



Review Article

Chinese Herb *Patrinia Herba* (Bai Jiang Cao) for Acute Respiratory Tract Infections: A Systematic Review of Clinical Studies



R.-X. Zheng^a, Z.-Y. Yu^a, C. Shen^a, M. Willcox^b, J. Trill^b, M. Moore^b, X.-Y. Hu^{b,1}, J.-P. Liu^{a,*,1}

^a Center for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing 100029, China

^b Primary Care, Population Sciences, and Medical Education, Faculty of Medicine, Southampton SO16 5ST, UK

ARTICLE INFO

Keywords:

Patrinia Herba

Chinese herb

Systematic review

Clinical trials

Acute respiratory tract infections

ABSTRACT

Introduction: Acute respiratory tract infections (ARTIs) are a group of common diseases with a high incidence that cause tremendous pressure on the healthcare system globally. *Patrinia Herba* (Bai Jiang Cao) has a long history of use in China. This systematic review aimed to evaluate the clinical effectiveness and safety of *Patrinia Herba* for ARTIs.

Methods: We searched the Chinese and English databases from their inception to March 2022 for clinical studies that tested single-herb preparations or formulae containing *Patrinia Herba* for ARTIs. We used the Cochrane Risk of Bias 2 and non-randomised studies as intervention tools for quality assessment. The review protocol was registered with PROSPERO (CRD42021260330).

Results: Six trials (2 107 participants) were identified. Two trials were pooled. The results showed that, in adults and children with influenza, single *Patrinia Herba* granules or injections improved the participants' feelings of aversion to cold, general malaise, nasal obstruction, runny nose, sore throat, cough, headache, and dizziness after a two-day treatment. For adults and children with pneumonia, *Patrinia Herba* compound preparations plus antibiotics appeared better than antibiotics alone in relieving fever, cough, shortness of breath, and chest pain. The overall methodological quality of the included randomised controlled trials was rated as unclear, low, or moderate for controlled clinical trials. No severe adverse events were reported.

Discussion: Low- or moderate-quality evidence demonstrates that single herb or compound preparations of *Patrinia Herba* may be effective for ARTIs in terms of symptom remission. Further high-quality studies are needed to confirm their potential for treating ARTIs.

Introduction

Acute respiratory tract infections (ARTIs), such as otitis media, sinusitis, pharyngitis, acute bronchitis, influenza, and pneumonia, as well as non-specific upper respiratory tract infections, cause tremendous pressure on health systems globally (Rashidi et al., 2021; Renati and Linder, 2016). According to the World Health Organization's (2020) list of the top 10 causes of death globally, lower respiratory tract infections are listed as the fourth most important (World Health Organization, 2020). Additionally, 17.1 billion cases of upper respiratory tract infections were reported in 2017 (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Since its emergence in 2019, COVID-19 has caused over 500 million confirmed cases and over 6 million deaths and is still mutating (World Health Organization, 2021a). In the United States, seasonal influenza is estimated to impose

an average annual economic burden of \$11.2 billion on healthcare systems and society (Putri et al., 2018).

At present, the treatment of ARTIs includes symptomatic and antibiotic treatments, where the effectiveness of symptomatic treatment is uncertain (Harris et al., 2016; National Institute for Health and Care Excellence, 2018). Moreover, there is a risk of adverse events (AEs) when using symptomatic treatments. For example, non-steroidal anti-inflammatory drugs may cause nephrotoxicity, and the combination of analgesic and decongestive agents could cause various AEs such as drowsiness, difficulty sleeping, lethargy, indigestion, nervousness, palpitations, and light headedness (De Sutter et al., 2012; Little, 2020). Antibiotic treatment faces a shortage of innovative antibiotics to cope with the growing emergence and spread of antibiotic resistance (World Health Organization, 2021b).

Herbal medicine has a long history of treating ARTIs and has been widely studied in modern times. In China, one of the earliest extant

* Corresponding author.

E-mail address: liujp@bucm.edu.cn (J.-P. Liu).

¹ These authors have contributed equally to this work and share corresponding authorship.

studies on Chinese medicine named ‘Shennong’s Classic of Materia Medica’ recorded 365 different kinds of Chinese medicine. Of these, 41 Chinese herbs have been used to treat various heat syndromes, as classified in traditional Chinese medicine (TCM) (Wang and Su, 2021). Most of the symptoms and signs of ARTIs, such as fever, sore throat, discoloured sputum, and dry mouth, are part of these syndromes. Huang et al. (2019) performed a review of Chinese herbal medicine for ARTIs and found seven clinical studies which showed that herbal medicine may relieve symptoms such as fever, headaches, coughing, myalgia, cold, sore throat, and nasal obstruction. The review listed several frequently used herbs for relieving heat, including *Patrinia Herba* (Bai Jiang Cao).

Patrinia Herba has a long history of use in China. According to the TCM theory, *Patrinia Herba* has a pungent and bitter flavour, is cooling, and relates to the stomach, large intestine, and liver meridians (Gao, 2007). There are two official species, *Patrinia Herba* and *Patrinia scabiosaefolia* Fisch. (*P. scabiosaefolia*) and *Patrinia villosa* Juss. (*P. villosa*) (Zhang and Cao, 1996). According to the ‘Tang materia medica’ and the ‘Compendium of Materia Medica,’ both *P. scabiosaefolia* (Supplementary Fig. S1) and *P. villosa* (Supplementary Fig. S2) were used as *Patrinia Herba* in Chinese history (Zhang and Cao, 1996). *P. scabiosaefolia* is found in most parts of China, whereas *P. villosa* grows in northern, eastern, central, and southwestern China (Yang, 2005). Pharmacological studies have shown that *Patrinia Herba* has antibacterial effects against *Staphylococcus aureus*, *Streptococcus*, and *Escherichia coli* (Tan et al., 2003). Anti-inflammatory (Lee et al., 2012; Lin et al., 2018), antioxidant (Lin et al., 2018; Sun et al., 2018; Xie et al., 2008; Xie et al., 2018), sedative, and hypnotic effects (Gong et al., 2021; Tan et al., 2003; Xu et al., 2007) have also been reported. Another possible mechanism of action for the effectiveness of *Patrinia Herba* might be the large intestine-lung pairing viscera theory in TCM (Ni and Gao, 2012).

