG, HbA1C, TC, TG, LDL-C and HDL-C decreased in observation group compared with the control group with significant difference. No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion
Study details	Duration of intervention: 90 days Duration of Follow-up: not reported

	Run-in period: not described	
Stated aim of study	"Effect of Chinese medicine in the treatment of type 2 and application value"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that "patients were divided into observation group and control group by random number method"
Allocation concealment (selection bias)	low risk	It mentioned in the trial that "patients were divided into two observation group and control group by random number method"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Sun H 2013

Modified Lianmei Granule Treatment for Type 2 Diabetes with Obesity in Early Satage

Methods	<p>Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone</p> <p>Randomisation ratio: 1:1</p>
Participants	<p>Ethnic: Chinese n=60</p> <p>Inclusion criteria: T2DM China 1994 and combine with obesity: BMI <math>\geq 25</math> kg/m<sup>2</sup>; TCM differentiation: qi and yin deficiency, phlegm and turbid stagnation; cases which are not in exclusion criteria</p> <p>Exclusion criteria: not meet above diagnostic criteria; age: &lt;18y, &gt;65y; pregnancy or breastfeeding; TCM herb and metformin, ARB allergy; have severe heart, liver, kidney complications or combine other severe primary diseases, psychosis; have diabetes ketoacidosis, hypertonicity coma and combine with infections within one month; type 1 diabetes</p>
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients and inpatients in TCM hospital</p> <p>Intervention:</p> <p>treatment group: TCM prescription modified Lianmei granule (Huanglian, Renshen, Wumei, Dahuang, Maidong, Sheng Dihuang, Shanzhuyu, Danshen, Cangzhu) on the basis of control group</p> <p>control group: diet control and exercise therapy + oral intake western medicine: raigor column nai</p>
Outcomes	<p>The improvement of the clinical symptoms and weight loss in treatment groups for obese patients with type 2 diabetes with high blood sugar, high cholesterol are better than that in control group.</p> <p>No detail information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>
Stated aim of study	<p>“To observe modified Lianmei granule the clinical curative effect of early treatment of obesity with type 2 diabetes”</p>
Risk of bias	

Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Gao SQ 2015

Clinical Application Study of Yiqi yangyin huoxue Method in Type 2 Diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=100 Inclusion criteria: T2DM WHO, FBG $\geq$ 7mmol/L, 2hPG $\geq$ 11.1mmol/L, diagnosis as type 2 diabetes by laboratory test. TCM diagnostic criteria China 1992, TCM differentiation : qi and yin deficiency , blood stasis

	Exclusion criteria: diabetes ketoacidosis and severe infection, hyper thyroidism or hepatitis or other diseases which can cause hyperglycemia; have severe complications with heart, brain, liver, kidney and so on; pregnancy and breastfeeding	
Interventions	Number of study centres: 1 Location: China Setting: inpatients in TCM hospital Intervention: experimental group: yiqi yangyi huoxue herbal treatment programs (Huangqi, Taizishen, Danshen, Mudanpi, Suoyanghua, Shanyao, Sheng Dihuang, Wuweizi, Hesouwu, Huangjing, Dahuang) on the basis of control group control group: extension of diabetic knowledge, dietary and exercise therapy auxiliary metformin	
Outcomes	Both groups have FBG, 2hPG and GHbA1c under control. The experimental group had significant statistical difference in the changed improve the efficacy of TCM symptoms compare to control group No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 4 months Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	"To explore the effects of Yiqi yangyi huoxue method of type 2 diabetes, summarize new clinical thinking"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into experimental group and control group"
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into experimental group and control group"
Blinding of participants and personnel (performance bias)	Unclear risk	The information was not reported in this study

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	No clear information mentioned in the trial that "no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Jia QL 2014

Clinical observation of 45 cases of Qingreyiqi decoction compatibility in the treatment of type 2 diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=90 Inclusion criteria: T2DM WHO, voluntary to the study and signed consent form, first diagnosed with type 2 diabetes, Age: 53-67 years Exclusion criteria: not described
Interventions	Number of study centres: 1 Location: China Setting: inpatients in TCM hospital Intervention: Observation group: oral Qingreyiqi decoction Sheng Dahuang, Sheng Huangqi, Shanyao, Gegen, Danshen, Sheng Dihuang, Sheng Huangqi, Gouqizi, Chishao, Danggui, Zhimu, Chuanxiong, Tianma) on the basis of control group

	Control group: conventional treatment: health education, dietary and exercise therapy and conventional oral hypoglycemic agents like metformin etc.	
Outcomes	<p>Total effective rate of observation group was apparently higher than the control group. The fasting blood glucose ( FBG), 2 hours postprandial blood glucose (2hPG), glycosylated haemoglobin ( GHbA1c), and blood lipid index (TG, TC, LDL-C0 of two group were obviously decreased, but the observation group decreased more significantly.</p> <p>Blood routine examination, liver and kidney function were supervised to measure adverse effect of drug. No abnormal was observed in blood routine examination, liver and kidney function. One case had nausea and vomiting.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	"To discuss the efficacy and safety of the Qingreyiqi decoction compatibility in the treatment of type 2 diabetes"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that "patients were divided into observation group and control group by random file number method"
Allocation concealment (selection bias)	low risk	It mentioned in the trial that "patients were divided into observation group and control group by random file number method"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study



Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on sex, age, disease course, FBG and blood lipid. Other aspects of bias were unclear

Zhang XL 2013

Clinical Observation of traditional Chinese Medicine Combing with Insulin on Treating 38 Cases of Asymptomatic Type 2 Diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=74 Inclusion criteria: T2DM China 2012, asymptomatic type 2 diabetes, agree with insulin treatment; age: 28-76y, average age 54.3 y; average FBG=13.4mmol/L (treatment group), 13.1mmol/L (control group), average blood sugar after three meals=18.4mmol/L (treatment group), 17.9mmol/L (control group) Exclusion criteria: not described
Interventions	Number of study centres: 1 Location: China Setting: inpatients in TCM hospital Intervention: treatment group: TCM prescription Erzhi Siwu decoction (Nvzhenzi, Hanliancao, Sheng Dihuang, Chishao, Chuangxiong, Danggui, Huanglian, Gegen, Huangqi, Tianhuafen and add Shigao, Xuanshen, Dahuang, Zhimu, Shanzhuyu,

	Sangpiaoxiao, Xianlingpi, Fuling, Baizhu, Dangshen, Cangzhu based on syndrome differentiation) on the basis of control group control group: conventional diabetes health education, diabetes diet and insulin therapy	
Outcomes	Fasting blood glucose was controlled within 3.9-7mmol/L and postprandial blood glucose 2 hours was less 10mmol/L, observing the difference of the amount of insulin and incidence of hypoglycemia between two groups. The incidence of hypoglycemia of the treatment group was lower than the controlled group. No detail information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 3 months Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	"To observe the curative effect of combining traditional Chinese medicine and insulin to treat asymptomatic type 2 diabetes"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into two groups"
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into two groups"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study

Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Jiang YC 2004

Clinical observation on Combination of Chinese Medicine and Western Medicine for the Treatment of 51 Cases of Type 2 Diabetes Mellitus

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 37 in control group, 51 in treatment group
Participants	Ethnic: Chinese n=88 Inclusion criteria: T2DM WHO 1999; diagnosed with type 2 diabetes after blood sugar, urine sugar and insulin function test; can follow up according to doctor's advice, informed and signed consent Exclusion criteria: combine with nephrosis, ketoacidosis and other severe complications
Interventions	Number of study centres: 1 Location: China Setting: outpatients or inpatients in hospital Intervention: treatment group: TCM prescription compound hypoglycemia decoction (Huangqi, Shanzhuyu, Renshen, Jiegeng, Gegeng, Yuzhu, Nvzhenzi, Sheng Dihuang, Shanqifen, Gancao, and add Zhimu for thirsty, Digupi for wasting, Sangpiaoxiao for diuresis) on the basis of control group control group: oral intake gliclazide plus strict diet control
Outcomes	Treatment group had better improvement in clinical effects and glucose metabolism (FBG, PBG, 24h urine blood sugar) No adverse effect was observed in both groups during the treatment

	Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 2 months Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	"To discuss the curative effect of combining traditional Chinese medicine and western medicine to treat type 2 diabetes"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds like age, sex and disease course etc. Other aspects of bias were unclear

Clinical observation on 30 Cases of Type 2 Diabetes Mellitus Treated with the Method of Relieving Liver and Reinforcing Spleen

Methods	<p>Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone</p> <p>Randomisation ratio: 1:1</p>
Participants	<p>Ethnic: Chinese n=60</p> <p>Inclusion criteria: T2DM ADA 1999, TCM diagnostic criteria China 2002, TCM differentiation: liver stagnation and spleen deficiency; age: 18-70 years with both sex; no distinct diabetic acute and chronic complications; no insulin treatment before, no herb treatment and medicine which affect blood lipid before 2 weeks of study</p> <p>Exclusion criteria: type 1 diabetes and diabetes with special causation, pregnant diabetes; pregnancy, breastfeeding and allergy to the study drugs and not suitable to the study; combine with cardiovascular, renal, hemopoietic system and other severe primary diseases, psychosis; have diabetes acute complications within recent one month</p>
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients and inpatients in TCM hospital</p> <p>Intervention:</p> <p>Basic treatment: life style regulation and diet therapy; control general calorie intake; insist rational aerobic exercise, prevent or reduce obese, maintain healthy weight</p> <p>Treatment group: TCM prescription: smoothing the liver and strengthening the spleen decoction (Sheng Huangqi, Shanyao, Fuling, Yiyiren, Chaihu, Baishao, Shanyurou, Suanzaoren, Gegen, Sangye) on the basis of control group</p> <p>Control group: basic treatment + conventional treatment: oral intake metformin enteric coatel tablets or acarbose</p>
Outcomes	<p>There is significant difference between treatment group and control group in glucose and lipid acid level (FBG, 2hPPG, HbA1c), insulin resistance index ( IRI ) and traditional Chinese clinical symptoms</p>

	Blood , urine, and stool routine examination, liver and kidney function test were measure for adverse effect, and no abnormal and adverse effects were observed during the treatment Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 8 weeks Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	"To observe the effect of treatment of smoothing the liver and strengthening the spleen with type 2 diabetes in clinic"	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into two groups"
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into two groups"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds like age, sex and disease course etc. Other aspects of bias were unclear

## Clinical Observation of Traditional Chinese Medicine Coptis Chinensis Treatment of Type 2 Diabetes Mellitus

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=75 Inclusion criteria: T2DM WHO 1999; have never used other hypoglycemia medicine within half month before the study; informed and signed written consent before the study Exclusion criteria: FBG $\geq$ 14mmol/L and/or 2hPBG $\geq$ 18mmol/L; liver and kidney function distinct abnormal; younger than 30years; BMI $\geq$ 30kg/m <sup>2</sup>
Interventions	Number of study centres: 1 Location: China Setting: patients in TCM hospital Intervention: observation group: TCM prescription: coptis granules on the basis of control group control group: oral intake metformin tablet
Outcomes	FBG and 2hPBG were statistically significant lower in observation group than control group after 30 days treatment. The improving of insulin resistance and abnormal metabolism of lipid in control group were ineffective; observation group has better clinical effect in improving insulin resistance and recovery of islet function and significantly improved in patients with dyslipidemia. No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion
Study details	Duration of intervention: 60 days Duration of Follow-up: not reported Run-in period: not described
Stated aim of study	"To investigate the clinical effect of coptis chinensis in treating type 2 diabetes mellitus"
Risk of bias	

Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into observation group and control group by using random number table method”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into observation group and control group by using random number table method”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds of sex, age and disease course. Other aspects of bias were unclear

Ye LF 2013

Effect of Sanhuang Tang on Insulin Resistance Index and Inflammatory Factors of Obese Type 2 Diabetes



Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=69 Inclusion criteria: T2DM WHO 1999 diabetes diagnostic criteria: clinical symptoms + anytime blood sugar $\geq$ 7.0mmol/L; OGTT2h $\geq$ 11.1mmol/L; TCM differentiation: phlegm hot junction; BMI $\geq$ 25kg·m <sup>-2</sup> ; age: 18-75 year; informed consent Exclusion criteria: not accord with inclusion criteria; type 1 diabetes, pregnant diabetes and other types of diabetes; have diabetes ketoacidosis, diabetes hyperglycemia hypertonicity status and other acute complications; combine with heart, brain, liver, kidney and other severe diseases; have used insulin and other similar treatment; pregnancy or breastfeeding; not good at comply with treatment or psychosis
Interventions	Number of study centres: 1 Location: China Setting: outpatients and inpatients in TCM hospital Intervention: Sanhuang tang group: plus Sanhuang tang (Huanglian, Huangqin, Dahuang) on the basis of control group Western medicine group: lifestyle intervention plus metformin
Outcomes	Sanhuang tang group is statistically significant in improving clinical symptoms, glucose and lipid metabolism and insulin resistance and reduce the level of inflammatory factors (FBG, 2hPBG, HbA1C, TC, TG, TNF- $\alpha$ , IL-6, HOMA-IR) compare to western medicine group blood, urine, stool routine examination and liver, kidney function test had been taken, but no other details were mentioned about adverse effect. Outcomes were assessed at baseline and trial completion
Study details	Duration of intervention: 3 months Duration of Follow-up: not reported Run-in period: not described
Stated aim of study	“To observe the efficacy of Chinese herbal formula Sanhuang tang in treating obese type 2 diabetes”
Risk of bias	

Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly distributed into Sanhuang tang group and western medicine group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly distributed into Sanhuang tang group and western medicine group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on age, sex and disease course etc. Other aspects of bias were unclear

Cai Z 2015

Effects of Fructus Schisandrae Decoction on the Changes of Serum IL-2 and IL-6 of Patients with type 2 Diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
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Participants	<p>Ethnic: Chinese n=88</p> <p>Inclusion criteria: up-to-date diabetes diagnostic criteria: polydipsia, polyuria, polyphagia and no other reasons weight loss plus one of following: random blood sugar<math>\geq</math>11.1mmol/L; FBG<math>\geq</math>7.0mmol/L; OGTT2h<math>\geq</math>11.1mmol/L. on the basis of above plus one of followings can be diagnosed as T2DM: low insulin level, insulin resistance. Age<math>\leq</math>70y; involuntary to the study and signed consent and meet with ethical criteria</p> <p>Exclusion criteria: not meet with T2DM diagnostic criteria; severe liver and gallbladder disease; malignant tumour; age <math>\leq</math>40y, <math>\geq</math>70y; have mental disease</p>	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients and inpatients in TCM hospital</p> <p>Intervention:</p> <p>Experimental group: TCM herb Schisandra chinensis (Wuweizi) on the basis of control group</p> <p>Control group: conventional treatment: oral intake of Metformin Hydrochloride Capsules</p>	
Outcomes	<p>The cytokines (IL-2 and IL-6 levels) were improved in both groups after treatment and more statistically significantly improved in experimental group. The level of glycated haemoglobin (HbA1c) was reduced in both groups after treatment and the decrease were more statistically significant in experimental group than control group. Level of blood lipid (TC, TG and LDL) were improved and the improvement was more statistically significant in experimental group</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To investigate the clinical curative effect of Fructus Schisandra Decoction on type 2 diabetes mellitus disease and the change of serum IL-2, IL-6 levels”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement

Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Guan X 2006

Influence of Liuweidihuang Pill and Ginkgoibca Leave to the Lipotoxicity and Insulin Resistance in Early Time of Type 2 Diabetes Mellitus

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=104 Inclusion criteria: T2DM WHO 1999, polydipsia, polyuria, weight loss and repetitive infection, random blood sugar $\geq$ 11.1mmol/L; FBG $\geq$ 7.0mmol/L; OGTT2h $\geq$ 11.1mmol/L; TCM differentiation: internal heat from yin deficiency and blood stasis in meridians; age: 30-70 years; have no distinct diabetes complication, diagnosis with diabetes

	<p>over three months; BP≤180/110mmHg; BMI≤30; have used no more than two kinds of hypoglycemic medicine and blood sugar is under control when enrolled with the study; informed consent and voluntary to the study</p> <p>Exclusion criteria: not meet with inclusion criteria; type 1 diabetes and diabetes due to special reason and pregnant diabetes; diabetes severe acute complication like ketoacidosis, diabetes hypertonicity; vascular complications: myocardial infarction, cerebrovascular accident, lower limb angionosis; severe heart, liver, lung, kidney, blood or other life-threatening disease like tumor or AIDS; pregnancy, breastfeeding; easy lost follow-up; current use medicine affect blood sugar, BP and blood lipid; in other study currently</p>
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients in TCM hospital</p> <p>Intervention:</p> <p>Basic treatment: dietary and exercise therapy + no more than two kinds of hypoglycemia medicine: insulin inhibitor, alpha glucosidase inhibitor, metformin, insulin, glimepiride</p> <p>experimental group: basic treatment plus TCM herb Liuweidihuang capsule and Yinxyngye tablet</p> <p>control group: basic treatment plus TCM herb placebo</p>
Outcomes	<p>TC, TG, LDL-C, FFA and TNF-α had better control in experimental group than control group with FFA and TNF- α has statistical difference. No difference for FBG, 2hPBG, and HbA1c in both groups before and after treatment. Clinical symptoms, FINS and IR changes also have no statistically significance.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>
Study details	<p>Duration of intervention: 6 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>
Stated aim of study	<p>“evaluate the influence and clinical application of Jinqi hypoglycemic tablet on vascular endothelial cells active factor of patients with diabetes mellitus by observing the change of correlation factor about vascular endothelial cells damage before and after therapy ”</p>

Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into experimental group and control group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into experimental group and control group”
Blinding of participants and personnel (performance bias) All outcomes	low risk	Double-blinded and placebo controlled for both researcher and patients
Blinding of outcome assessment (detection bias) All outcomes	low risk	Double-blinded and placebo controlled for both researcher and patients
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	low risk	The protocol of the trial was strictly double-blinded for both researcher and patients
Other bias	low risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds of sex, age and disease course. SBP, DBP, FBG, HbA, TC, TG, ALT, Cr, FFA, TNA, IR and TCM symptom score are also have no statistically significant difference in both groups before study.

Shen LX 2007

Study on improvement of islet  $\beta$ cell function in patients with type 2 diabetes by integrative Chinese and Western medicine

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1:1
Participants	Ethnic: Chinese n=65 (group A:23, group B:25, group C:24) Inclusion criteria: T2DM WHO 1999, age ≤65y, have no pharmacotherapy within 3 months; FBG, PG2h and HbA1c are all increase (FBG≤7.0mmol/L, PG2h≤11.1mmol/L, HbA1c≥6.5%) Exclusion criteria: stress status, severe liver and kidney dysfunction, have disease which affect glucose metabolism
Interventions	Number of study centres: 1 Location: China Setting: patients in medical college hospital Intervention: diabetes health education, diet control and proper exercise therapy for all three groups Group A: sulfonylurea oral intake Group B: insulin Group C: insulin + TCM prescription Dachaihu decoction (Chaihu, Huangqin, Zhishi, Huanglian, Dahuang, Banxia)
Outcomes	After treatment, the damaged islet β cell function was not improved and the secretive peak value of C2 peptide was still low and delayed in group A. but it shifted earlier and indicated a certain degree of improvement and recovery of islet β cell function in group B and C with statistically significant in Group C. FBG, P2BG and HbA1c decreased after treatment in three groups with more decreased in Group B and C and Group C was more significant. No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion
Study details	Duration of intervention: 1 year Duration of Follow-up: not reported Run-in period: not described
Stated aim of study	“evaluate the influence of eliminating heat by nourishing Yin and activating blood and removing stasis TCM on inflammatory factor of type 2 diabetes in earlier period ”
Risk of bias	

Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into 3 groups”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into 3 groups”
Blinding of participants and personnel (performance bias) All outcomes	unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	7 cases lost follow up in three groups (2 in Group A, 3 in Group B and 2 in Group C) with same reasons as lost contact with across three groups.
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Liu HZ 2007

Effects of Danzhi Jiangtang Capsule on  $\beta$ -cell Function of pancreatic Islet in Type 2 Daibetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=62 Inclusion criteria: T2DM WHO 1999; TCM differentiation China Zhengzhou conference 1986: qi deficiency, yin deficiency, and China Beijing conference 1988: blood stasis. Age: 56-87year;



	Exclusion criteria: not described	
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients and inpatients in TCM university hospital</p> <p>Intervention:</p> <p>Conventional hypoglycemia treatment: sulfonylurea, glucosidase inhibitor or insulin treatment; hypertension and coronary disease treatment</p> <p>Treatment group: conventional treatment + TCM Danzhi Jiangtang Capsules oral intake (Taizishen, Sheng Dihuang, Tusizi, Mudanpi, Zexie, Shuizhi)</p> <p>Control group: conventional treatment + rosiglitazone</p>	
Outcomes	<p>Comparing with those of control group, the score of TCM syndrome, indexes of FBG, 2hPG, blood insulin (empty, 30min, 2h and 3h), ISI, Homa-IR, Homa-B were significantly improved (<math>P &lt; 0.05</math>, <math>P &lt; 0.01</math>).</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 2 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To observe the effects of Danzhi Jiangtang Capsules on B-cell function of pancreatic islet in patients with type 2 diabetes and explore its contribution to treating and delaying the development of type 2 diabetes.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general baseline and clinical backgrounds of sex, age, disease course, score of TCM syndrome, BMI, FPC and HbA1c. Other aspects of bias were unclear

Shi XD 2015

The curative effect observation of Xiaoke pill and glibenclamide treatment of type 2 diabetes mellitus

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=100 Inclusion criteria: T2DM WHO 1999; age: 46-62, all cases ≤65 years; 24 cases combined with hypertension. FPG mean= 8.4-8.5mmol/L, 2hPG mean=12.5-12.8mmol/L, HbA1c mean=7.4-7.6%; both groups have DM clinical symptoms; no insulin treatment before, liver and kidney function normal, whole blood test normal Exclusion criteria: diabetes complication; combined coronary heart disease and brain infarction; weak constitution; hypocortisonism; hypoanteriorpituitarism
Interventions	Number of study centres: 1 Location: China Setting: inpatients in hospital

	<p>Intervention: both groups have general treatment: quit smoking and alcohol, lifestyle intervention and dietary plan, regular exercise and exercise therapy</p> <p>Treatment group: glibenclamide and aspirin therapy oral intake</p> <p>Control group: Xiaoke pill(Huangqi, Dihuang, Shanyao, Wuweizi, Tianhuafen, Gegen, Yumixu) and aspirin therapy oral intake</p>	
Outcomes	<p>The symptoms of diabetes were significantly improved with 56% in treatment group and 82% in control group respectively.</p> <p>Peripheral blood sugar, urine sugar, urine ketone bodies, urine protein and blood picture were observed for measurement of efficacy.</p> <p>BP, liver and kidney function, fundus examination was measures and no abnormal was observed. 4 cases in treatment group had hypoglycemic reaction and 2 cases out of 4 had mild nausea and vomiting. No any adverse effects were observed in control group.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 90 days</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To discuss the effect of Xiaoke pill and glibenclamide treatment of type 2 diabetes mellitus”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias)	Unclear risk	The information was not reported in this study

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear

Lan KJ 2011

23 Cases of the Traditional Chinese Medicine Combined Insulin Treatment for Type 2 Diabetes of the Clinical Effect of analysis

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=43 Inclusion criteria: T2DM WHO 1999; need insulin treatment; average age: 58.7±6.4 year, average disease course: 5.4±2.6, BMI: 23.1±3.3 kg/m Exclusion criteria: not described
Interventions	Number of study centres: 1 Location: China Setting: inpatients in army hospital Intervention: dietary control and exercise therapy Combined group: insulin treatment + TCM herb decoction (Huangqi, Dannanxing, Chuanxiong, Gualou, Fuling, Zexie, Xiangfu, Shu Dihuang, Huanglian, Gegen, Danshen) Control group: insulin treatment
Outcomes	Outcomes were assessed at baseline and trial completion at 2 weeks for FPG, 2hPBG, and at 3 months for HbA1c

