



Clinical studies of several well-known and valuable herbal medicines: a narrative review

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Background and Objective: Valuable Chinese medicines have a long history in China and are the jewel of traditional Chinese culture. Both plant-origin and animal-origin, occupy a considerable proportion of the health care market due to their various pharmacological activities. But their clinical data is still far from enough. Further clinical trials are needed to successfully obtain evidence of efficacy. Thus, we intend to make an overview of the current clinical use of eight valuable Chinese medicines: *Cordyceps sinensis* (Berk.) Sacc. (*Cordyceps*), *Crocus sativus* Linn. (*Saffron*), *Ganoderma lucidum* (Leyss. Ex Fr.) Karst. (*Ganoderma*), *Collocalia esculenta* L. (*Bird's nest*), *Panax ginseng* C. A. Meyer (*Ginseng*), *Colla corii asini* (*Ejiao*), *Panax notoginseng* (Burk.) F.H.Chen (*Notoginseng*) and *Dendrobium officinale* Kimura et Migo (*Dendrobium*), which are widely known and used by the public.

Methods: We collected some clinical trial data from electronic databases via Google Scholar, PubMed, Web of Science and CNKI (from January 2001 to June 2021 containing both English and Chinese literatures), most were randomized, double-blind, and placebo-controlled trials and a summary was provided in the form of tables.

Key Content and Findings: In this narrative review, we have summarized eight representative valuable herbs, mainly focused on their current clinical applications, intending to provide a comprehensive background for the further development of their clinical use.

Conclusions: Since these herbal medicines are used widely, more clinical studies should be designed to provide more reliable data on their efficacy.

Keywords: Valuable herbal medicines; clinical; double-blind; randomized trials

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Introduction

Practitioners of traditional Chinese medicine (TCM) have accumulated a wealth of experience in the use of medicine over more than two thousand years of clinical practice, resulting in the formation of well-known ancient prescriptions that have been handed down for hundreds of years. Valuable Chinese medicines such as ginseng, cordyceps, ganoderma, etc. occupy a considerable

proportion of the health care market due to their various bioactive components with innumerable health benefits and striking efficacy. However, further clinical trials are needed to successfully obtain evidence of efficacy. In this review, we will focus on eight typical valuable Chinese herbal medicines, containing a representative selection of five plant origins [*Crocus sativus* Linn. (*Saffron*), *Ganoderma lucidum* (Leyss. Ex Fr.) Karst. (*Ganoderma*), *Panax ginseng*

Table 1 The search strategy summary

Items	Specification
Date of Search	1 st July 2021
Databases and other sources searched	Google Scholar, PubMed, Web of Science, CNKI
Timeframe	From January 2001 to June 2021
Inclusion and exclusion criteria	Inclusion: Clinical trial, Randomized Controlled Trial, Review Systematic Review; Both English and Chinese literatures
Selection process	Wenhui Zhang and Lin Xu conducted the selection together. Consensus was obtained by Man Yuan, Wenhui Zhang and Lin Xu through comparing the sample size.

Table 2 The search terms used

Database	Search terms
Google Scholar	" <i>Cordyceps sinensis</i> (Berk.)Sacc.", " <i>Crocus sativus</i> Linn.", " <i>Ganoderma lucidum</i> (Leyss. Ex Fr.) Karst.", " <i>Collocalia esculenta</i> L.", " <i>Panax ginseng</i> C. A. Meyer", " <i>Colla corii asini</i> ", " <i>Panax notoginseng</i> (Burk.) F. H. Chen", " <i>Dendrobium officinale</i> Kimura et Migo", "clinical trial"
PubMed	" <i>Cordyceps sinensis</i> (Berk.)Sacc.", " <i>Crocus sativus</i> Linn.", " <i>Ganoderma lucidum</i> (Leyss. Ex Fr.) Karst.", " <i>Collocalia esculenta</i> L.", " <i>Panax ginseng</i> C. A. Meyer", " <i>Colla corii asini</i> ", " <i>Panax notoginseng</i> (Burk.) F. H. Chen", " <i>Dendrobium officinale</i> Kimura et Migo", "clinical trial"
Web of Science	" <i>Cordyceps sinensis</i> (Berk.)Sacc.", " <i>Crocus sativus</i> Linn.", " <i>Ganoderma lucidum</i> (Leyss. Ex Fr.) Karst.", " <i>Collocalia esculenta</i> L.", " <i>Panax ginseng</i> C. A. Meyer", " <i>Colla corii asini</i> ", " <i>Panax notoginseng</i> (Burk.) F. H. Chen", " <i>Dendrobium officinale</i> Kimura et Migo", "clinical trial"
CNKI	" <i>Cordyceps sinensis</i> (Berk.)Sacc.", " <i>Crocus sativus</i> Linn.", " <i>Ganoderma lucidum</i> (Leyss. Ex Fr.) Karst.", " <i>Collocalia esculenta</i> L.", " <i>Panax ginseng</i> C. A. Meyer", " <i>Colla corii asini</i> ", " <i>Panax notoginseng</i> (Burk.) F. H. Chen", " <i>Dendrobium officinale</i> Kimura et Migo", "clinical trial" are searched by Chinese characters