This systematic review aimed to evaluate the clinical effectiveness and safety of *Patrinia Herba* in ARTIs.

Methods

This review was registered in PROSPERO (CRD42021260330) and reported according to the PRISMA 2020 statement (Page et al., 2021). See Supplementary Table S1 for the checklist.

We made a few changes to the protocol during the research.

1. Case control studies were removed from the inclusion criteria because they did not reflect the effectiveness of *Patrinia Herba*.
2. We used the risk of bias in non-randomised studies of intervention tool for assessing controlled clinical trials (CCTs) to make the quality assessment more accurate and specific.
3. To minimise this limitation, we conducted a second-stage search to retrieve formulae and patents that could not be identified during the first stage. The first-stage search strategy only refers to publications which clearly reported the use of *Patrinia Herba*.

Eligibility Criteria

Study design: Prospective controlled studies, such as randomised controlled trials (RCTs), CCTs, and cohort studies, qualified for inclusion.

Participants: Patients of all age groups were included if they had a confirmed or suspected diagnosis of ARTI. Conditions included common cold, influenza, rhinosinusitis, laryngitis, tonsillitis, pharyngitis, croup, acute otitis media, bronchitis, pneumonia, and acute exacerbation of chronic obstructive pulmonary disease. Symptoms of suspected ARTIs included cough, sore throat, fever, runny nose, and discoloured sputum for a duration of 4 weeks or less.

Patients with life-threatening conditions were excluded from the study. Patients with chronic infections and ambiguity regarding the presence of infection were excluded.

Interventions and comparators: *Patrinia Herba* (Bai Jiang Cao), either as a single herb or as a component of an Herbal mixture, qualified for inclusion. Any form of herbal preparation, such as decoction, granule, injection, paste, pills, and steam, provided with or without conventional therapies, was included. There were no limits on the dosage or duration of treatment. For comparators, placebo, no treatment, waitlist control, and usual care such as antipyretics, antivirals, antibiotics, anti-inflammatory drugs, steroids, or corticosteroids were included.

Shufeng Jiedu capsules (containing *Patrinia Herba*) are widely used as ARTIs. There have been systematic reviews on the effectiveness and safety of ARTIs and acute exacerbation of chronic obstructive pulmonary disease (Xia et al., 2020; Zhang et al., 2021). Therefore, we excluded this patented herbal medicine.

Main outcomes: Time to complete resolution of systemic symptoms (such as fever, pain, and aversion to cold) and respiratory symptoms (such as runny nose, cough, and sore throat) in days or the proportion of patients resolved at a predefined time.

Secondary outcomes: (1) Changes in the use of antibiotics, such as dosage, duration, and class. (2) Absent days from work or school or the proportion of participants who had days off due to ARTIs. (3) Proportion of participants who needed to be admitted to the hospital and length of hospitalisation. (4) AEs (any anaphylactic, allergic reactions, hypersensitivity reactions, or complications that resulted from *Patrinia Herba*, as well as any herbal-drug interactions).

Serious AEs were defined according to the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use guidelines as follows (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, 2016).

As a result, serious AEs were considered to be any event that leads to death, is life-threatening, requires hospitalisation, leads to persistent or significant disability, or causes congenital anomaly or birth defect.

Search Strategy

There were two stages of literature search conducted.

The first stage focused on identifying publications that clearly reported *Patrinia Herba* as ARTIs. The China National Knowledge Infrastructure, Wanfang Database, Chinese Scientific Journals Database (VIP), SinoMed, EMBASE, MEDLINE, CINAHL, Cochrane Central Register of Controlled Trials, and PubMed were searched from their inception to 3 March 2022.

Search terms related to *Patrinia Herba* (Bai Jiang Cao) were identified from the ‘National Compilation of Chinese Herbal Medicine,’ ‘A Quick-consultative Dictionary of World Medicinal Planta,’ the ‘Standard List of Chinese Medicinal Materials,’ and the ‘Chinese Materia Medica: volume 20.’

Search terms related to acute respiratory infections were developed based on Medical Subject Headings.

The second stage was performed to minimise the limitations of this review. We searched for trials of patent TCMs and formulae containing *Patrinia Herba*, which had been identified in the first stage. The same databases as in the first phase were searched from their inception to 3 March 2022, and we conducted backward citation searching for the included studies.

(See Supplementary Table S2 for the full strategy of the stage 1 search and Supplementary Table S3 for the stage 2 search.)

Study Selection and Data Extraction

After removing duplicates, three authors (ZYY, RXZ, and CS) independently assessed eligibility. A third author (JPL or XYH) was asked to make the final decision if consensus could not be reached.

A predesigned Excel sheet was piloted and used to extract the data. The authors were contacted if additional information was required.

Assessment of Risk of Bias

The Cochrane Risk of Bias 2 tool was used to assess RCTs (Higgins et al., 2022). The risk of bias in non-randomised studies of intervention tool was used to assess the CCTs (Sterne et al., 2016). The Newcastle-Ottawa Scale was used for cohort studies (Ottawa Hospital Research Institute, 2021).

Two authors (ZYY and RXZ) independently evaluated the risk of bias. Disagreements were resolved through discussion among the authors (RXZ, ZYY, CS, MW, JT, MM, XYH, and JPL).