	<p>Mean 2h PBG and FBG decreased significantly at endpoint in the combination group compared with control group (<math>P &lt; 0.05</math>). The HbA1C excursion were significant lower after 3 months (<math>P &lt; 0.05</math>)</p> <p>No information was reported in terms to adverse effect in this study</p>	
Study details	<p>Duration of intervention: 3months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To compare the level of HbA1c in insulin-requiring patients with diabetes (T2DM) treated twice daily with Chinese herbal remedies combined with insulin.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general

		backgrounds of age, sex, disease course, BMI and so on. Other aspects of bias were unclear
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Yang LQ 2010

Clinical observation of Dangua Prescription on Type 2 Diabetes Patients with long-term hyperglycosemia

	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 2:1
Participants	Ethnic: Chinese n=126 Inclusion criteria: T2DM WHO 1999; blood sugar control is not ideal for long time, HbA1C>7.5% last for one year; not included in exclusion criteria. TCM differentiation China 2002: phlegm dampness symptoms and blood stasis symptoms Exclusion criteria: pregnant or breast-feeding; severe heart, liver, kidney and brain complications, or combine other severe primary diseases; have diabetes ketosis, ketoacidosis, hypertonic coma and infections; not accord with TCM differentiation
Interventions	Number of study centres: 1 Location: China Setting: outpatients and inpatients in TCM university hospital Intervention: both groups have diabetes education, diet control and exercise therapy Treatment group: Dangua prescription (Danshen, Gualou, Chuanxiong, Chishao, Banxia, Xiebai) on the basis of control group Control group: insulin, hypoglycemia medicine: gliclazide, metformin and rosiglitazone, single or combined.
Outcomes	Compared with control group, 2hPG, HbA1C, c peptide, 2h postprandial C peptide, high shear viscosity of whole blood, low shear viscosity of whole blood, fibrinogen and cumulative score of symptoms were decreased (P<0.05). The average dosage of insulin in treatment group was less than that in control group (P<0.05). The total effective rate was 92.68% in the treatment group and 77.27% in control group with P<0.05 Liver and kidney function, ECG were measured before and after the treatment and no adverse effect or complication were observed in both intervention group

	Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 90 days Duration of Follow-up: not reported Run-in period: none	
Stated aim of study	"To observe the effect of Dangua prescription on type 2 diabetes patients with long-term hyperglycosemia."	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned that the "patients were randomly divided into control group and treatment group"
Allocation concealment (selection bias)	unclear risk	It only mentioned that the "patients were randomly divided into control group and treatment group"
Blinding of participants and personnel (performance bias) All outcomes	unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general background of sex, age, disease course, complications and so on. Other aspects of bias were unclear

Zhang YH 2008

Effect of Didang Tang on type 2 diabetes with insulin resistance

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=73 Inclusion criteria: T2DM WHO 1999, no sensitive to insulin treatment with high blood insulin level. age: 35-77 years Exclusion criteria: liver and kidney dysfunction, type 1 diabetes, tumor, hemopoietic system disease, psychotic, acute myocardial infarction, severe arrhythmia, acute heart failure or chronic heart dysfunction over grade three.
Interventions	Number of study centres: 1 Location: China Setting: patients in TCM hospital Intervention: treatment group: sulfonylurea, metformin and alpha glucosidase inhibitor routine treatment for 4 weeks and plus TCM formula Didang Tang (Dahuang, Taoren, Shuizhi, Mengchong) for 8 weeks control group: sulfonylurea, metformin and alpha glucosidase inhibitor routine treatment
Outcomes	After treatment, TC, TG, LDL-C, FBG, FINS and ISI in treatment group have decreased compared to control group and with statistical significant. Outcomes were assessed at baseline and trial completion Chest x-ray, blood and urine routine examination, liver and kidney function test have been measured for safety and no abnormal had been observed in terms to adverse effect related to study drugs. No complication and other severe adverse effects were observed during the intervention.
Study details	Duration of intervention: 8 weeks Duration of Follow-up: 12 weeks Run-in period: 4 weeks
Stated aim of study	“to observe the effect of Didang Tang on type 2 diabetes with insulin resistance and discuss the prevention and treatment of type 2 diabetes with TCM principle of moving blood and clearing stagnation ”
Risk of bias	



Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into experimental group and control group by computer random table method”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into experimental group and control group by computer random table method”
Blinding of participants and personnel (performance bias) All outcomes	unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds of sex, age and distribution of complications between both groups. Other aspects of bias were unclear

Ji LN 2013

Efficacy and Safety of Traditional Chinese Medicine for Diabetes: A Double-Blinded, Randomised, Controlled Trial

Methods	<p>Parallel randomised controlled, double blinded, multicentre non-inferiority clinical trial of Chinese herbal medicine with or without other pharmaceuticals compared with other pharmaceuticals alone</p> <p>Randomisation ratio: 1:1</p>
Participants	<p>Ethnic: Chinese n=800</p> <p>Inclusion criteria: drug naïve patients with BMI within 18kg/m<sup>2</sup>-28kg/m<sup>2</sup>; patients who received treatment with metformin at a stable dose ≥750mg/day for at least 3 months before screening with BMI within 18kg/m<sup>2</sup>-35kg/m<sup>2</sup>; stable body weight within at least 3 months before screening; poor glycemic control with FPG between 126-234mg/dl (7.0-13mmol/L) and HbA1c≥7.0% at screening.</p> <p>Exclusion criteria: FPG≥13mmol/L or HbA1c≥11%, more than 3 episodes of severe hypoglycemia within 6 months before screening, allergic to sulfonylureas or their ingredients, treatment with glucose-lowering agents other than metformin or insulin within 3 months before screening or with exogenous insulin for more than 1 week within 3 months before screening, a history of heart disease within 1 year before screening, a history of abnormal kidney function or serum creatinine levels reaching the upper limit of normal, ALT or AST≥2.5 times the upper limit of normal, suffering from acute or chronic hepatitis, haemoglobin disease or chronic anemia, or underlying conditions that could lead to poor complication.</p>
Interventions	<p>Number of study centres: 20</p> <p>Location: 19 participant centres in China and 1 participant centre in Queensland, Australia</p> <p>Setting: patients in hospitals</p> <p>Intervention: control diet and do exercise</p> <p>Drug naïve group: Xiaoke Pill (Radix Puerariae, Radix Rehmanniae, Radix Astragali, Radix, Trichosanthis, Stylus Zeae Maydis, Fructus Schisandrae Sphenantherar and Rhizoma Dioscoreae) in Xiaoke Pill arm, Glibenclamide in Glibenclamide arm</p> <p>Metformin group: Xiaoke Pill + Metformin in Xiaoke Pill arm, Glibenclamide + Metformin in Glibenclamide arm</p>
Outcomes	<p>Clinical and Biochemical measurements: HbA1c, FPG, C-peptide, hsCRP, adiponectin and lipids, LDL-C, HDL-C, triglyceride, liver function test, complete blood</p>

	<p>count, urine routine assay, kidney function test, twelve-lead ECG, physical examination;</p> <p>Outcome in drug naïve group: patients in the Xiaoke Pill arm were 38% less likely to have any hypoglycemia compared to those in the Glibenclamide arm. The average annual rate of hypoglycemia was 24% lower in patients treated with Xiaoke Pill. Patients in Xiaoke Pill arm were also 41% less likely to have a mild hypoglycemic episode compared to those in the Glibenclamide arm. All with statistically significant with above outcome.</p> <p>Outcome in Metformin Group: patients in Xiaoke Pill arm were 24% less likely to have any hypoglycemia compared to those in the Glibenclamide arm. The average annual rate of hypoglycemia was 62% lower in patients treated with Xiaoke Pill. All with statistically significant with above outcome.</p> <p>Safety and Efficacy outcomes were measured by incidence of hypoglycaemia, change in HbA1c level, change in fasting glucose level, <math>\beta</math>-cell function, insulin resistance levels; fasting lipid profiles and TCM symptoms score.</p> <p>No serious adverse event was reported during the study.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 48 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: 4 weeks</p>	
Stated aim of study	<p>“To establish the safety and efficacy of traditional Chinese medicine combined with glibenclamide to treat type 2 diabetes mellitus.”</p>	
Notes	<p>Randomised controlled trial with 2 arms</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “randomization was performed centrally and was concealed and stratified in blocks of four”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “randomization was performed centrally and was concealed and stratified in blocks of four”

Blinding of participants and personnel (performance bias) All outcomes	low risk	Double-blinded and placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	low risk	Double-blinded and placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 2 patients in TCM group early stopped.
Selection reporting (reporting bias)	low risk	The protocol of the trial was clear, so the possibility of selection outcome reporting could be examined by the review authors.
Other bias	unclear risk	The intervention groups were comparable, as it listed characteristics of the patients at baseline in the trial and no significant difference was found between groups on demographics and anthropometric characteristics as well as blood pressure, metabolic characteristics and lipids. Other aspects of bias were unclear

Chen ZH 2014

Treatment of Type 2 Diabetes Mellitus Patients of Qi-Yin Deficiency Phlegm-Stasis Inter-obstruction Syndrome by Jiangtang Xiaozhi Capsule and Pioglitazone Tablet: a Non-inferiority Randomized Controlled Trial

Methods	Randomised parallel controlled prospective clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=73 Inclusion criteria: T2DM WHO 1999, have diabetes history, FBG 7.0-11.1mmol/L or 2hPBG 11.1-16.6 mmol/L and blood sugar keep the same level after 2 weeks run-in-period; age 30-70 years old, both sex; have no insulin treatment before and good for

	<p>comply with therapy; informed and signed consent; TCM diagnostic criteria China 2002, TCM differentiation: qi- yin deficiency phlegm-stasis inter-obstruction syndrome</p> <p>Exclusion criteria: liver and kidney dysfunction; combine severe cardiovascular and hemopoietic system disease or other severe primary disease as well as psychosis; have diabetes ketoacidosis and other acute metabolism disorder within one month; pregnancy and breastfeeding; combine with severe infections in recent one month; allergic constitution; not comply in run-in period; have history of excessive drinking and drug taking; use Pioglitazone or patent herb which can affect the evaluation of the therapeutic effect</p>
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients in TCM hospital</p> <p>Intervention:</p> <p>Run-in period: dietary and exercise therapy under the supervisor of physician and nutritionist</p> <p>JTXZC group: TCM prescription: Jiangtang Xiaozhi capsule (Huangqi, Nuzhenzi, Lizhihe, Kunbu, Jianghuang, Huanglian)</p> <p>Pioglitazone group: Pioglitazone tablet</p>
Outcomes	<p>BW, BMI (waist circumference, hip circumference, waist-to-hip ratio), HbA1c, FBG or 2h PBG, TNF-<math>\alpha</math> and PAI-1 were lower after treatment in both groups. The level of NF-<math>\kappa</math>B was apparently lowed after treatment in Pioglitazone group, but also decreased in JTXZC group with statistical difference. The scoring of TCM symptoms improved after treatment in both groups with statistically significant in experimental group.</p> <p>Blood, urine and stool routine examination, liver and kidney function examination as well as ECG were measured before and after the study. No abnormal were observed in above test.</p> <p>I case in JTXZC group had nausea symptom after initial take the herb and better later change to taking herb after meal; 3 cases in Pioglitazone group had some mild adverse effects. No severe adverse reactions were observed in both intervention groups.</p> <p>Outcomes were assessed at baseline and trial completion</p>
Study details	<p>Duration of intervention: 8 weeks</p>

	Duration of Follow-up: every 2 weeks Run-in period: 2 weeks	
Stated aim of study	“To evaluate the efficacy and safety of Jiangtang Xiaozhi capsule in treating type 2 diabetes mellitus of qi- yin deficiency phlegm-stasis inter-obstruction syndrome and to observe its effect on inflammatory factors and fibrinolytic factors”	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into two groups by statistical software random digit table method ”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were randomly divided into two groups by statistical software random digit table method ”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors, except only mentioned full analysis set was adopted for the outcome
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds of sex, age, and disease course, distribution of

		complication in both groups and disease condition. Other aspects of bias were unclear
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Niu XX 2014

Clinical Observation of Panax Quinquefolium Hypoglycemic Pills on Treatment of Type 2 Diabetes

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=180 Inclusion criteria: T2DM WHO 1999, average age: 53.80±9.75, average disease course: 4.31 year Exclusion criteria: not described
Interventions	Number of study centres: 1 Location: China Setting: outpatients in TCM hospital Intervention: both groups have exercise therapy and diet control Experimental group: Panax quinquefolium hypoglycemic pills (Xiyangshen, Shu Dihuang, Sheng Dihuang, Maidong, Tiandong, Huangqi, Shihu, Zhiqiao, Zexie, Pipaye) oral intake Control group: Metformin Hydrochloride tablet oral intake
Outcomes	The improvement of clinical test result in experimental group was better than that in control group with statistically significant. HbA1c rate of experimental group was significantly increased, 2hPBG and FBG both decreased significantly. The total effects including clinical symptoms in experimental group are statistically higher than that in control group. No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion
Study details	Duration of intervention: 4 months Duration of Follow-up: not reported Run-in period: not described
Stated aim of study	"To observe the clinical effect of type 2 diabetes mellitus with the treatment of Panax quinquefolium Hypoglycemic pill"

Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into two groups”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds of disease course, age and sex. Other aspects of bias were unclear.