C. A. Meyer (Ginseng), *Panax notoginseng* (Burk.) F. H. Chen (Notoginseng) and *Dendrobium officinale* Kimura et Migo (Dendrobium)] and three animal-origin herbs [*Cordyceps sinensis* (Berk.)Sacc. (Cordyceps), *Collocalia esculenta* L. (Birds' nest) and *Colla corii asini* (Ejiao)], to provide an in-depth understanding of the valuable cultural and medicinal heritage left by our ancestors.

We present the following article in accordance with the Narrative Review reporting checklist (available at <https://lcm.amegroups.com/article/view/10.21037/lcm-21-56/rc>).

Methodology

Electronic databases viz. Google Scholar, PubMed, Web of Science and CNKI were explored extensively using keywords including "*Cordyceps sinensis* (Berk.)Sacc.", "*Crocus sativus* Linn.", "*Ganoderma lucidum* (Leyss. Ex Fr.) Karst.", "*Collocalia esculenta* L.", "*Panax ginseng* C. A. Meyer", "*Colla corii asini*", "*Panax notoginseng* (Burk.) F. H. Chen",

"*Dendrobium officinale* Kimura et Migo", and "clinical trial". Eventually, relevant literatures published prior to October 2021 were collected, curated and critically evaluated in order to extract necessary information. The recognized accepted plant names and their respective synonyms were validated according to The Plant List (Tables 1,2).

Cordyceps sinensis (Berk.)Sacc.

Cordyceps sinensis (Berk.)Sacc. is a fungus of the ergot family that parasitizes the larvae of Lepidoptera. Chinese Cordyceps is a well-known traditional Chinese medicine with substantial benefits to human health. It is popularly referred to as "Dong Chong Xia Cao" (summer plant, winter worm) (1). With its reputation as a medicinal cure-all with few documented adverse effects, it is no surprise that it has garnered such popularity worldwide in recent years. It has the functions of tonifying the kidney, benefiting the lung, stopping bleeding and resolving

Table 3 Comparison and analysis of clinical studies on *Cordyceps sinensis* (Berk.)Sacc.

No.	Study design	Sample size	Duration	Dosage	Test sample	Conditions	Effect	Main conclusion	Ref
1	Randomized	62 patients	12 months	5 capsules/ 3 times a day	Observation index	Pulmonary tuberculosis	Pulmonary tuberculosis clinical symptoms	Jinshuibao capsule combined therapy has satisfactory clinical effects on newly diagnosed pulmonary tuberculosis	(10)
2	Randomized, double-blind	106 patients	16 weeks	4 capsules/ 3 times a day	Blood	Hypertensive patients with yin and yang deficiency syndrome	Renal function	Jinshuibao capsule combined with losartan potassium showed better effects in treating early renal damage of hypertension patients with yin and yang deficiency syndrome	(14)

Sample size includes the sum of all groups.

phlegm, according to TCM theory. Cordyceps contains various active ingredients, such as cordycepin, adenosine, cordyceps polysaccharide, ergosterol and multiple amino acids (2). Cordycepin, also known as 3-deoxyadenosine, is the most well-studied compound and has been suggested to have many pharmacological effects, such as antitumor (3), antidiabetic (4), anti-inflammatory (5), antimicrobial (6) and immunomodulatory (7) effects.