Data Synthesis

RevMan 5.3 software was used to pool the data where possible. If reported, intention-to-treat data and treatment scores at the end of treatment were used for the analysis. Binary data were presented as a risk ratio (RR) with a 95% confidence interval (CI) and continuous data as the mean difference (MD) with a 95% CI. If the units of the outcome measures used across studies were not consistent, the effects of standardised MD were used. The overall effect size of 0.2–0.5 was regarded as small, 0.5–0.8 as moderate, and more than 0.8 as large.

Statistical heterogeneity was assessed using the I^2 statistic (Higgins et al., 2022). When I^2 was greater than 0% and lower than 30%, the heterogeneity was considered not important; when I^2 was greater than 30% and lower than 50%, it was considered moderate heterogeneity; when I^2 was greater than 50% and lower than 75%, it was considered substantial heterogeneity; when I^2 was greater than 75%, it was considered considerable heterogeneity. Where substantial heterogeneity existed, a sensitivity analysis was conducted to further investigate potential sources of heterogeneity. Sensitivity analyses were performed for the primary outcomes to determine whether the review conclusions would have differed if eligibility was restricted to trials with a low risk of selection bias.

Analyses of subgroups were based on different preparations of *Patrinia Herba* (such as granules or capsules), pathogens (such as bacterial infection or virus infection), study design (such as RCT, CCT, and cohort study), age groups (under 18 years were defined as children), and comparators (such as symptomatic relief, antibiotics, antiviral agents, and/or steroids).

Results

Study Selection

Four thousand and eighty-two studies were identified from the databases. After removing 931 duplicates, 3 097 records were screened. Of these, 2 954 records were excluded, and 143 were assessed for eligibility. Six studies were included after the full-text screening. The details are shown in Figure 1.

Study Characteristics

All included trials were conducted in China as single-centre studies. There were two CCTs (Li and Qin, 2019; Research Cooperation Group of Influenza Prevention and Control in Yichun Region of Jiangxi Province [Yichun], 1981) and four RCTs (Hu, 2010; Liu, 2008; Zhan, 2021; Zheng, 2017). The included conditions varied and comprised influenza (Yichun, 1981), community-acquired pneumonia (CAP) (Li and Qin, 2019; Zhan, 2021; Zheng, 2017), childhood pneumonia (Hu, 2010), and CAP with underlying diseases (Liu, 2008). The interventions used varied and included *Patrinia Herba* as a monotherapy using different forms of administration (granules versus injection) (Yichun, 1981); in five trials, *Patrinia Herba* was a component of different formulae, such as decoctions (Li and Qin, 2019; Zhan, 2021; Zheng, 2017), a syrup (Hu, 2010), and an oral solution (Liu, 2008). The comparators included antiviral agents, antibiotics, and symptomatic and supportive treatment. Further details are provided in Table 1.

Critical Appraisal of Methodological Quality

Of the six included trials, four were RCTs (Hu, 2010; (Liu, 2008); Zhan, 2021; Zheng, 2017), one of which used a random number table (Zhan, 2021), whereas the other three did not provide details of randomisation. One trial stated that participants were randomised by the classes at school they were in, so that, it was defined as CCT (Yichun, 1981). The other CCT did not mention any information on randomisation (Li and Qin, 2019). None of the included trials reported allocation concealment. Blinding was not used in any trial. All included trials failed to mention any missing data, patients' loss to follow-up, or any information regarding the protocol. Figures 2 and 3 show the risk of bias graphs of the included CCTs and RCTs.

Effectiveness and Safety

Six trials on single *Patrinia Herba* preparation and herbal mixtures containing *Patrinia Herba* were included for analysis. Two RCTs of herbal mixture named Huatan Qingfei decoction on patients with CAP were pooled for meta-analysis (Zhan, 2021; Zheng, 2017). One CCT of single-herb preparation *P villosa* on patients with flu (Yichun, 1981), one CCT of Huatan Qingfei decoction on patients with CAP (Li and Qin, 2019), one RCT of Qingre Huatan decoction on patients with CAP (Liu, 2008), and one RCT of sugar syrup containing *Patrinia Herba* on patients with pneumonia (Hu, 2010) were unable to be pooled due to high heterogeneity. Findings from one trial (Hu, 2010) were reported narratively as they did not report the standard deviation; therefore, the effective estimation could not be made.

A summary of *Patrinia Herba* preparations used in patients with ARTIs is shown in Table 2.

P villosa for Flu (One Trial)

There was one CCT regarding the use of *P villosa* as a single-herb preparation (Yichun, 1981). The trial compared the effectiveness of *P villosa* granules or injections as monotherapy (intervention group) with the antiviral agent moroxydine (control group) against influenza.

After a 2-day treatment, the trial indicated that *P villosa* had better effects than moroxydine on fever (RR: 1.57, 95% CI [1.23, 2.00], 334 participants), aversion to cold (RR: 1.42, 95% CI [1.11, 1.81], 261 participants), general malaise (RR: 1.61, 95% CI [1.26, 2.05], 341 participants), nasal obstruction (RR: 1.63, 95% CI [1.26, 2.09], 331 participants), runny nose (RR: 4.44, 95% CI [2.47, 8.00], 189 participants), sore throat (RR: 2.39, 95% CI [1.48, 3.87], 144 participants), cough (RR: 2.10, 95% CI [1.50, 2.93], 294 participants), headache (RR: 2.01, 95% CI [1.49, 2.71], 341 participants), and dizziness (RR: 2.13, 95% CI [1.59, 2.87], 308 participants) (Yichun, 1981).

There was no significant difference between the *P villosa* and antiviral groups for sneezing (RR: 1.21, 95% CI [1.00, 1.47], 199 participants), backache (RR: 1.38, 95% CI [0.96, 1.97], 137 participants), conjunctival congestion (RR: 1.32, 95% CI [0.33, 5.35], 67 participants), and throat congestion (RR: 1.10, 95% CI [0.92, 1.30], 138 participants) (Yichun, 1981).