Song W 2014

Clinical Research of Chinese Medicine in Treating Patients with type 2 Diabetes

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=128



	<p>Inclusion criteria: T2DM WHO 1999, disease course within 5 years, have never taken any hypoglycemia drug and lipid decrease drug before 2 month of study; age: 25-80y; informed and signed consent</p> <p>Exclusion criteria: FBG&gt;10mmol/L, 2hPGB or random blood sugar&gt;15mmol/L; HbA1c&gt;10.0%; have recent distinct liver kidney dysfunction and infection, trauma, cardiovascular accident etc. stress status; combine with diabetic acute complications and pregnant diabetes or breastfeeding as well as potential pregnancy, hyperthyroid or other disease which lead to hyperglycemia and type 1 diabetes; possible allergy to study drug or have severe intestine absorption dysfunction</p>
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients and inpatients in TCM hospital</p> <p>Intervention:</p> <p>Basic therapy: diet, exercise and diabetic education</p> <p>Treatment group: basic therapy + TCM prescription based on syndrome differentiation (Kidney tonify:Gouji, Chuanxuduan, Nuzhenzi, Hanliancao; Nourish Qi and Yin: Bei Huangqi, Dihuang, Digupi; Soothe liver and regulate Qi: Chaihu, Baishao, Bohe, Yujin; clear heat and generate fluid: Shigao, Zhimu, Gegen, Liaoqiao; clear fu and reduce heat: Dahuang, Zhishi, Huomaren; nourish heart calm spirit: Yejiaoteng, Yuanzhi, Shuanzhaoren; clear ying cool blood: Mudanpi, Maidong, Xuanshen, Chishao; clear damp-heat: Cangzhu, Huangbai, Yiyiren, Cheqiancao, Mianyinchen, add Fuling, Chaobaizhu, Fabanxia, Shenqu for damp restrict spleen; add Laifuzi, Zhiqiao, Chuanxiaopu for stomach bloat; add Gualoupi, Xiebai for depressed chest; move blood to clear stasis: Danshen, Sanling, Ezhu, Zelan)</p> <p>Control group: basic therapy + acarbose</p>
Outcomes	<p>The total effective rate improved after treatment in both group without significant difference. The total effective rate in TCM symptoms improved and showing significant difference of better in treatment group. FBG, 2hPBG and HbA1c were significantly improved in both group. The BMI, AUCi, blood lipid (TC, TG, LDL-C, HDL-C) level in treatment group were significantly improved compared to control group.</p> <p>Blood routine examination, liver and kidney function were measured before and after treatment and no abnormal was observed. 16 case in control group had bloating and</p>

	diarrhoea and was under control without any impact on study. No adverse effects were observed in treatment group. Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 6 months Duration of Follow-up: 3 month Run-in period: not described	
Stated aim of study	"To observe the clinical efficacy on type 2 diabetes treated with professor FAN Guanjie's experienced prescription of Chinese medicine."	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that "patients were randomly divided into control group and treatment group by random number table"
Allocation concealment (selection bias)	low risk	It mentioned in the trial that "patients were randomly divided into control group and treatment group by random number table"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds"

		of sex, age and disease course. Other aspects of bias were unclear.
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Ye RQ 2014

Effect of Jianpi Zengmin Decoction on Insulin Resistance in Type 2 Diabetes Mellitus

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=100 Inclusion criteria: T2DM WHO 1999, HOMA-IR $\geq$ 2.8; TCM diagnostic criteria China 2002, obesity diagnostic criteria China 1997; age: 20-70 year, informed consent with the study and can complete the treatment, observation and examinations. Exclusion criteria: type 1 diabetes or other kinds of diabetes and pregnant diabetes; combine with acute diabetes complication; have severe heart, kidney and liver etc. complications, severe hypertension or combine other severe primary disease; pregnancy or breastfeeding, psychosis and potential allergy to the study drug; cannot comply with prescription, diet and exercise therapy and affect the treatment
Interventions	Number of study centres: 1 Location: China Setting: outpatients in TCM hospital Intervention: Basic treatment: diet therapy, exercise therapy and same type of hypoglycemic drug (apart from metformin etc. which may have relative allergy ingredients as the study herb) Treatment group: basic therapy + TCM prescription Jianpi Zengmin decoction (Dangshen, Fuling, Baizhu, Fabanxia, Chenpi, Huangqi, Danshen, Shanyao, Gegen, Shanzha, Chishao, Zhigancao) Control group: basic therapy + metformin hydrochloride
Outcomes	The total effective rate was 90% in treatment group with significant difference compare to 70% in control group. HOMA-IR, BMI, TG, CHOL, FBG and 2hPG were reduced significantly in both group. The difference of HOMA-IR and TG levels in treatment group compare to control group was statistically significant.

	No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 8 weeks Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	"To observe the effect of Jianpi Zengmin decoction on insulin resistance in type 2 diabetes."	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear.

## Therapeutic Effect of Middle-warming and Spleen-strengthening and Kidney-tonifying therapy for Type 2 Diabetes Mellitus

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 2:1
Participants	Ethnic: Chinese n=99 (Chinese medicine group 66, control group 33) Inclusion criteria: T2DM WHO 1999; 7.8mmol/L≤FBG≤13.9mmol/L and/or 11.1mmol/L≤2hPBG≤25mmol/L; FINS≥15mU/mL; have done dietary and exercise therapy for 2 weeks; age: 30-70 y Exclusion criteria: acute stress status like severe infection; severe liver and kidney dysfunction
Interventions	Number of study centres: 1 Location: China Setting: outpatients and inpatients in TCM hospital Intervention: diet and weight control plan Chinese medicine group: TCM prescription: middle-warming, spleen-strengthening and kidney-tonifying (Shu Fuzi, Sheng Huangqi, Ganjiang, Zhigancao, Hongshen, Rougui, Baizhu, Yunling, Shu Dihuang, Shanyurou, Huaishanyao, Wuzhuyu, Danggui, Zhuyizang) Control group: metformin tablet oral intake
Outcomes	After treatment, insulin sensitivity index and HDL-C were improved and FBG, 2hPG, HbA1c, TG, FINS, BMI decreased in the Chinese medicine group. The effect on lowering TG, FINS, BMI and improving efficacy of ISI, HDL-C was better in Chinese medicine group than that in control group with statistically significant. No examination was reported in terms to adverse effect in this study. It was only mentioned in the discussion that no complication or adverse effects were observed in Chinese medicine group. Outcomes were assessed at baseline and trial completion
Study details	Duration of intervention: 8 weeks Duration of Follow-up: not reported Run-in period: 2 weeks

Stated aim of study	“To observe the effect of middle-warming, spleen-strengthening and kidney-tonifying therapy on lowering glucose, regulating blood lipid, increasing insulin sensitivity and decreasing body mass index in type 2 diabetes mellitus patients.”	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were divided into Chinese medicine group and control group by random number table method”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were divided into Chinese medicine group and control group by random number table method”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Exclusion or losses were reported before the intervention, and the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on clinical backgrounds. Other aspects of bias were unclear.

Zhu HY 2012

The Chinese Medicine Syndrome Differentiation Treatment of Type 2 Diabetes with Insulin Resistance

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1	
Participants	Ethnic: Chinese n=80 Inclusion criteria: T2DM WHO 1999 with insulin resistance, TCM differentiation China 2004: yin deficiency with excess heat, qi and yin deficiency, yin and yang deficiency Exclusion criteria: combine with ketoacidosis, hyperosmolar coma, severe infection and other acute complications, or severe heart failure and other severe primary disease; heart rate increase no more than 30% after daily continuous exercise for half hour; secondary diabetes, psychosis; use insulin treatment	
Interventions	Number of study centres: 1 Location: China Setting: patients in TCM hospital Intervention: Observation group: TCM syndrome differentiation treatment (Sheng Dihuang, Maidong, Niuxi, Zhimu and Shigao for yin deficiency with excess heat; Taizishen, Huangqi, Huaishanyao, Xuanshen, Maidong, Shanzhuyu for Qi and Yin deficiency; Gan Dihuang, Shanyao, Shanzhuyu, Zexie, Fuling, Mudanpi, Paofuzi for Yin Yang deficiency) Control group: topiramate glibenclamide ketone	
Outcomes	Compared with the control group, the fasting insulin (Fins) and pancreatic $\beta$ cell function index (Homa-IS) were increased and the total efficacy was improved in observation group with statistically significant. No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 8 weeks Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	"To study the Chinese medicine syndrome differentiation treatment of type 2 diabetes with insulin resistance."	
Risk of bias		
Bias	Authors judgement	Support for judgement

Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were divided into control group and observation group by random number table method”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were divided into control group and observation group by random number table method”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear.

Zheng J 2013

Clinical Study of Qingre Zaoshi Jianpi Traditional Chinese Medicine in the Treatment of Shire Kunpi Syndrome Primary Type Diabetes

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=82 Inclusion criteria: T2DM WHO 1999, TCM differentiation China 2002: heat and dampness syndrome primary type 2 diabetes



	Exclusion criteria: heart, brain and other severe physical and psychological disorders; other types diabetes; combine with ketoacidosis, hypertonic status and other diabetes acute complications within one month	
Interventions	Number of study centres: 1 Location: China Setting: outpatients and inpatients in TCM hospital Intervention: Treatment group: clearing heat and dispelling dampness tonifying spleen TCM herb formula (Banxia, Cangzhu, Chenpi, Fuling, Huangqin, Huanglian, Xuanshen, Ganjiang, Danshen) Control group: metformin hydrochloride tablet	
Outcomes	The difference of total effective power in two groups was statistically significant with 65% in control group and 85.7% in treatment group. FPG, PFG and HbA1c were all decreased after treatment and more decrease in treatment group with statistical significance No information was reported in terms to adverse effect in this study Outcomes were assessed at baseline and trial completion	
Study details	Duration of intervention: 8 weeks Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	“To observe the clinical curative effect of clearing heat and dispelling dampness tonifying spleen traditional Chinese medicine in the treatment of heat and dampness syndrome primary type 2 diabetes.”	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “patients were divided into treatment group and control group according to random number table method”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “patients were divided into treatment group and control group according to random number table method”

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds of sex, age and disease course. Other aspects of bias were unclear.