As cordyceps is a rare herbal medicine rich in pharmacological activities, we also paid full attention to its clinical application. Several nutraceutical preparations made from cordyceps are marketed and reported to have various functions, such as improving intracellular energy exchange, controlling blood glucose levels and lipid profiles, and nourishing the body's immune system (8,9).

Jinshuibao (JSB) capsule, a kind of clinical drug derived from purified and fermented *Cordyceps sinensis*, has been demonstrated to have good effects in the treatment of many diseases and is commonly used to protect the liver, kidney, and other organs. Sixty-two newly diagnosed pulmonary tuberculosis patients achieved a satisfactory clinical effect with JSB capsule combined treatment. In addition, the JSB capsule strongly nourishes, regulates and improves the body's energy metabolism, thus prompting bodily recovery (10). A meta-analysis of randomized controlled trials showed that JSB is an effective accessory therapeutic medicine for patients with early diabetic nephropathy (11), with its contribution to decreasing blood pressure and the level of triglycerides. It can remove urinary proteins, arrest and suspend the progression of diabetic nephropathy (12,13). A double-blind, randomized clinical trial showed that JSB combined with losartan potassium can protect and stabilize the renal function of

hypertensive patients (14) (Table 3). However, as a result of shortages of naturally occurring fungi, there is still a lack of direct clinical studies on cordyceps itself, especially double-blind, randomized clinical trials. Therefore, there is still a need to further verify the therapeutic effect of cordyceps with more strictly and systematically designed clinical tests with large sample sizes in the future.

Crocus sativus Linn.

Crocus sativus Linn. is an herbaceous plant that belongs to the family Iridaceae. It is commonly known as saffron, which is native to southern Europe and cultivated in Beijing, Shandong, Zhejiang, Sichuan, Xinjiang and other places in China (15). *Crocus sativus* Linn. is traditionally used to promote blood circulation, relieve blood stasis, cool the blood and detoxify the body, relieving depression and calming the mind. It has been developed and used in medical supplies, health care products, food, spices and other products, with a wide range of applications and high economic value (16).

The main constituents of saffron are carotenoids, glycosides, flavonoids and terpenoids (17). Over the past two decades, active components, including safranal, crocin, picrocrocin and crocetin, have gained importance in modern pharmacological studies and have shown several properties, including antitumour, antioxidant (18), anti-inflammatory (19), antifibrosis (20), anxiolytic and neuroprotective (21) properties.

There are relatively few clinical studies that use saffron as a therapeutic agent in China, and most of them have focused on efficacy observations. Several double-blind, randomized trials have been conducted to preliminarily evaluate the clinical effect of saffron. Saffron seems to be

Table 4 Comparison and analysis of clinical studies on *Crocus sativus* Linn.

No.	Study design	Sample size	Duration	Dosage	Test sample	Conditions	Effect	Main conclusion	Ref
1	Double-blind clinical trial	64 patients	3 months	30 mg/day	Blood	Type 2 diabetes	Diabetes	Improved hyperglycaemia and lipid profiles in type 2 diabetic patients	(28)
2	Randomized, double-blind, and placebo-controlled trial	84 patients	8 weeks	30 mg/day	Body mass index	Coronary artery disease (CAD)	Obesity	Antiobesity feature of SAE and crocin in patients with CAD	(26)
3	Randomized, double-blind, and placebo-controlled trial	80 patients	8 weeks	50 mg/day	Blood	Allergic asthma	Asthma	Improved clinical symptoms of patients with allergic asthma	(22)
4	Randomized, double-blind	40 patients	6 weeks	30 mg/day	Blood	A prior history of percutaneous coronary intervention (PCI)	Depression	Short-term therapy with saffron capsules showed antidepressant efficacy	(23)
5	Randomized, double-blind, placebo-controlled, pilot clinical trial	40 patients	4 weeks	30 mg/day	Based on the DSM-IV	MDD	Depression	Improved depression and could be an adjunctive treatment in MDD	(24)
6	Randomized	50 patients	3 months	200 mg/day	Blood	Ischaemic stroke	Neuroprotection	Aqueous extract of saffron has short-and long-term neuroprotective effects against ischaemic stroke in humans	(29)
7	Randomized, triple-blind and placebo-controlled trial	66 patients	12 weeks	30 mg/day	Blood	Schizophrenia	Metabolic syndrome	SAE could prevent metabolic syndrome and increases in blood glucose	(25)