There is uncertainty regarding the data of this trial (Yichun, 1981), especially regarding fever and throat congestion. The baseline health information of the patients and the evaluation of efficacy differed according to the number of patients with fever and throat congestion. The author was a Collaborative Research Group of Influenza Prevention and Control in Yichun, Jiangxi Province, and did not provide any contact details. As the trial was conducted in the early 1980s, no relevant information on the research team was found on the Internet; thus, we could not contact them.

Herbal Mixtures Containing *Patrinia Herba* for Community-Acquired Pneumonia (Four Trials)

There were four papers that studied the effects of herbal mixtures containing *Patrinia Herba* for CAP (Li and Qin, 2019; Liu, 2008; Zhan, 2021; Zheng, 2017).

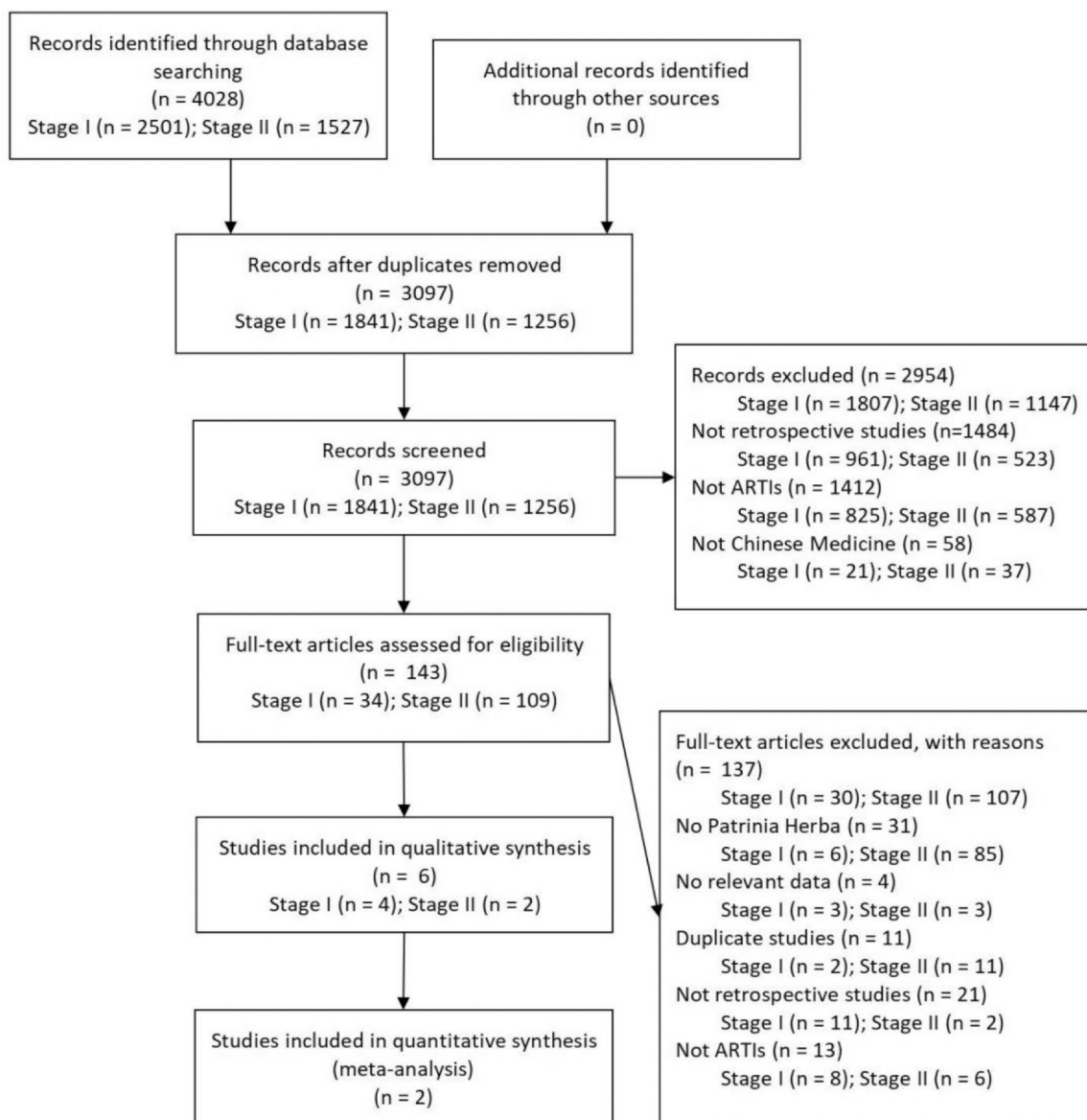


Fig. 1. Flow diagram of literature retrieval. ARTI, acute respiratory tract infection.

One RCT compared Qingre Huatan oral solution plus standard care with standard care alone (intravenous antibiotics, oxygen inhalation, and supportive treatments) (Liu, 2008). The trial included patients with CAP with underlying diseases, such as pulmonary heart disease, pharyngitis, and coronary heart disease.

After 10–14 days of treatment, there was a significant difference between the treatment and control groups for the resolution time of fever (MD: -2.72 days, 95% CI $[-3.71, -1.73]$, 74 participants), cough (MD: -3.35 days, 95% CI $[-4.63, -2.07]$, 81 participants), shortness of breath (MD: -2.8 days, 95% CI $[-3.83, -1.77]$, 66 participants), chest pain (MD: -3.05 days, 95% CI $[-4.24, -1.86]$, 54 participants), and constipation (MD: -2.46 days, 95% CI $[-3.55, -1.37]$, 61 participants) (Liu, 2008).

Two RCTs and one CCT compared Huatan Qingfei decoction plus acupoint application combined with antibiotics versus antibiotics alone (Li and Qin, 2019; Zhan, 2021; Zheng, 2017).