Zhou C 2013

Clinical Curative Effect Observation on TCM Treatment in Different Time of 317 Incident Cases of Type 2 Diabetes

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=317 Inclusion criteria: T2DM WHO 1999, new-onset of type 2 diabetes and have never used medicine before; have diabetes education, reasonable exercise and diet, active coordination with the treatment and adhere to treatment for 2 months Exclusion criteria: severe complication such as ketoacidosis, hepatitis, TB, severe infection and so on.
Interventions	Number of study centres: 1 Location: China

	<p>Setting: outpatients and inpatients in TCM hospital</p> <p>Intervention: diabetes education, reasonable exercise and diet</p> <p>Treatment group: TCM formula of hypoglycemic by regulate qi benefit spleen and reinforce kidney (Yipijiangtangwan: Shanyao, Baizhu, Jinei jin, Sharen, Yunling, Wumei, Zexie, Peilan, Heye; Tiaoqijiangtangwan: Chaihu, Yujin, Jiangchan, Nuzhenzi, Wuweizi, Huangqi, Maidong, Xiyangshen, Huangqin, Banxia; Tangshenkangwan: Fuzi, Shanzhuyu, Sheng Dihuang, Xinyangshen, Bajitian, Taoren, Honghua, Yinyanghuo, Mugua)</p> <p>Control group: metformin</p>	
Outcomes	<p>The curative effect and clinical symptoms, blood fat and islet function improvement (FPG, 2hPG, TC, TG, HDL-C, INS, C peptide, GLU) in treatment group were statistically significant compared with control group.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To observe the curative effect of traditional Chinese medicine on treating new-onset type 2 diabetes.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias)	Unclear risk	The information was not reported in this study

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds. Other aspects of bias were unclear.

Du LK 2014

Mechanism of improving insulin resistance in type 2 diabetes with the method of supplementing qi and nourishing Yin, removing phlegm to resolve blood stasis

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=80 Inclusion criteria: T2DM WHO 1999, IR China Li XJ 2001. TCM differentiation, China 2002: spleen qi deficiency with phlegm obstructing Exclusion criteria: not described
Interventions	Number of study centres: 1 Location: China Setting: inpatients and outpatients in TCM hospital Intervention: Basic treatment: dietary and exercise therapy, hypertension and regulating lipid treatment Treatment group: basic treatment + TCM formula of supplementing qi and nourishing Yin, removing phlegm to resolve blood stasis (Huangqi, Renshen, Danshen, Huangjin, Chishao, Cangzhu, Xuanshen) Control group: basic treatment + Avandia

Outcomes	<p>The treatment group improved TNF-<math>\alpha</math>, leptin, ADP level and better than control group with statistically significance; two groups had equal effect in improving insulin resistance; the treatment group significantly improved blood lipid level (TC, TG, LDL-C) and the indexes were superior to those in control group with statistically significance.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 8 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To discuss the possible mechanism of improving insulin resistance in Type 2 diabetes mellitus with the method of supplementing qi and nourishing Yin, removing phlegm to resolve blood stasis.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study

Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds of sex, age and disease course. Other aspects of bias were unclear.

Guan Y 2015

Clinical efficacy of spleen-strengthening, heat-clearing and turbidity-eliminating therapy in treatment of insulin resistance type 2 diabetes

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=62 Inclusion criteria: T2DM WHO 2007; Obesity international obesity organisation 2000, BMI $\geq$ 25kg/m <sup>2</sup> ; insulin resistance China 2007; TCM differentiation China 2002: spleen deficiency with dampness excess and phlegm-heat with internal depression; age: 40-70 year. Exclusion criteria: not described
Interventions	Number of study centres: 1 Location: China Setting: outpatients or inpatients in TCM university hospital Intervention: Basic treatment: diabetes prevention and treatment education, diet and exercise control Treatment group: basic treatment + TCM formula of spleen-strengthening, heat-clearing and turbidity-eliminating therapy (Fuling, Shanyao, ChaoYiyiren, ChaoBaizhu, Cangzhu, Sharen, Chaozhizi, Juhong, DanJuye, Guijianyu, Heye, Sangye) Control group: basic treatment + metformin enteric-coated tablet

Outcomes	<p>There was a significant difference in overall response rate between the treatment group and the control group (87.5% vs 53.33%, <math>P &lt; 0.01</math>). After treatment, both groups showed significant improvement in FBG, 2hPG, FINS, IRI, TC, and TG (<math>P &lt; 0.01</math> or <math>P &lt; 0.05</math>), and the treatment group showed significant improvements in 2hPG, TC and APN than the control group (<math>P &lt; 0.01</math> or <math>P &lt; 0.05</math>).</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 8 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To observe the clinical efficacy of spleen-strengthening, heat-clearing and turbidity-eliminating therapy in treating obese patients with type 2 diabetes and insulin resistance.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No detail information was reported in this study, and only mentioned it was single-blinded trial.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No detail information was reported in this study, and only mentioned it was single-blinded trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study

Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on general backgrounds of sex, age and disease course. Other aspects of bias were unclear.

Yu DQ 2004

Effect and security of traditional Chinese medicine prescription on urine albumin excreting rate type 2 diabetes

Methods	Randomised controlled clinical trial of Chinese herbal medicine compared with placebo Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=71 Inclusion criteria: T2DM WHO 1999; age: 45-75year; course of diabetes over 3 months and blood sugar is stable in recent 2 month Exclusion criteria: type 1 diabetes or special type of diabetes or combine acute diabetic complication and acute or chronic infection; pregnancy or breastfeeding; ALT $\geq$ 113U/L; Cr $\geq$ 170 $\mu$ mol/L, have history of other chronic renal disease before; had malignant tumour before; combine other severe disease, cannot follow up on time; have used ACEI or ARB medicine within 1 month
Interventions	Number of study centres: 1 Location: China Setting: outpatients in university hospital Intervention: both groups have diet control, hypoglycemia, hypo tension and hypo lipid treatment Treatment group: TCM prescription of clearing heat and detoxicating, promoting blood circulation and removing blood stasis (Huangqi, Baihuasheshecao, Banzhilian, Baizhu etc.) control group: placebo



Outcomes	<p>Albumin excreting rate (UAER), microcirculation nail bed flow, HbA1c, FBG, 2hPG, TC, TG, HDL-c, LDL-c, Apo-a, Apo-b and BMI were measured. At the end of trial, the treatment group showed decrease of UAER level with P=0.000.</p> <p>Liver, kidney function and routine blood test were measured before and after the treatment, no abnormal was observed.</p> <p>Adverse effects were observed. Two cases in treatment group and four cases in control group had adverse effects of stomach and they are tolerable.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 24 weeks</p> <p>Duration of Follow-up: 4, 8, 12, 16, 20, and 24 weeks after treatment</p> <p>Run-in period: not described</p>	
Stated aim of study	<p>“To evaluate the effect and safety of traditional Chinese medicine prescription on urine albumin excreting rate of type 2 diabetes.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that “patients were randomly divided into treatment group and control group”
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No detail information was reported in this study, and only mentioned it was single-blinded trial.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No detail information was reported in this study, and only mentioned it was single-blinded trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	11 losses were reported (5 in treatment group 6 in control group) with similar reasons for missing data across groups

Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	No information was reported in the trial about general backgrounds of study groups. Other aspects of bias were unclear.

Wang SH 2014

A randomized, double-blinded, multicentre clinical trial for Tangke Soft Capsules in the treatment of Type 2 diabetes

Methods	Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with placebo alone Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=200 Inclusion criteria: T2DM China 2007, FPG $\geq$ 7.0mmol/L, or 2hPG $\geq$ 11.1mmol/L; or random blood sugar $\geq$ 11.1mmol/L; TCM differentiation China 2002: Qi and Yin deficiency; diabetes for over 3 months; have done diet control and/or exercise therapy, or oral intake hypoglycemic western medicine besides diet control and exercise therapy, and condition is stable for over 2 months but blood sugar is still under the normal: 7.0mmol/L $\leq$ FPG $\leq$ 13.3mmol/L, or 11.1mmol/L $\leq$ 2hPG $\leq$ 22.9mmol/L; age: 18-70 years old; informed and signed consent Exclusion criteria: pregnant or breast-feeding woman, patients with severe complications on heart, brain, liver and kidney or combine with other severe primary diseases, psychotic; sensitivity patients; patients with ketosis and associated infections within one month; ALT 1.5 time over than normal; Cr over than normal; can't take medicine based on prescription; current attending other clinical trial
Interventions	Number of study centres: multicentre (5) Location: China Setting: outpatients and inpatients in five TCM university hospital Intervention: basic treatment: hypoglycemia agents, exercise and dietary therapy Treated group: basic treatment plus TCM medicine: Tangke soft Capsules (Wuweizi) Control group use basic treatment plus placebo soft capsules

Outcomes	<p>FBG, 2hBG, TCM pattern changes, ECG and adverse events monitor of function of liver and kidney, blood and urine, safety problems were observed. Compared with the baseline, the level of HbA1C, FPG and 2h PG after treatment in the Tangke group decreased significantly (<math>P &lt; 0.01</math>), but no markedly compared with placebo group. So was for FPG. There was a significant difference in the drop of 2hPG between Tangke and placebo group (<math>P = 0.044</math>).</p> <p>No serious adverse events and hypoglycemic episodes were observed in both intervention groups.</p> <p>Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: none</p>	
Stated aim of study	<p>“To evaluate the efficacy and safety of Tangke Soft Capsules (extract of Schisandrae chinensis Fructus) for the treatment of Type 2 diabetes.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned that the trial was randomised in two treatment groups
Allocation concealment (selection bias)	unclear risk	It only mentioned that the trial was randomised in two treatment groups
Blinding of participants and personnel (performance bias) All outcomes	low risk	It mentioned double-blinded, placebo-controlled clinical trial
Blinding of outcome assessment (detection bias) All outcomes	low risk	It mentioned double-blinded, placebo-controlled clinical trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	19 losses were reported with 9.5% general lost rate at the endpoint of study with balanced missing outcome data in numbers across intervention groups
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors

Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that “no significant difference was found between groups on baseline data of age, body lengths, BMI, disease course and medical conditions. Other aspects of bias were unclear
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Chao ML 2009

Improving insulin resistance with traditional Chinese medicine in type 2 diabetes patients

Methods	Parallel randomised double-blinded, placebo-controlled, clinical trial of Chinese herbal medicine compared with placebo Randomisation ratio: 1:1
Participants	Ethnic: Chinese n=43 Inclusion criteria: newly diagnosed T2DM WHO 1999, FPG $\geq$ 7mmol/L and/or OGTT 2h $\geq$ 11.1mmol/L; age range: 18-70 years; overweight with BMI 23-35 kg/m <sup>2</sup> and with poor glucose level after a 1-month diet control, two FPG concentrations between 7-10 mmol/L within a month Exclusion criteria: had used any antidiabetic drugs; with health problems of cardiac, hepatic, renal, other chronic diseases, or acute diabetic complications including diabetic ketoacidosis or hyperosmolar hyperglycemic non-ketotic coma, as determined by history, examination and routine blood chemistry; women of childbearing age were pregnant or planning for pregnancy
Interventions	Number of study centres: 2 Location: China Setting: patients in university affiliated hospital Intervention: diet and exercise advise TCM group: TCM prescription: compound powder form with 50 mag of Coptis chinensis, 30mg of Astragalus membranescus and 120mg of Lonicera japonica Placebo group: placebo in indistinguishable tablets
Outcomes	BMI, waist-hip, SBP, DBP, FPG, PPG, HbA1c, TG, TC, HDL, LDL, INS0, INS120, GDR, CRP, IL-6, RBP4, adiponectin, ALT were assessed at baseline and trial completion

	<p>Glucose disposal rate in the TCM group was significantly improved as compared to that in the placebo group (<math>P &lt; 0.05</math>)</p> <p>Renal and hepatic function, blood counts were assessed at baseline and the end of the study for safety purpose. Only mild adverse symptoms were observed for 5 cases and the frequency of side effects was not significantly different between the two groups. No severe side effect occurred during the study, no episode of hypoglycemia was reported.</p>	
Study details	<p>Duration of intervention: 3 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: 2 weeks</p>	
Stated aim of study	<p>“To evaluate the efficacy of TCM on insulin sensitivity and other related metabolic factors in type 2 diabetes patients.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “randomization was performed centrally and was concealed and stratified in blocks of four”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “randomization was performed centrally and was concealed and stratified in blocks of four”
Blinding of participants and personnel (performance bias) All outcomes	low risk	Double-blinded and placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	low risk	Double-blinded and placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 2 patients in TCM group early stopped.
Selection reporting (reporting bias)	low risk	The protocol of the trial was clear, so the possibility of selection outcome reporting could be examined by the review authors

Other bias	Unclear risk	The intervention groups were comparable, as it listed comparison of clinical characteristics between two groups and no significant difference was found. Other aspects of bias were unclear
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Tong XL 2013