MDD, major depressive disorder. SAE, saffron aqueous extract.

an effective and safe option as a supplement to improve the clinical symptoms of patients with allergic asthma (22). However, the toxicity and long-term effects remain unknown. For antidepressant efficacy, short-term therapy with saffron capsules showed improvement in patients with depression after percutaneous coronary intervention (23). Crocin, the main active constituent of saffron, has also been proven to be an adjunctive treatment in major depressive disorder (MDD) (24). Saffron also shows good application potential in metabolic diseases. In a randomized triple-blind placebo-controlled study, 66 patients were allocated to the group receiving saffron aqueous extract (SAE)

capsules. The trial showed that SAE could prevent metabolic syndrome and insulin resistance without serious adverse effects (25). Improvement in appetite, dietary intake and body composition can be observed in patients with coronary artery disease (26). A study has shown that saffron and its derivatives suppress hyperglycaemia in experimental models (27). This effect was also demonstrated in a double-blind randomized clinical trial, where saffron consumption improved hyperglycaemia and the lipid profile in type 2 diabetic patients (28) (Table 4).

As a valuable herbal medicine, *Crocus sativus* Linn. has accumulated a certain clinical background, but limitations

Table 5 Comparison and analysis of clinical studies on *Ganoderma lucidum* (Leyss. Ex Fr.) Karst.

No.	Study design	Sample size	Duration	Dosage	Test sample	Conditions	Effect	Main conclusion	Ref
1	Unknown	18 patients	8 weeks	1000 mg each time, 3 times daily	QOLIE-31	Epilepsy	Seizure frequency	GLSP may help to reduce the weekly seizure frequency in patients with epilepsy	(40)
2	Unknown	48 patients	2 weeks	1,000 mg each time, 3 times daily	Blood	Old myocardial infarction, sequelae of cerebral thrombosis and diabetes mellitus	Platelet aggregation	GL is an effective anti-platelet aggregation agent	(38)
3	Randomized	90 patients	28 days	1,500 mg each time, 3 times daily	Blood	Cervical cancer	Cellular immune function	GLSP can significantly improve cell immunity in elderly patients with cervical cancer and reduce the expression of VEGF	(41)
4	Unknown	19 patients	6 months	3 capsules each time, 3 times daily	Blood, CAT score	Moderate to severe COPD	CAT symptom	improved the CAT symptom score of patients with moderate to severe COPD	(42)

GLSP, ganoderma lucidum spore powder; VEGF, vascular endothelial growth factor; CAT, copd assessment test; COPD, chronic obstructive pulmonary disease.

still exist. Relatively small sample sizes, poor patient compliance with medications and short observational periods are the main problems. Short trials have difficulty achieving a thorough evaluation of the related medications, and larger sample sizes are also required.

Ganoderma lucidum (Leyss. Ex Fr.) Karst.

Ganoderma lucidum (Leyss. Ex Fr.) Karst., commonly known as Lingzhi, is the dried seed entity of the porous fungus purple ganoderma or red ganoderma. It is widely used in China and other Asian countries (30). Historically, Lingzhi has been viewed as a magical herb as well as an auspicious symbol written in Shen Nong Ben Cao Jing by Chinese people. Therefore, it has the reputation of “Mushroom of Immortality” with the meaning of good fortune and mysterious power (31). In TCM theory, Ganoderma can tonify Qi, calm the mind and relieve cough and asthma.

Species of ganoderma have been widely studied and cultivated due to their highly prized medicinal value, and ganoderma is well known as a valuable herbal medicine (32). Recent experimental investigations have confirmed that ganoderma exhibits various pharmacological actions, such as immunomodulatory (33), anticancer (34), antidiabetic (35)

and antioxidant (36) activities. Polysaccharides and triterpenoids are considered to be the main active compounds in ganoderma (37).