In terms of symptom remission, the pooled results of the RCTs showed that the treatment group had a shorter duration of cough (MD: -1.97 days, 95% CI $[-2.04, -1.90]$, I^2 : 0%) and fever (MD: -2.7 days, 95% CI $[-2.77, -2.63]$, I^2 : 0%) than the control group at week 4. There was no statistically significant difference between the two groups in terms of headache improvement (Zhan, 2021; Zheng, 2017).

Herbal Mixtures Containing *Patrinia Herba* for Pneumonia in Children (One Trial)

One trial in children with pneumonia compared conventional therapy (intravenous antibiotics) combined with a sugar syrup containing *Patrinia Herba* versus conventional therapy alone (Hu, 2010). The trial measured the mean resolution time of fever (treatment group: 1.88 days; control group: 2.86 days) and cough (treatment group: 4.63 days; control group: 6.48 days).

No study has reported the outcomes of the changes of the antibiotics usage or other outcomes of interest.

Summary of Adverse Events

One CCT and two RCTs compared Huatan Qingfei decoction combined with acupoint and antibiotics versus antibiotics for CAP-measured AEs (Li and Qin, 2019; Zhan, 2021; Zheng, 2017). Pruritus, nausea, vomiting, dizziness, headache, and gastrointestinal reactions were also observed. There were no statistically significant differences between the treatment and control groups in any of the trials.

One CCT included patients with CAP with underlying diseases compared to Huatan Qingfei decoction plus acupoint application combined with antibiotics versus antibiotics used alone. There was no

Table 1
Characteristics of included trials.

Study ID	Study design	Disease (course)/ Settings (severity)	Control group		Treatment group		Pauritia Herba content	Course of treatment	OTP	Outcome indicators
			Sample size (male–female)/ age (M ± SD)	Intervention (comparators)	Sample size (male–female)/age (M ± SD)	Intervention				
Jiangxi KYZ 1981	CCT	Flu (unclear)/ inpatients (unclear)	78 (unclear)/ (unclear)	Moroxydine: > 15 y: 0.3–0.4 g; 7–15 y: 0.2 g; < 7 y: 0.1 g, three times a day, PO	401 (341–138)/ > 15 y: 371; 7–15 y: 93; < 7 y: 15	<i>P. villosa</i> granules ² , 1 pack (17 g) – 0.5 pack (8.5 g), three times a day, PO, for 2 d; <i>P. villosa</i> injections ³ , 2 ml (8 g) – 1 ml (4 g), IM	1 (100%)	2 D	2 D	1. Effective rate; systemic symptoms resolution: fever ^{4,5} , aversion to cold ^{4,6} , general malaise ^{4,6} 2. Respiratory symptoms resolution: nasal obstruction ^{4,6} , runny nose ⁴ , sneezing ⁴ , sore throat ⁴ , cough ⁴ , headache ^{4,6} , dizziness ^{4,6} , backache ⁴ , conjunctival congestion ⁴ , throat congestion ^{4,5} 3. AEs: skin itching ⁴ , nausea and vomiting ⁴ , dizziness ⁴
Li YC 2019	CCT	CAP (CG: 4–12 mo; TG: 3–11 mo)/unclear (unclear)	50 (25–25)/ (44.9 ± 3.3)	Levofloxacin, 0.4 g, Qd, plus normal saline 100 ml, intravenous drip, for 10 d	50 (27–23)/ (45.6 ± 3.2)	Huatan Qingfei decoction ⁷ , one set, twice a day, PO + acupoint application ⁸ , Qd, for 10 d + comparators	1 (combined with acupoint application, unable to calculate)	10 D	10 D	1. Effective rate 2. Laboratory indices: WBC, N, PCT, CRP, HsCRP 3. AEs: skin itching ⁴ , nausea and vomiting ⁴ , dizziness ⁴
Zhan SN 2021	RCT	CAP (CG: 4–15 d; TG: 4–12 d)/unclear (unclear)	46 (25–21)/ (37.18 ± 9.53)	Azithromycin injection, 10 mg/(kg*d ⁻¹), IV, for 6 d. Then azithromycin tablets, 10 mg/(kg*d ⁻¹), PO, for 4 wk	45 (26–19)/ (36.9 ± 9.36)	Huatan Qingfei decoction ⁹ , one set, twice a day, PO + acupoint application ¹⁰ , Qd, for 4 wk + comparators	1 (combined with acupoint application, unable to calculate)	4 W	4 W	1. TCM clinical syndrome integral 2. Systemic symptoms resolution: fever ^{4,6} 3. Respiratory symptoms resolution: cough ^{4,6} , lung rale ⁶ 4. Laboratory indices: WBC, PCT ⁶ , CRP ⁶ , IgM ⁶ , IgA ⁶ , IgG ⁶ 5. AEs: nausea ⁴ , vomiting ⁴ , headache ⁴
Zheng LT 2017	RCT	CAP (CG: 3–12 d; TG: 3–15 d)/unclear (mild: 34; moderate: 38; severe: 8) ¹¹	80 (46–34)/ (36.91 ± 9.35)	Azithromycin injection, 10 mg/(kg*d ⁻¹), IV, for 5 d. Then azithromycin tablets, 10 mg/(kg*d ⁻¹), PO, QD, for 3 d, stopped for 4 d, and start taking for 3 d.	80 (43–37)/ (37.19 ± 9.52)	Huatan Qingfei decoction ¹² , one set, twice a day, PO + acupoint application ¹³ , Qd, for 4 wk + comparators	1 (combined with acupoint application, unable to calculate)	4 W	4 W	1. Effective rate 2. Systemic symptoms resolution: fever ^{4,6} 3. Respiratory symptoms resolution: cough ^{4,6} , lung rale ⁶ 4. Laboratory indices: WBC ⁶ , N ⁶ , IL-6 ⁶ , IL-10 ⁶ , IgM ⁶ , IgA ⁶ , IgG ⁶ 5. AEs: headache ⁴ , gastrointestinal reactions ⁴ , dizziness ⁴
Hu HC 2010	RCT	Pneumonia (5–28 d)/unclear (unclear)	596 (unclear)/ (children)	Routine antibiotics intravenously administered; symptomatic treatments	600 (unclear)/ (children)	Pneumonia sugar syrup ¹⁴ , one set per day, three times a day, PO, for 1 wk + comparators	2 (without modification 8.3%)	1 W	1 W	1. Effective rate 2. Systemic symptoms resolution: fever ⁴ 3. Respiratory symptoms resolution: cough ⁴ , lung rale, tongue coating, and nature