The safety and effectiveness of TM81, a Chinese herbal medicine, in the treatment of type 2 diabetes:  
a randomised double-blind placebo-controlled trial

Methods	Parallel randomised large-scale, placebo-controlled, clinical trial of Chinese herbal medicine compared with placebo Randomisation ratio: 3:1
Participants	Ethnic: Chinese n=480 (TM81 group 360, placebo group 120) Inclusion criteria: T2DM early-stage WHO 1999, 30-65 years old, BMI $\geq$ 24kg/m <sup>2</sup> . After the initial screening, subjects entered a 2-week run-in period with diet control and programmed daily exercise. Then subjects still with HbA1C $\geq$ 7.0% and FPG level between 7.0 and 13.9mM or 2hPG>11.1mM were enrolled. A consent form was signed by all subjects prior to enrolment Exclusion criteria: have been treated for diabetes for > 1 month by conventional medications, physical therapy, psychological therapy, herbal medicine or dietary supplements; have been treated with antidiabetic drugs 3 weeks prior to screening; have had diabetic ketoacidosis or serious infections within 1 month; have uncontrolled hypertension; pregnant females, or those planning to be pregnant; breast feeding; have hepatic and renal dysfunctions, pulmonary function insufficiency, cardiac failure, acute myocardial infarction and other serious diseases; have severe chronic diabetic complications; chronic gastrointestinal diseases, or that are generally not healthy; allergic to Chinese herbal medicines; have mental disorders; on-going allergic symptoms; participating in other clinical trials or prior participation in TM81 trials; alcoholism, taking antipsychotic agents or substance abuse or dependence; have factors that may affect trial execution based on investigator's judgement, such as changeable working and living environments that may lead to withdrawal from the trial; have unstable antihypertension effects during drug administration; or taking weight-loss medicines

Interventions	<p>Number of study centres: 10</p> <p>Location: China</p> <p>Setting: patients in university affiliated hospital</p> <p>Intervention: both groups have diet control and programmed daily exercise</p> <p>TM81 group: TM81 (Tang-Min-Ling-Wan) formula: quantitative control limits raw herbs of Rhizoma Coptidis, Radix Paeoniae Alba, radix Scutellariae, Pericarpium Citri Reticulatae, Rhizoma Rhei and other Chinese herbs</p> <p>Placebo group: placebo capsulated in similar packing, appearance, shape, size and colour with TM81 capsule</p>	
Outcomes	<p>After treatment, the decrease of HbA1C, FPG and PG is statistically significant in TM81 group compared to placebo group. The TM81 was more effective for patients with higher baseline HbA1C levels. The TM81 group also showed improved <math>\beta</math>-cell function and increased homeostatic model assessment. Body weight, BMI and waist circumference of subjects in TM81 group were reduced and the symptoms related to diabetes were improved.</p> <p>During the trial, there were no medium or serious adverse events reported. 24 mild adverse events were reported in the TM81 group versus 7 mild adverse events reported in the placebo group. There was one case with abdominal cramping and diarrhoea which disappeared shortly without treatment. No abnormal ECG, hepatic functions or renal functions were observed at week 12. There were no significant differences in the types and frequency of adverse reactions between two groups. Outcomes were assessed at baseline and trial completion</p>	
Study details	<p>Duration of intervention: 12 weeks</p> <p>Duration of Follow-up: week 0. Week 4, week 8 and week 12</p> <p>Run-in period: 2 weeks</p>	
Stated aim of study	<p>“To evaluate the safety and effectiveness of TM81 in the treatment of type 2 diabetes patients.”</p>	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	low risk	It mentioned in the trial that “randomization and blinding were conducted by personnel who did not participate in data acquisition and evaluation. A computer program

		was used to generate the subject assignment. Each subject was given a unique number and this number was used throughout the trial.”
Allocation concealment (selection bias)	low risk	It mentioned in the trial that “randomization and blinding were conducted by personnel who did not participate in data acquisition and evaluation. A computer program was used to generate the subject assignment. Each subject was given a unique number and this number was used throughout the trial.”
Blinding of participants and personnel (performance bias) All outcomes	low risk	All investigators were blinded from the study drug assignment, in which only a randomization code was disclosed. Unblinding was conducted only after all study data were collected
Blinding of outcome assessment (detection bias) All outcomes	low risk	All investigators were blinded from the study drug assignment, in which only a randomization code was disclosed. Unblinding was conducted only after all study data were collected
Incomplete outcome data (attrition bias) All outcomes	Low risk	68 subjects in the TM81 group and 13 subjects in the placebo group dropped out. The proportion of missing outcomes is 16.88% which is not enough to have a clinically relevant impact on the intervention effect estimate compared with observed event risk
Selection reporting (reporting bias)	low risk	The protocol of the trial was clear, so the possibility of selection outcome reporting could be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it listed comparison of baseline data between two groups and no significant difference was found for most of baseline items apart from HbA1C and 2hPG. Other aspects of bias were unclear



Study on Treatment of Reinforcing Spleen and dissipating Dampness and Promoting Blood Circulation (TRDP) on the Function of Pancreatic  $\beta$ Cells in Patients with Type 2 Diabetes Mellitus

Methods	<p>Randomised controlled clinical trial of combined medicine (Chinese herbal medicine + other pharmaceuticals) compared with other pharmaceuticals alone and Chinese herbal medicine alone</p> <p>Randomisation ratio: 1:1:1</p>
Participants	<p>Ethnic: Chinese n=90 (30 in each of TCM, western medicine and TCM combined with western medicine)</p> <p>Inclusion criteria: T2DM WHO 1999; TCM differentiations: spleen deficiency with dampness stagnation and blood stasis, blood sugar is still abnormal after dietary and exercise therapy, initially occurred T2DM</p> <p>Exclusion criteria: type 1 diabetes ketoacidosis or diabetes hypertonic coma, or combine with moderate or over hypertension, coronary disease myocardial infarction, severe arrhythmia, liver kidney hemopoietic system and other severe complications, allergy to the study drugs or have acute hyperglycemia due to other diseases</p>
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: patients in TCM university hospital</p> <p>Intervention: dietary control and exercise therapy</p> <p>TCM group: strengthen spleen eliminate dampness and move the blood</p> <p>Western medicine group: Pioglitazone</p> <p>TCM combined with western medicine group: TCM (Cangzhu, Baizhu, Fuling, Chenpi, Houpo, Cheqianzi, Zexie, Honghua, Sangshen, huzhang, Guijianyu) + Pioglitazone</p>
Outcomes	<p>After treatment, FBG, PBG, HbA1c, FINS, IAI, HOMA-IR, HOMA-<math>\beta</math>, IL-6, TNF-<math>\alpha</math> of three groups decreased significantly than those before treatment (<math>P&gt;0.05</math>). TCM combined western medicine group was more effective than the two other groups (<math>P&lt;0.05</math>).</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion:</p>
Study details	<p>Duration of intervention: 2 months</p> <p>Duration of Follow-up: not reported</p> <p>Run-in period: not described</p>

Stated aim of study	"To explore the effects of TRDP on $\beta$ cell function in treatment of type 2 diabetes mellitus."	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into treatment group and control group"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The information was not reported in this study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The information was not reported in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds of age, sex and medical conditions. Other aspects of bias were unclear

Ge SM 2012

Clinical effect of the "Eight method of Fan's in the treatment of early type 2 diabetes in 30 patients

Methods	<p>Randomised controlled clinical trial of Chinese herbal medicine compared with other pharmaceuticals alone as well as diet control and exercise therapy</p> <p>Randomisation ratio: 1:1:1</p>
Participants	<p>Ethnic: Chinese n=90 (30 in each of TCM treatment group, WM treatment group and control group)</p> <p>Inclusion criteria: T2DM WHO 1999; early diagnosed T2DM within half year; age≥30 y; have or not used hypoglycemia treatment with western medicine or insulin; stop using western medicine, insulin, TCM or patent TCM for over 2 weeks; cooperate with diet and exercise therapy; have no significant life event before and after treatment; stable emotion, regular life, diet and exercise are stable.</p> <p>Exclusion criteria: not described</p>
Interventions	<p>Number of study centres: 1</p> <p>Location: China</p> <p>Setting: outpatients in medical university hospital</p> <p>Intervention:</p> <p>Chinese medicine treatment group: pure TCM treatment with The Eight method of Fan's method based on syndrome differentiation (Kidney deficiency: Gouji, Chuanduan, Nuzhenzi, Hanliancao; Qi and Yin deficiency: Beiqi, Shengdi, Digupi; Liver qi stagnation: Chaihu, Baishao, Bohe, Danpi; Lung Stomach heat: Shigao, Zhimu, Gegen, Lianqiao; Fuexcess with constipation: Dahuang, Zhishi, Huomaren; Heart spirit lose nourishment: Yejiaoteng, Yuanzhi, Suanzhaoren; Heat into blood fen: Danpi, Chishao, Maidong, Yimi, Mianyinchen; Excess dampness restrict spleen: Fuling, Chaobaizhu, Fabanxia, Shenqu; add Laifuzi, Zhiqiao, Chuanpu for stomach bloat; add Gualoupi, Xiebai for chest depression; Blood stasis: Danshen, Sanleng, Ezhu, Zelan)</p> <p>Acarbose treatment group: acarbose</p> <p>Control group: dietary and exercise therapy</p>
Outcomes	<p>FBG, PBG, HbA1c, TG, CH, Cr, clinical symptoms were measured. The effective rates were 83.3% in Chinese medicine treatment group and 80% in acarbose treatment group with no significant difference. The effective rates of two groups were higher than that of the control group with statistically significant difference.</p> <p>No information was reported in terms to adverse effect in this study</p> <p>Outcomes were assessed at baseline and trial completion</p>

Study details	Duration of intervention: 6 months Duration of Follow-up: not reported Run-in period: not described	
Stated aim of study	"To observe clinical effect of 'The Eight method of Fan's' to treat type 2 diabetes."	
Risk of bias		
Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into Chinese medicine group, the acarbose treatment group and the control group"
Allocation concealment (selection bias)	unclear risk	It only mentioned in the trial that "patients were randomly divided into Chinese medicine group, the acarbose treatment group and the control group"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No detail information was reported in this study, and only mentioned it was single-blinded trial.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No detail information was reported in this study, and only mentioned it was single-blinded trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusion or losses were reported, but the number of participants remained the same at the endpoint of study
Selection reporting (reporting bias)	Unclear risk	The protocol of the trial was not available, so the possibility of selection outcome reporting could not be examined by the review authors
Other bias	Unclear risk	The intervention groups were comparable, as it mentioned in the trial that "no significant difference was found between groups on general backgrounds of sex, age and so on. Other aspects of bias were unclear.