In early clinical research, ganoderma was found to have an antiplatelet aggregation effect without any obvious side effects (38). Ganoderma is generally clinically applied in the form of Chinese patented medicine or health care products. *G. lucidum* polysaccharide (GLPS) was developed into a drug named “Ji 731 Injection” in China in 1973 and was approved by the Chinese FDA as “Ling Bao Duo Tang Zhu She Ye” to treat various myopathies (39). Ganoderma Lucidum Spore Powder (GLSP) has all the genetic material and health effects of ganoderma and can be used as a representative for clinical research. A retrospective study that included 18 eligible patients demonstrated the reduction effect of GLSP on the weekly seizure frequency in patients with epilepsy (40). Chinese researchers also found that GLSP could improve postoperative cellular immunity in elderly cervical cancer patients and improve the chronic obstructive pulmonary disease (COPD) assessment test (CAT) symptom score of patients with moderate to severe COPD (Table 5).

Currently, we cannot find successful randomized, double-blind trials on the medicinal efficacy of ganoderma.

Evidence from a placebo-controlled trial of *Ganoderma lucidum* (Leyss. Ex Fr.) Karst. does not support the use of ganoderma for the treatment of cardiovascular risk factors in people with diabetes mellitus or metabolic syndrome (43).

Another double-blind, randomized, placebo-controlled pilot trial for the efficacy of ganoderma water extract in patients with rheumatoid arthritis also failed (44). Therefore, more clinical studies should be carried out to provide convincing scientific data to meet the criteria for new drug development.

Collocalia esculenta L.

Collocalia esculenta L., commonly known as Edible bird's nest (EBN), is the saliva produced by certain types of swiftlets belonging to the family Apodidae and the genus *Aerodramus*. It is regarded as both a valuable herbal medicine and a nutrient food in China. Traditional Chinese medicine believes that EBN has the functions of nourishing the stomach, moistening the lung and relieving cough (45).

The main chemical components of EBN include proteins, carbohydrates, sialic acid, amino acids and a small amount of fat and trace minerals (46). The chemical composition and characteristics of bird nests vary depending on the source, type, harvesting season and other factors (47). It is thought to have immunoregulatory (48), antiviral and anti-inflammatory (48), antioxidant (49) and neuroprotective (50) properties.

Since bird's nest is a rare tonic that can be used as both medicine and food, its production is limited due to constraints on the environment, resulting in an increasing demand and a high price. To date, EBN is still used as a safe, palatable nutritional supplement. Although many believe and claim that EBN has various health-promoting effects and medicinal value (51), its clinical data are far from sufficient. At present, we did not find any systematic, double-blind, randomized clinical trials conducted on EBN.

Panax ginseng C. A. Meyer

Ginseng, one of the most well-known Chinese herbal medicines, is widely used in many different traditional medical recipes. It is a dry rhizome belonging to *Araliaceae ginseng*. According to Oriental medicine theory, it can invigorate qi, enhance the body's immune system, promote tissue regeneration, induce more rapid diuresis, expel pus, and reduce swelling. Therefore, ginseng is considered "The

Lord of herbs" (52). Pharmacological studies in recent decades have shown that ginsenosides are the mechanism underlying the effects of ginseng (53). Ginsenosides, which include Rb1, Rb2, Rb3, Rc, Rd, Rg3, Re, Rg1, Rg2, and Rh1 (54), contribute to ginseng's antioxidant (55), antinociceptive, anti-inflammatory (56), antimicrobial (57), anti-cardiovascular disease (58), antidiabetic (59), anti-central nervous system disorder (60) and anticancer (61) effects. Additionally, there is evidence showing that ginseng can enhance energy and sexuality (62,63).

Demonstration of the various effects of ginseng in both *in vivo* and *in vitro* experiments has attracted attention to its clinical manifestations. We needed a control group to confirm the effectiveness of ginseng. Several clinical trials have been organized globally to identify the actual efficacy of ginseng.

According to a double-blind, randomized, controlled experiment, ginseng has significant effects in improving sexual function and quality of life and mitigating menopausal symptoms (64). Ginseng has also been found to be safe for people with COPD, including those taking standard inhaled therapies for COPD (65), although its effects are similar to those of the placebo (Table 6).