(continued on next page)

Table 1 (continued)

Study ID	Study design	Disease (course)/ Settings (severity)	Control group		Treatment group		Patrinia Herba content ¹	Course of treatment	OTP	Outcome indicators
			Sample size (male-female)/age (M ± SD)	Intervention (comparators)	Sample size (male-female)/age (M ± SD)	Intervention				
Liu SX 2008	RCT	CAP with underlying diseases (unclear)/ Inpatients and outpatients (unclear)	40 (19-21)/ (56)	Antibiotics intravenous drip according to sensitive test, oxygen inhalation, supportive treatment, for 10-14 d	41 (21-20)/(54)	Qingre Huatan oral solution ¹⁵ , 10 ml, three times a day, PO, for 10-14 d + comparators	1 (10.4%)	10-14 D	Unclear	1. Effective rate 2. Systemic symptoms resolution: fever and dry mouth ^{1,6} , constipated ^{1,6} 3. Respiratory symptoms resolution: cough and sputum ^{4,6} , shortness of breath ^{4,6} , chest pain ^{4,6} , lung rale ⁶ 4. X ray: inflammation total absorption ⁶

OTP, observation time point; M, mean; SD, standard deviation; CAP, community-acquired pneumonia; CCT, controlled clinical trial; RCT, randomised controlled trial; CG, control group; TG, treatment group; *P villosa*, *Patrinia villosa* Juss.; Qd, once a day; Mo, month (s); D, day (s); W, week (s); PO, oral administration; IV, injection of vein; AE, adverse event; TCM, traditional Chinese medicine.

¹ *Patrinia Herba* content: the ranking of the content of the *Patrinia Herba* in the interventions (*Patrinia Herba* as a percentage of all herbs).

² *P villosa* granules: *Patrinia villosa* Juss. granules 13 g plus white sugar, and dextrin, made in Yichun regional pharmaceutical factory, Yichun Xiujiang pharmaceutical factory.

³ *P villosa* injections: *Patrinia villosa* Juss. distillation plus benzyl alcohol, and normal saline, 2 ml, made in Gao'an County People's Hospital.

⁴ Interested outcome in this review.

⁵ The data are questionable.

⁶ There was significant statistical difference between the treatment group and the control group ($P < 0.01$).

⁷ Huanan Qingfei decoction: *Herba Hououmyniae* (Yuxingcao) 20 g, *Patrinia Herba* (Baijiangcao) 20 g, *Trichosanthes kirilowii* Maxim. (Gualou) 15 g, *Fructus Perillae* (Suzi) 10 g, *Cortex Mori* (Sangbaipi) 10 g, *Semen Armeniacae Amarum* (Xingren) 10 g, *Radix Astragalii* (Huangqi) 10 g, *Bombyx Batryticatus* (Jiangcan) 10 g, *Rhizoma Belamcandae* (Shegan) 10 g, *Herba Ephedrae* (Mahuang) 5 g, *Radix Platycodonis* (Jiegeng) 5 g, *Radix Et Rhizoma Glycyrrhizae* (Gancao) 5 g.

⁸ Acupoint application: RN17 (Danzhong), BL13 (Feishu), RN22 (Tiantu), EX-B1 (Dingchuan), BL43 (Gaohuang), etc. Plaster application. Made in Ye Hall, Xingjia, Wuhan. No. 20180708. Made of: non-woven fabrics, far-infrared power powder, medical grade pressure-sensitive adhesive, and magnetic materials.

⁹ Huanan Qingfei decoction: *Fructus Perillae* (Suzi) 10 g, *Herba Ephedrae* (Mahuang) 5 g, *Cortex Mori* (Sangbaipi) 10 g, *Radix Platycodonis* (Jiegeng) 5 g, *Radix Astragalii* (Huangqi) 10 g, *Patrinia Herba* (Baijiangcao) 20 g.

¹⁰ Acupoint application: RN17 (Danzhong), BL23 (Shenshu), EX-B1 (Dingchuan), BL13 (Feishu), BL43 (Gaohuang), *Semen Sinapis albae* (Baijiezi), *Cortex Cinnamomi* (Rougui), etc. ground to powder, and mixed with white vinegar. Then stirred to form a paste prepared as 5.5 cm × 3 cm ointment patch. Once a day.

¹¹ The diagnosis of the severity of CAP was from "Respiratory Society of Chinese Medical Association, 1999. Guidelines for the diagnosis and treatment of community-acquired pneumonia. 20 (4): 158-160.

¹² Huanan Qingfei decoction: *Fructus Perillae* (Suzi) 10 g, *Herba Ephedrae* (Mahuang) 5 g, *Herba Hououmyniae* (Yuxingcao) 20 g, *Trichosanthes kirilowii* Maxim. (Gualou) 15 g, *Cortex Mori* (Sangbaipi) 10 g, *Radix Platycodonis* (Jiegeng) 5 g, *Semen Armeniacae Amarum* (Xingren) 10 g, *Radix Astragalii* (Huangqi) 10 g, *Patrinia herba* (Baijiangcao) 20 g, *Bombyx Batryticatus* (Jiangcan) 10 g, *Rhizoma Belamcandae* (Shegan) 10 g, *Radix Et Rhizoma Glycyrrhizae* (Gancao) 5 g. Boiled.