**Characteristics of excluded studies** [ordered by study ID]

Study	Reason for exclusion
Cao YX 2015	Duration of study 30 days
Deng LN 2007	Duration of study 2 weeks
Zeng YP 2006	Duration of study 2 weeks
Fan GJ 2006	Duration of study 4 weeks
Shi YH 2014	Duration of study 4 weeks
Tong BL 2007	Duration of study 6 weeks
Chen ZQ 2006	Duration of study 4 weeks
Lv WZ 2008	Duration of study 1 month
Yu H 2009	Duration of study 2 weeks
Chen XJ 2010	Duration of study 4 weeks
Wang GL 2012	Duration of study 20 days
Han F 2014	Duration of study 4 weeks
Liu YH 2015	Duration of study 30 days
Tian YH 2010	Duration of study 30 days
Wu WY 2004	Duration of study 4 weeks
Hu MF 2008	Duration of study 45 days
Xu MY 2013	Duration of study 30 days
Hu JG 2013	Duration of study 30 days
Shi J 2011	Duration of study 4 weeks
Tang XY 2012	Duration of study 4 weeks
Wang JS 2008	Duration of study 4 weeks
Guo YQ 2015	Duration of study 30 days
Zhong YZ 2012	Not mention the duration of study
Chen Q 2006	Not mention the duration of study, non-randomised study
Zhu YL 2015	Duration of study 4 weeks, non-randomised study
Liu Y 2014	Duration of study 2 weeks, testing TCM herb extract
Xie XN 2012	Duration of study 4 weeks, combined acupoint injection with TCM herb extract therapy
Huang TS 2015	Duration of study 1 month, combined acupoint injection with TCM herb extract therapy

Yan YJ 2007	Duration of study 1 month, combined with ear acupuncture treatment
Chen DS 2007	Multiple study centre randomized single-blinded controlled trial, duration of study 4 weeks
Ning HJ 2015	Non-randomized study, combined with acupuncture and Tui Na treatment
Liu HY 2008	RCT testing TCM herb extract berberine
Gan JR 2012	RCT testing TCM herb extract berberine in treatment of adverse effect caused by T2DM drug
Zhao MY 2013	Non-randomized controlled study
Zhang LB 2014	Non-randomized controlled study (pseudo RCT)
Li MH 2011	Non-randomized controlled study (pseudo RCT)
Zhou XL 2013	Non-randomized control study (pseudo RCT)
Ren C 2012	Non-randomized controlled study (pseudo RCT)
Lin ZR 2010	Non-randomized controlled study
Mo JF 2013	Non-randomized concurrent controlled trial
Yu ZF 2011	Non-randomized controlled study
Jin YH 2015	Retrospective randomized controlled study
Chen GH 2006	Case series
Zheng M 2006	RCT compared different herbal medicines
Wang WH 2010	Randomized double blinded controlled trial compared different herbal medicines
Su XY 2015	RCT compared different herbal medicines
He CL 2013	Case series study of carotid artery intima-media thickness and lipid of type 2 diabetes artery atherosclerosis
Ma RW 2010	RCT study of treating T2DM complication – diabetic macro-vascular disease
Fang ZH 2009	RCT study of impaired blood vessel endothelium in prothrombotic state of T2DM
Sun XZ 2011	RCT study of treating T2DM carotid atherosclerotic plaque
Jiang T 2014	RCT study of treating T2dM with carotid plaques
Peng GH 2015	RCT study of treating T2DM with peripheral neuropathy
Li C 2012	Non-randomized controlled trial study of treating T2DM peripheral neuropathy
Zhang XZ 2014	RCT study of treating peripheral neuropathy in T2DM due to damp-heat flowing down
Shu JP 2014	RCT study of treating nerve condition velocity in T2DM peripheral nerve
Shen XR 2015	RCT study of treating T2DM angiopathy
Xiao RR 2013	RCT study of treating T2DM with peripheral neuropathy

Chen Y 2014	RCT study of treating T2DM peripheral neuropathy
Sun YR 2012	RCT study of treating T2DM peripheral neuropathy
Wen ZM 2012	Non-randomized controlled trial study of treating T2DM complication – diabetic nephropathy
Xu ZL 2014	RCT study of treating early T2DM nephropathy
Li JW 2013	RCT study of preventing early T2DM nephropathy
Kong LX 2014	RCT study of treating T2DM with membranous nephropathy
Du YB 2011	RCT study of treating early and metaphase T2DM nephropathy
Jiang XY 2005	RCT study of treating late T2DM nephropathy
Feng SH 2015	RCT study of treating elderly T2DM nephropathy
Wei QL 2006	RCT study of early diabetic nephropathy
Miao JY 2013	RCT study of treating T2DM complicated with non-alcoholic steatohepatitis
Xiao FY 2012	RCT study of treating T2DM complicated with non-alcoholic fatty liver disease
Wu LK 2012	RCT study of treating T2DM combined with fatty liver disease
Zou H 2012	RCT study of treating T2DM with fatty liver disease
Wu LK 2011	RCT study of treating fatty liver in T2DM
Meng LW 2015	RCT study of treating T2DM and dyslipidemia
Zhao FH 2012	RCT study of treating T2DM with dyslipidemia and its effect to weight, BMI, FBG, P2HBG, HbA1c and blood fat
Zhao X 2012	RCT study of treating T2DM complicated with depression
Jia SQ 2009	RCT study of treating T2DM accompanied by depression
Sui JX 2015	RCT study of prevention of diabetic retinopathy
Zhang M 2010	RCT study of treating obese diabetes eyeground hemorrhage
Huo JJ 2015	RCT study of treating T2DM with hyperuricemia
Lu XR 2013	RCT study of treating T2DM and hypertension
Jiang D 2009	RCT study of treating T2DM complicated with hypertension
Jiao YP 2013	RCT study of treating hypertension with T2DM
Dang ZL 2014	RCT study of treating T2DM complicated with gastroesophageal reflux disease
Su H 2008	RCT study of treating T2DM gastroparesis
Xu HJ 2014	RCT study of treating T2DM secondary constipation
Zhang YD 2009	RCT study of treating constipation in T2DM
LJ 2015	RCT study of T2DM cardiovascular disease autonomic neuropathy heart rate variability

Shi BD 2015	RCT study of treating T2DM urinary tract infection
Guan JT 2014	RCT study of treating T2DM with acute cerebral infarction
Shen HH 2013	RCT study of treating T2DM and periodontal disease
Li SF 2011	Prospective randomised controlled study of treating chronic diabetic foot ulcers
Liu Q 2013	RCT study of treating T2DM by pharmaceuticals with total alkali from morus folium jiangtang capsule
Xu J 2008	RCT study of changes in vascular endothelial cell active factors in T2DM and treating of diabetes complications
Wang X 2007	RCT study of TCM on inflammatory factor of earlier period T2DM. and the protocol and drugs of the trial are very similar with one of included studies (Guan X 2006)
Ye X 2014	RCT study of treating T2DM, but have no mention of treatment method and intervention medicine.
Li XH 2010	RCT study of treating T2DM, but have no mention of intervention medicine for control group.
Cai HZ 2015	RCT study of testing TCM herb extract
Qiang G 2015	RCT study of treating T2DM with vascular dementia
Shi G 2015	RCT study of treating T2DM complicated with pulmonary tuberculosis
Li ZQ 2013	RCT study of T2DM treatment with TCM herb, but no details of treating herbs due to full text is not available
Leung P.C 2012	RCT study of TCM herbal formula treatment for T2DM patients with chronic ulcers
Fang ZH 2013	RCT study of treating T2DM vascular lesions
Ni Q 2012	RCT study of treating type 2 pre-diabetes
Tian GQ 2008	RCT study of treating T2DM complicated with hyperlipidemia, but no details of treating herbs due to full text is not available
Zuo GL 2009	RCT study of treating T2DM with atherosclerosis
Uno T 2005	Non-RCT study with study duration 1 month
Zhang Y 2015	RCT study of treating T2DM with multi-centres and big samples, but won't be completed until early-2016 (only available for the letter to the editor)



## APPENDICES

### Appendix 1. List of Chinese herbal medicines used as treatment for type 2 diabetes

No.	Pharmaceutical name	Botanical name	Chinese name (Pinyin)
1	Astragali Radix	<i>Astragalus membranaceus</i> (Fisch.) Bge.	Huangqi
2	Rehmanniae Radix	<i>Rehmannia glutinosa</i> Libosch.	Shengdihuang
3	Rehmanniae Radix Praeparata	<i>Rehmannia glutinosa</i> Libosch.	Shudihuang
4	Salviae Miltiorrhizae Radix et Rhizoma	<i>Salvia miltiorrhiza</i> Bge.	Danshen
5	Achyranthis Bidentatae Radix	<i>Achyranthes bidentata</i> Bl.	Niuxi
6	Paeoniae Rubra Radix	<i>Paeonia lactiflora</i> Pall.	Chishao
7	Coptidis Rhizoma	<i>Coptis chinensis</i> Franch.	Huanglian
8	Polygonati Rhizoma	<i>Polygonatum sibiricum</i> Red.	Huangjing
9	Puerariae Radix	<i>Pueraria lobata</i> (Willd.) Ohwi	Gegen
10	Epimedii Folium	<i>Epimedium brevicornu</i> Maxim.	Yinyanghuo
11	Talcum	Magnesium Silicate	Hua Shi Fen
12	Artemisiae Scopariae Herba	<i>Artemisia capillaris</i> Thunb.	Yinchen
13	Scutellariae Radix	<i>Scutellaria baicalensis</i> Georgi	Huangqin
14	Acori Tatarinowii Rhizoma	<i>Acorus tatarinowii</i> Schott; <i>Acorus gramineus</i> Soland.	Shichangpu
15	Agastaches Herba	<i>Agastache rugosa</i> (Fisch & Mey.) O. Ktze.	Huoxiang
16	Fritillariae Cirrhosae Bulbus	<i>Fritillaria cirrhosa</i> D. Don	Chuanbeimu
17	Forsythiae Fructus	<i>Forsythia suspensa</i> (Thunb.) Vahl	Lianqiao
18	Coicis Semen	<i>Coix lacryma-jobi</i> L. var. <i>mayuen</i> (Roman.) Stapf	Yiyiren
19	Dioscoreae Rhizoma	<i>Dioscorea opposita</i> Thunb.	Shanyao
20	Crataegi Fructus	<i>Crataegus pinnatifida</i> Bge.	Shazha
21	Hirudo	<i>Hirudo orientalis</i> , <i>Hirudo troctina</i> , and <i>Hirudo verbana</i>	Shuizhi
22	Semen Sinapsis seu Brassicae	<i>Sinapis alba</i> (L.) Boiss.; <i>Brassica Juncea</i> (L.) Czern.	Baijiezi

23	Litchi Semen	Litchi chinensis Sonn.	Lizhihe
24	Ecliptae Herba	Eclipta prostrata L.	Mohanlian
25	Eupatorii Herba	Eupatorium fortunei Turcz.	Peilan
26	Atractylodis Rhizoma	Atractylodes chinensis (DC.) Koidz.	Cangzhu
27	Centellae Herba	Centella asiatica (L.) Urb.	Jixuecao
28	Smilacis Glabrae Rhizoma	Smilax glabra Roxb.	Tufuling
29	Trichosanthis Radix	Trichpsanthes kirilowii Maxim./ Trichosanthes rosthonii Harms	Tianhuafen
30	Gypsum Fibrosum	Gypsum fibrosum	Shigao
31	Anemarrhenae Rhizoma	Anemarrhena asphodeloides Bge.	Zhimu
32	Ophiopogonis Radix	Ophiopogon japonicus (L.f) KerGawl.	Maidong
33	Radix Aconiti Lateralis Praeparata	Aconitum carmichaeli Debx.	Fuzi
34	Cinnamomi Cortex	Cinnamomum cassia Presl	Rougui
35	Cornu cervi pantotrichum	Cervus elaphus, Cervus nippon	Lurong
36	Rubi Fructus	Rubus chingii Hu	Fupenzi
37	Granati Pericarpium	Punica granatum L.	Shiliupi
38	Persicae Semen	Prunus persica (L.) Batsch/ Prunus davidiana (Carr.) Franch.	Taoren
39	Carthami Flos	Carthamus tinctorius L.	Honghua
40	Massa Fermentata Medicinalis	Artemisiae Annuae, Fructus Xanthii, Semen Armeniacae Amarum, Semen Phascoli Calcarati	Shenqu
41	Hordei Fructus Germinatus	Hordeum vulgare L.	Maiya
42	Corydalis Rhizoma	Corydalis yanhusuo W.T. Wang	Yanhusuo
43	Bombyx Batryticatus	Bombyx mori L. (Fam. Bombycidae)	Jiangcan
44			Quanxie
45	Curcumae Radix	Curcuma wenyujin Y.H.Chen et C.Ling	Yujin
46	Codonopsis Radix	Codonopsis pilosula (Franch.) Nannf.	Dangshen
47	Glehniae Radix	Glehnia littoralis Fr. Schmidt ex Miq.	Beishashen
48	Pseudostellariae Radix	Pseudostellaria heterophylla (Miq.) Pax ex Pax et Hoffm.	Taizishen