Additionally, in stark contrast to an empirical advisory rejecting ginseng on the grounds that it possesses antiplatelet and anticoagulation effects, a study in 2016 confirmed that the combination of ginseng products with aspirin did not further aggravate the platelet inhibition caused by aspirin and that ginseng did not impair partial thromboplastin time (PTT)/activated PTT (APTT) or thrombin generation (66) (Table 6).

Ginseng was further found to possess antioxidant properties by enhancing the antioxidant defence mechanism in healthy populations (67). Moreover, ginseng was found to be capable of enhancing cognitive performance in AD patients in an experiment conducted in 2008 (68) (Table 6).

However, ginseng was also found to be ineffective in treating patients with fibromyalgia (69), as well as patients with cancer-related fatigue (70).

Colla corii asini

Colla corii asini (CCA), also known as Ejiao, is one of the oldest Chinese medicines and is made from the skin of a donkey. In particular, it is the water extraction of the donkey skin. CCA has been used in life nourishing and clinical haematic anti-anaemia therapy for more than 2,000 years in Asia (71). According to previous reports, the main

Table 6 Comparison and analysis of clinical studies on *Panax ginseng* C. A. Meyer

No.	Year	Study design	Sample size	Duration	Dosage	Test sample	Conditions	Effect	Main conclusion	Ref.
1	2019	Double-blind, randomized	62 patients	4 weeks	500 mg twice daily	Female sexual function index, menopause-specific quality of life, Green menopausal symptom scale	Menopausal period and sexual performance	Performance enhanced and menopausal effect mitigated	According to the analysis of the result, Ginseng has significant effects in improving sexual function and quality of life and mitigating menopausal symptoms	(64)
2	2018	Multicentre, randomized, double-blind,	168 patients	24 weeks	100 mg twice daily	the St George's Respiratory Questionnaire, the COPD assessment test and the Short Form Health Survey	Health-related quality of life in COPD patients	Same effect as placebo but safe to take	The results showed that ginseng and placebo demonstrated similar benefits in health-related quality of life, but ginseng was safe for people with COPD, including those taking standard inhaled therapies for COPD	(65)
3	2016	Randomized, double-blind, placebo-controlled	25 patients	3 weeks	1,000 mg once daily	PT/APTT, platelet function by light transmission aggregometry and thrombin generation assay by calibrated automated thrombogram were measured at baseline and after each phase. Information on adverse reactions including bleeding manifestations	Test on antithaemostatic effect	No evidence of platelet inhibition or anticoagulation effect	According to the results, they concluded that the combination of ginseng products with aspirin did not further aggravate platelet inhibition caused by aspirin and that ginseng did not impair PT/APTT or thrombin generation	(66)
4	2011	Randomized, placebo-controlled	82 patients	4 weeks	1,000 mg twice daily	Serum level of reactive oxygen species (ROS), malondialdehyde (MDA), total antioxidant capacity (TAC), the activities of catalase, superoxide dismutase (SOD), glutathione reductase (GSH-Rd), and peroxidase (GSH-Px), and total glutathione content	Antioxidant effect	It can act as an antioxidant	In conclusion, the findings indicated that ginseng had antioxidant properties. It enhanced the antioxidant defence mechanism in healthy populations	(67)

Table 6 (continued)

Table 6 (continued)

No.	Year	Study design	Sample size	Duration	Dosage	Test sample	Conditions	Effect	Main conclusion	Ref.
5	2008	Randomized, double blinded, placebo controlled	58	12 weeks	4.5 g once daily	Mini-Mental State Examination and cognitive disease assessment scale	Alzheimer Disease	Clinically effective		(68)
6	2011	Double-blind, randomized, placebo-controlled	38 patients	12 weeks	100 mg once daily	Ratings on the Visual Analogue Scale and Fibromyalgia Impact Questionnaire - FIQ	fibromyalgia	Did not seem to have an effect	However, there were no significant differences between groups	(69)
7	2017	Randomized, double-blind, placebo-controlled	112 patients	28 days	400 mg twice daily	Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) subscale	Cancer-related fatigue	No evidence of effectiveness	No evidence of effectiveness	(70)

COPD, chronic obstructive pulmonary disease.