¹³ Acupoint application: RN17 (Danzhong), BL23 (Shenshu), RN22 (Tiantu), BL17 (Geshu), EX-B1 (Dingchuan), BL43 (Gaohuang). Once a day.

¹⁴ Pneumonia sugar syrup: *Radix Scutellariae* (Huangqin) 9 g, *Herba Hououmyniae* (Yuxingcao) 9 g, *Patrinia Herba* (Baijiangcao) 9 g, *Cortex Magnoliae Officinalis* (Houpo) 9 g, *Semen Raphani* (Laiyuzi) 9 g, *Radix Et Rhizoma Salviae Miltiorrhizae* (Danshen) 9 g, *Rhizoma Chuanxiong* (Chuanxiong) 9 g, *Pheretima* (Dilong) 9 g, *Fructus Crataegi* (Shanzha) 15 g, *Fructus Forsythiae* (Lianqiao) 6 g, *Radix Et Rhizoma Glycyrrhizae* (Gancao) 6 g. For children under 5 years old, reduce all herbs by 3 g. Children with clean nasal discharge added *Ramulus Cinnamomi* (Guizhi) 3 g, *Rhizoma Et Radix Cynanchi Stauntonii* (Baiqian) 6 g; children with nasal discharge thick and yellow added *Radix peucedani* (Qianhu) 6 g, *Bulbus Fritillariae Thunbergii* (Zhebeimu) 3 g; children with shortness of breath added *Herba Ephedrae* (Mahuang) 3 g, *Semen Armeniacae Amarum* (Xingren) 6 g. Self-formulated decoction.

¹⁵ Qingre Huatan oral solution: *Patrinia Herba* (Baijiangcao) 15 g, *Herba Hououmyniae* (Yuxingcao) 15 g, *Flos Farfarae* (Kuandonghua) 15 g, *Semen Lepidii Semen Descurainiae* (Tinglizi) 15 g, *Fructus Forsythiae* (Lianqiao) 15 g, *Concretio Silicea Bambusae* (Tianzhuhuang) 10 g, *Pheretima* (Dilong) 10 g, *Bulbus Fritillariae Thunbergii* (Zhebeimu) 10 g, *Rhizoma Phragmitis* (Lugen) 12 g, *Rhizoma Anemarrhenae* (Zhimu) 12 g, boiled and filtrated, concentrating filtrate, 10 ml. Hospital preparation.

¹⁶ There was statistical difference between the treatment group and the control group ($P < 0.05$).

Study ID	D1	D2	D3	D4	D5	D6	D7	Overall
<i>P. villosa granules/injections v. antiviral agents</i>								
Jiangxi KYZ	L	L	L	?	L	M	?	M
<i>Huatan Qingfei decoction+acupoint application+ iv levofloxacin v. iv levofloxacin alone</i>								
LI YC	L	L	L	L	L	M	?	M

Fig. 2. Risk of bias assessment of controlled clinical trials of *Patrinia Herba* for ARTIs. D1, bias due to confounding; D2, bias in selection of participants into study; D3, bias in classification of intervention; D4, bias due to deviations from intended intervention; D5, bias due to missing data; D6, bias in measurement of outcomes; D7, bias in selection of the reported result; ?, no information; L, low risk of bias; M, moderate risk of bias; H, high risk of bias.

Study ID	Comparisons and outcomes	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
<i>Huatan Qingfei decoction+acupoint application+ iv levofloxacin v. iv levofloxacin alone</i>							
Zheng LT	fever	?	?	L	?	?	?
	cough	?	?	L	H	?	H
	nausea	?	?	L	?	?	?
	vomiting	?	?	L	?	?	?
	headache	?	?	L	?	?	?
Zhan SN	fever	?	?	L	?	?	?
	cough	?	?	L	H	?	H
	headache	?	?	L	?	?	?
	gastrointestinal reaction dizziness	?	?	L	?	?	?
<i>Pneumonia sugar syrup+usual care v. usual care alone (Antibiotics+symptomatic treatments)</i>							
Hu HC	fever	?	?	L	?	?	?
	cough	?	?	L	H	?	H
<i>Qingre Huatan oral solution+usual care v. usual care alone (antibiotics+oxygen+supportive treatments)</i>							
Liu SX	fever	?	?	L	?	?	?
	cough	?	?	L	H	?	H
	shortness of breath	?	?	L	H	?	H

Fig. 3. Risk of bias assessment of randomised controlled trials of *Patrinia Herba* for ARTIs. ?, unclear risk of bias; L, low risk of bias; H, high risk of bias.

statistically significant difference between the treatment and control group in terms of pruritus (RR: 3.00, 95% CI [0.13, 71.92], 100 participants), nausea and vomiting (RR: 0.5, 95% CI [0.05, 5.34], 100 participants), and dizziness (RR: 3.00, 95% CI [0.13, 71.92], 100 participants) (Li and Qin, 2019).

The two RCTs involving patients with CAP compared Huatan Qingfei decoction plus acupoint application and antibiotics versus antibiotics used alone. In terms of headache (RR: 0.34, 95% CI [0.01, 8.15], 251 participants), dizziness (RR: 1.00, 95% CI [0.06, 15.71], 160 participants), gastrointestinal reactions (RR: 2.00, 95% CI [0.19, 21.62], 160 participants), nausea (RR: 1.02, 95% CI [0.07, 15.85], 91 participants), and vomiting (RR: 1.02, 95% CI [0.07, 15.85], 91 participants), there were no statistically significant differences between the treatment and control groups (Zhan, 2021; Zheng, 2017).

Discussion

Summary of Main Results

Comprehensive searches of English and Chinese databases identified six clinical studies on *Patrinia Herba* for ARTIs, including four RCTs

(1528 participants) (Hu, 2010; Liu, 2008; Zhan, 2021; Zheng, 2017) and two CCTs (579 participants) (Li and Qin, 2019; Yichun, 1981).