49	Phellodendri Chinensis Cortex	Phellodendron chinense Schneid.	Chuanhuangbai
50	Chuanxiong Rhizoma	Ligusticum chuangxiong Hort.	Chuanxiong
51	Pheretima Earthworm	Pheretima aspergillum	Dilong
52	Dendrobii Caulis	Dendrobium nobile Lindl.	Shihu
53	Asparagi Radix	Asparagus cochinchinensis (Lour.) Merr.	Tianmendong
54	Citri Reticulatae Pericarpium	Citrus reticulata Blanco	Chenpi
55	Pinelliae Rhizoma	Pinellia ternata (Thunb.) Breit.	Banxia
56	Cassiae Semen	Cassia obtusifolia L.	Juemingzi
57	Alismatis Rhizoma	Alisma orientalis (Sam.) Juzep.	Zexie
58	Bambusae Caulis in Taenia	Bambusa tuldoides Munro	Zhuru
59	Arisaema Cum Bile	Arisaema erubescens (Wall.) Schott	Dannanxing
60	Scrophulariae Radix	Scrophularia ningpoensis Hemsl.	Xuanshen
61	Lycii Cortex	Lycium chinense Mill.	Digupi
62	Corni Fructus	Cornus officinalis Sieb. et Zucc.	Shanzhuyu
63	Schisandrae Chinensis Fructus	Schisandra chinensis (Turcz.) Baill.	Wuweizi
64	Mume Fructus	Prunus mume (Sieb.) Sieb. et Zucc.	Wumei
65	Angelicae Sinensis Radix	Angelica sinensis (Oliv.) Diels	Danggui
66	Paeoniae Alba Radix	Paeonia lactiflora Pall.	Baishao
67	Spatholobi Caulis	Spatholobus suberectus Dunn	Jixueteng
68	Lonicerae Japonicae Caulis	Lonicera japonica Thunb.	Rendongteng
69	Moutan Cortex	Paeonia suffruticosa Andr.	Mudanpi
70	Lycopi Herba	Lycopus lucidus Turcz. var. hirtus Regel	Zelan
71	Gardeniae Fructus	Gardenia jasminoides Ellis	Zhizi
72	Atractylodis Macrocephalae Rhizoma	Atractylodes macrocephala Koidz.	Baizhu
73	Bupleuri Radix	Bupleurum chinense DC.	Chaihu
74	Herba Buchneriae	Winged Euonymus Twig, Ramulus Euonymi	Guijianyu
75	Polygoni Multiflori Radix	Polygonum multiflorum Thunb.	Heshouwu

76	Cuscutae Semen	Cuscuta chinensis Lam.	Tusizi
77	Morindae Officinalis Radix	Morinda officinalis How	Bazitian
78	Eucommiae Cortex	Eucommia ulmoides Oliv.	Duzhong
79	Polygonati Odorati Rhizoma	Polygonatum odoratum (Mill.) Druce	Yuzhu
80	Mori Cortex	Morus alba L.	Sangbaipi
81	Mori Folium	Morus alba L.	Sangye
82	Mori Ramulus	Morus alba L.	Sangzhi
83	Nelumbinis Rhizomatis Nodus	Nelumbo nucifera Gaertn.	Oujie
84	Glycyrrhizae Radix	Glycyrrhiza uralensis Fish.	Gancao
85	Lycii Fructus	Lycium barbarum L.	Gouqizi
86			Baikouren
87	Tetrapanacis Medulla	Tetrapanax papyrifer (Hook.) K. Koch	Tongcao
	Lablab Album Semen	Dolichos lablab L.	Baibiandou
	Nelumbinis Folium	Nelumbo nucifera Gaertn.	Heye
88	Lonicerae Flos	Lonicera macranthoides Hand. -Mazz. ; Lonicera hypoglauca Miq. ; Lonicera confuse DC. ; Lonicera fulvotomentosa Hsu et S.C. Cheng	Jinyinhua
89	Ginseng Radix	Panax ginseng C. A. Mey.	Renshen,
90	Dianthi Herba	Dianthus superbus L.	Qumai
91	Stephaniae Tetrandrae Radix	Stephania tetrandra S. Moore	Fangji
92	Tribuli Fructus	Tribulus terrestris L.	Cijili
93	Trichosanthis Fructus	Trichpsanthes kirilowii Maxim. ; Trichosanthes rosthonii Harms	Gualou
94	Allii Macrostemonis Bulbus	Allium macrostemon Bge. ; Allium chinense G. Don	Xiebai
95	Cynomorii Herba	Cynomorium songaricum Rupr.	Suoyang
96	Gastrodiae Rhizoma	Gastrodia elata Bl.	Tianma
97	Ootheca Mantidis	Paratenodera Sinensis, P. augustipennis Saussure, Statilia maculata...	Sangpiaoxiao

98	Herba Epimedii	<i>Epimedium grandiflorum</i> Morr.	Xianlingpi
99	Platycodonis Radix	<i>Platycodon grandiflorum</i> (Jacq.) A. DC.	Jiegeng
100	Ziziphi Spinosae Semen	<i>Ziziphus jujuba</i> Mill. var. <i>spinosa</i> (Bunge) Hu ex H. F. Chou	Suanzaoren
101	Aurantii Immaturus Fructus	<i>Citrus aurantium</i> L.	Zhishi
102	Cyperi Rhizoma	<i>Cyperus rotundus</i> L.	Xiangfu
103	Stylus Zeae Maydis		Yumixu
104	Ligustri Lucidi Fructus	<i>Ligustrum lucidum</i> Ait.	Nuzhenzi
105	Laminariae Thallus Eckloniae Thallus	<i>Laminaria japonica</i> Aresch. ; <i>Ecklonia kurome</i> Okam.	Kunbu
106	Aurantii Fructus	<i>Citrus aurantium</i> L.	Zhiqiao
107	Eriobotryae Folium	<i>Eriobotrya japonica</i> (Thunb.) Lindl.	Pipaye
108			Hanliancao
109	Cibotii Rhizoma	<i>Cibotium barometz</i> (L.) J. Sm.	Gouji
110	Dipsaci Radix	<i>Dipsacus asper</i> Wall. ex Henry	Xudian
111	Menthae Herba	<i>Mentha haplocalyx</i> Briq.	Bohe
112	Fructus Cannabis.	<i>Cannabis sativa</i> L. Common Name: Cannabis seed, Hemp seed.	Huomaren
113	Caulis Polygoni Multiflori.	<i>Polygonum multiflorum</i> Thunb.( <i>Polygonaceae</i> ).	Yejaoteng
114	Polygalae Radix	<i>Polygala tenuifolia</i> Willd. ; <i>Polygala sibirica</i> L.	Yuanzhi
115	Plantaginis Herba	<i>Plantago asiatica</i> L. ; <i>Plantago depressa</i> Willd.	Cheqiancao
116	Raphani Semen	<i>Raphanus sativus</i> L.	Laifuzi
117			Xiapu
118	Sparganii Rhizoma	<i>Sparganium stoloniferum</i> Buch. -Ham.	Sanleng
119	Curcumae Rhizoma	<i>Curcuma phaeocaulis</i> Val.	Ezhu
120			Ganjiang
121	Ginseng Radix et Rhizoma Rubra	<i>Panax ginseng</i> C. A. Mey.	Hongshen
122	Endothelium Corneum Gigeriae Galli.	<i>Gallus gallus domesticus</i> Brisson	Jineijin
123	Amomi Fructus	<i>Amomum villosum</i> Lour. ; <i>Amomum villosum</i> Lour. var. <i>xanthioides</i> T. L. Wu et Senjen ; <i>Amomum longiligulare</i> T. L. Wu	Sharen
124	Chaenomelis Fructus	<i>Chaenomeles speciosa</i> (Sweet) Nakai	Mugua
125	Citri Exocarpium Rubrum	<i>Citrus reticulata</i> Blanco	Juhong
126	Lophatheri Herba	<i>Lophatherum gracile</i> Brongn.	Danzhuye

127			Baihuasheshecao
128	Scutellariae Barbatae Herba	Scutellaria barbata D. Don	Banzhilian
129	Magnoliae Officinalis Cortex	Magnolia officinalis Rehd. et Wils.	Houpo
130	Plantaginis Semen	Plantago asiatica L. ; Plantago depressa Willd.	Cheqianzi
131	Mori Fructus	Morus alba L.	Sangshen
132	Polygoni Cuspidati Rhizoma	Polygonum cuspidatum Sieb. et Zucc.	Huzhang

## Appendix 2 Search strategy for included databases

Database & research strategies 2015-2016

Database	Key words & outcome/results	Refined & outcome/results	date of access	Time refined
Web of Science (Basic Search)	(patient safety) AND (type 2 diabetes) - 13,410	Chinese herbal Medicine - 5	From 11/11/2014	2004-2014
	(patient safety) AND (Chinese Medicine herbs) - 273	Diabet* - 12	To 24/11/2015	
	(type 2 diabet*) AND (Chinese Medicine herbs) - 151	Human research - 3 Patient safety – 5 Refine by looking the tile & abstract - 127		
	Half-life of Chinese herbs - 0	Nil	From 6/4/2015	
	Metabolomics and Chinese herbs – 104 Toxicogenomics and Chinese herbs - 3	Toxicogenomics - 2 Human research - 2	From 14/4/2015	
China Academic Journals Full-text Database (Basic Search)	“diabet*” And “(clinical trial)” (Medicine & Public Health initial trial) – 107	Refine by looking the tile & abstract link to safety - 10	From 21/10/2014 to 14/07/2015	
	“patient safety” And “diabet*”- 397	nil		

	"Chinese herb" And "patient safety"- 133	Refine by looking the tile & abstract link to diabetes- 5		
PubMed	Reference list of key articles	Relative title	From 24/11/2015	
Google Scholar	Reference list of key articles	Relative title	From 24/11/2015	
The University of Adelaide Library Research	Chinese herbs and diabetes  (Library loan: 5)	Anywhere in the records - 324 Refine by articles - 269 Refine by title – 25	From 15/3/2015	2004-2014
Cochrane Library/Wiley Online Library	type 2 diabet* AND Chinese medicine herbs - 3 patient safety and type 2 diabetes – 17 patient safety AND Chinese medicine herbs -10	Nil  Chinese medicine herbs – 1 Type 2 diabetes - 1	23/08/2015	2004-2014

#### Database & research strategies 2015-2016

Database	Key words & outcome/results	Refined & outcome/results	date of access	Time refined
China Academic Journals Full-text Database (Basic Search) China Dissertation Database CDDB China Knowledge Resource Integrated Database KNS	"type 2 diabetes treatment" And "Chinese medicine" (Medicine & Public Health initial trial) - 365	Refine by looking at the title & abstract link to RCT - 161	From 20/10/2015 to 10/11/2015	2004 - 2015
PubMed	Chinese herbal medicine AND type 2 diabetes (clinical trial	Refine by looking at the title & abstract link to type 2 diabetes treatment	From 24/11/2014 to 6/04/2016	

	& human research) - 36	with Chinese herbal medicine - 21		
Google Scholar	“traditional Chinese medicine” and “type 2 diabetes’ - 365	Clinical trial - 86	From 24/11/2015 to 25/03/2016	
Web of Science (Basic Search)	type 2 diabet* AND Chinese herbal medicine - 309	Clinical trial - 43	From 7/01/2016 to 7/04/2016	2004-2015

### Appendix 3 Abbreviations

T2DM	type 2 diabetes mellitus
TCM	Traditional Chinese Medicine
WM	Western Medicine
TGA	Therapeutic Goods Administration
WHO	World Health Organisation
ADA	American Diabetes Association
BMI	Body mass index
ECG	electrocardiogram
FBG	fasting blood glucose
FPG	fasting plasma glucose
OGTT	oral glucose tolerance test
HbA1C	Glycated haemoglobin
GHbA1C	Hemoglobiini-A1C
FINS	fasting insulin
TG	Triglyceride
TC	Total cholesterol
LDL-C	Low-density lipoprotein-cholesterol



HDL-C	High-density lipoprotein-cholesterol
IR	Insulin resistance
IRI	Insulin resistance Index
HOMA-IR	Homeostatic Model Assessment of Insulin Resistance.
APTT	Activated Partial Thromboplastin Time
ISI / IAI	insulin sensitivity index
QOL	quality of life
TNF $\alpha$	tumour necrosis factor alpha
ALT	Alanine transaminase
SCR	serum creatinine
BUN	blood urea nitrogen
UA	Urine Analysis
IL-2	Interleukin-2
IL-6	Interleukin-6
FFA	Free Fatty Acids