components of Ejiao are amino acids (72), proteins (73), gelatine (74), and polysaccharides (75). According to the theory of traditional Chinese medicine, it is mild in nature and has a good warming effect, which can help people with a relatively weak physique to increase their resistance and invigorate their spirits. In daily applications, Ejiao has been widely used in gynaecology, such as the treatment of dysmenorrhea, menoxenia, metrorrhagia, and abortion (76). Additionally, it has been used for chronic diseases such as anxiety, insomnia, apostaxis, haemoptysis, haematuria, and haemafecia (77). Recent experimental investigations have confirmed that Ejiao exhibits various bioactivities, such as anti-anaemia activity (78), thrombocytopenia therapeutic activity (79), leukocyte-increasing activity (80), antiageing activity (81), antitumour activity (82), immunomodulatory activity (83), anti-inflammatory activity (84), and antifatigue activity (85).

Although Ejiao has been used for a long time in TCM and various effects have been shown in both *in vivo* and *in vitro* experiments, its clinical manifestations remain to be confirmed. Controlled studies are needed to identify real-world data.

Unlike many other valuable Chinese medicines, the number of clinical trials of Ejiao is unexpectedly small. Apart from relatively prominent cases, such as a study performed in 2019 that concluded that CCA had an anti-anaemia effect on pregnant women with β -thalassemia through translation regulation (86), most studies are reports on clinical analysis instead of randomized, double-blind, placebo-controlled clinical trials. Since Ejiao has been used so widely regardless of medicinal methods or health supplies, more reliable data are required to verify its efficacy. Therefore, more clinical studies should be designed to provide convincing scientific data, which could greatly benefit the development of Ejiao and other related products.

Panax notoginseng (Burk.)F. H. Chen

Panax notoginseng (Burk.)F. H. Chen, also known as sanqi, is widely used in China. The medicinal part is the dry root. At first, it was originally used by ethnic minorities in southwestern China (87) and then became popular throughout China. According to the ancient Chinese medicine book “Ben Cao Gang Mu Shi Yi (Supplements to the Compendium of Materia Medica)”, ginseng was the first to nourish qi, notoginseng was the first to nourish blood, they tasted the same, and their effects were equal. Ginseng and notoginseng were the most valuable Chinese medicines.

Table 7 Comparison and analysis of clinical studies on *Panax notoginseng* (Burk.) F. H. Chen

No.	Year	Study design	Sample size	Duration	Dosage	Test sample	Conditions	Effect	Main conclusion	Ref.
1	2012	Double-blind, 20 randomized volunteers controlled		5 days	4,000 mg/day	Performance measures, pain assessments, blood analyses	Well-trained males	Delayed-onset muscle soreness and muscle damage	P. notoginseng did not convincingly have an effect on performance, muscular pain or the assessment of blood markers in well-trained males after an intense bout of eccentric exercise that induced delayed-onset muscled soreness (DOMS)	(96)
2	2012	Double-blind, 52 men randomized controlled		3 days	3 g/day	Exercise heart rate (HR), rating of perceived exertion (RPE), blood samples	Untrained, nondiabetic men	Postprandial glycaemia in nondiabetic adults	Notoginseng had a beneficial effect on postprandial glucose disposal in untrained males. Panax notoginseng had antihyperglycaemic activity	(97)
3	2005	Randomized, 29 adults double-blind, placebo-controlled		30 days	1,350 mg/day	Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) subscale	Untrained subjects	Enhanced physical performance during endurance exercise	Panax notoginseng could improve endurance time to exhaustion, and lowered mean blood pressure during endurance exercise	(98)

Compounds isolated from notoginseng include saponins, flavonoids, nonprotein amino acids, polysaccharides, fatty acids, aliphatic alkenes and peptides (88). Notoginseng contains some of the same ginsenosides as ginseng, including Rb1, Rd, Re, Rg1, Rg2 and Rh1. However, notoginseng contains some unique saponins, such as notoginsenosides R1, Rt, R2, R3, R4, and R6 (89). Different kinds of active compounds enable notoginseng to have various effects, such as cardioprotective effects (90), neuroprotective effects (91), anti-inflammatory effects (92), haemostasis and anticoagulation (93), antiaging effects (94) and antihypertension effects (95).

It can be seen from the above that some effects of *Panax notoginseng* have been pharmacologically proven, and the performance of it in clinical applications is also striking. Controlled group data are needed to confirm the real changes caused by *Panax notoginseng*.

For delayed-onset muscle soreness and muscle damage,

notoginseng did not show significant differences from placebo (96). According to a double-blind, randomized, controlled experiment, notoginseng was proven to be effective in postprandial glucose disposal, which showed its antihyperglycaemic activity (97). Additionally, notoginseng was found to improve the endurance time to exhaustion and lower the mean blood pressure during endurance exercise (98) (Table 7).

Although some of the effects have been proven, the common shortcomings of these trials are that the sample sizes were very small and the duration was not long enough. Therefore, it is necessary to conduct more trials to confirm the real effect of *Panax notoginseng* on the human body.

Dendrobium officinale Kimura et Migo

Dendrobium officinale Kimura et Migo is a valuable traditional herbal medicine that is distributed widely throughout

China and is usually found on trees and rocks. According to traditional Chinese medicine theory, it can nourish the stomach, nourish fluids, nourish yin and clear heat. The bioactive compounds of dendrobium are polysaccharides, alkaloids, bibenzyls, phenanthrenes, flavonoids and other constituents (99). However, the most important and extensively researched is polysaccharides. These different kinds of bioactive compounds enable dendrobium to have different effects. According to modern pharmacological studies, dendrobium has anticancer activity (100), antiangiogenic activity (101), immunomodulatory activity (102), hepatoprotective activity (103), anti-inflammatory activity (104), antidiabetic activity (105), and antioxidant activity (102). The fibrous stems of *Dendrobium officinale* can be directly cut into sections and dried or twisted into a spiral and dried as tiepifengdou (106), which is the most familiar form for consumers.

Although dendrobium has been widely used in both Chinese medicine and health care, there is not enough attention to its performance in clinical trials. At present, data are very scarce. A trial held in China in 2018 concluded that for patients with type 2 diabetes mellitus (T2DM), *Dendrobium officinale* powder could effectively relieve clinical symptoms, control blood sugar and improve islet function (107).

As the result of the clinical trial has been proven, the antidiabetic effect of *Dendrobium officinale* and its real-world effects have great potential, and it is necessary and helpful to conduct more trials to confirm other effects of this medicine. Additionally, larger sample sizes are required.

Discussion and conclusion

The eight typical valuable Chinese herbal medicines mentioned above have been well studied for their chemical properties and pharmacological mechanism in the laboratory. However, as a result of shortages of these naturally occurring herbs, there is still a need to further verify the therapeutic effects with double-blind, randomized clinical trials.

Ganoderma, bird's nest and dendrobium need more strictly and systematically designed clinical tests with large samples in the future. In particular, clinical data on dendrobium and Bird's nest, which could greatly benefit their development and other related products, are far from sufficient. For ganoderma, we cannot find successful randomized, double-blind trials on its medicinal efficacy at the present time. Evidence from a placebo-controlled

trial of *Ganoderma lucidum* does not support the use of ganoderma for the treatment of cardiovascular risk factors in people with diabetes mellitus or metabolic syndrome. Therefore, more clinical studies should be carried out to provide convincing scientific data to meet the criteria for new drug development.

Additionally, although a clinical drug (JSB capsule) derived from purified and fermented cordyceps has achieved some clinical trials, there is still a lack of direct clinical studies on *Cordyceps sinensis* (Berk.) Sacc. itself. It is necessary and helpful to conduct more trials to confirm other effects if we want to promote its clinical use.

Unlike those on many other valuable Chinese medicines, most studies about Ejiao report on clinical analysis instead of randomized, double-blind, placebo-controlled clinical trials. Since Ejiao is used widely, more clinical studies should be designed to provide more reliable data on its efficacy.

Saffron, ginseng and notoginseng have accumulated a certain clinical background, but limitations still exist. The relatively small sample sizes, poor patient compliance with medications and short observational periods are the main problems. Short trials have difficulty achieving a thorough evaluation of the related medications, and larger sample sizes are required. It is essential to conduct more trials to confirm the real effect of these medicines on the human body.

Here, we summarize the clinical advances of eight valuable Chinese herbal medicines with the intention of providing a basis for broadening their clinical use in the future.

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