One CCT compared the effectiveness of *Patrinia Herba* granules or injection as monotherapy with moroxydine against influenza. Other trials have studied *Patrinia Herba* as part of the herbal mixture.

For influenza, *Patrinia Herba* as a monotherapy administered as granules or injections might improve aversion to cold, general malaise, nasal obstruction, runny nose, sore throat, cough, headache, and dizziness after a 2-day treatment (Yichun, 1981).

For adult and child pneumonia, herbal mixtures containing *Patrinia Herba* combined with antibiotics might have advantages over antibiotics alone in relieving fever, cough, shortness of breath, and chest pain (Hu, 2010; Li and Qin, 2019; Liu, 2008; Zhan, 2021; Zheng, 2017).

Apart from safety, no results regarding the use of antibiotics or other secondary outcomes have been reported. Skin itching (1/50 participants for 10 days), nausea and vomiting (1/50 participants for 10 days, 2/45 participants for 4 weeks), dizziness (1/50 participants for 10 days), headache (1/125 participants for 4 weeks), dizziness (1/80 participants for 4 weeks), and gastrointestinal reactions (2/80 participants for 4 weeks) were reported in three trials (351 participants) (Li

Table 2
Summary of results on *Patrinia Herba* preparations for patients with ARTIs.

Comparisons and outcomes	Effect estimate [CI] (EST)	P-value	OTP	Study ID (No. of participants)
Disease: flu				
<i>P villosa granules/injections v. antiviral agents</i>				
Fever	RR: 1.57, [1.23, 2.00] (3.66)	< 0.01	2 D	Jiangxi KYZ 1981 (334)
Aversion to cold	RR: 1.42, [1.11, 1.81] (2.83)	< 0.01	2 D	Jiangxi KYZ 1981 (261)
General malaise	RR: 1.61, [1.26, 2.05] (3.84)	< 0.01	2 D	Jiangxi KYZ 1981 (341)
Nasal obstruction	RR: 1.63, [1.26, 2.09] (3.78)	< 0.01	2 D	Jiangxi KYZ 1981 (331)
Runny nose	RR: 4.44, [2.47, 8.00] (4.98)	< 0.01	2 D	Jiangxi KYZ 1981 (189)
Sneezing	RR: 1.21, [1.00, 1.47] (1.97)	0.05	2 D	Jiangxi KYZ 1981 (199)
Sore throat	RR: 2.39, [1.48, 3.87] (3.56)	< 0.01	2 D	Jiangxi KYZ 1981 (144)
Cough	RR: 2.10, [1.50, 2.93] (4.36)	< 0.01	2 D	Jiangxi KYZ 1981 (294)
Headache	RR: 2.01, [1.49, 2.71] (4.54)	< 0.01	2 D	Jiangxi KYZ 1981 (341)
Dizziness	RR: 2.13, [1.59, 2.87] (5.01)	< 0.01	2 D	Jiangxi KYZ 1981 (308)
Backache	RR: 1.38, [0.96, 1.97] (1.76)	0.08	2 D	Jiangxi KYZ 1981 (137)
Conjunctival congestion	RR: 1.32, [0.33, 5.35] (0.39)	0.69	2 D	Jiangxi KYZ 1981 (67)
Throat congestion	RR: 1.10, [0.92, 1.30] (1.06)	0.29	2 D	Jiangxi KYZ 1981 (138)
Disease: community-acquired pneumonia				
<i>Qingre Huatan oral solution + usual care v. usual care alone (antibiotics + oxygen + supportive treatments)</i>				
Fever	MD: -2.72, [-3.71, -1.73] (5.36)	< 0.01	10-14 D	Liu SX 2008 (74)
Cough	MD: -3.35, [-4.63, -2.07] (5.11)	< 0.01	10-14 D	Liu SX 2008 (81)
Shortness of breath	MD: -2.80, [-3.83, -1.77] (5.33)	< 0.01	10-14 D	Liu SX 2008 (66)
Chest pain	MD: -3.05, [-4.24, -1.86] (5.04)	< 0.01	10-14 D	Liu SX 2008 (54)
Constipation	MD: -2.46, [-3.55, -1.37] (4.41)	< 0.01	10-14 D	Liu SX 2008 (61)
<i>Huatan Qingfei decoction + acupoint application + iv levofloxacin v. iv levofloxacin alone</i>				
Skin itching	RR: 3, [0.13, 71.92] (0.68)	0.5	10 D	Li YC 2019 (100)
Nausea and vomiting	RR: 0.5, [0.05, 5.34] (0.57)	0.57	10 D	Li YC 2019 (100)
Dizziness	RR: 3, [0.13, 71.92] (0.68)	0.5	10 D	Li YC 2019 (100)
Nausea	RR: 1.02, [0.07, 15.85] (0.02)	0.99	4 W	Zhan SN 2021 (91)
Vomiting	RR: 1.02, [0.07, 15.85] (0.02)	0.99	4 W	Zhan SN 2021 (91)
Headache	RR: 0.34, [0.01, 8.15] (0.01)	0.99	4 W	Zhan SN 2021; Zheng LT 2017 (251)
Dizziness	RR: 1.00, [0.06, 15.71] (0.00)	1	4 W	Zheng LT 2017 (160)
Gastrointestinal reactions	RR: 2.00, [0.19, 21.62] (0.57)	0.57	4 W	Zheng LT 2017 (160)
Cough	MD: -1.97, [-2.04, -1.9] (56.99), I ² : 0%	< 0.01	4 W	Zhan SN 2021; Zheng LT 2017 (251)
Fever	MD: -2.7, [-2.77, -2.63] (77.66), I ² : 0%	< 0.01	4 W	Zhan SN 2021; Zheng LT 2017 (251)
<i>Pneumonia sugar syrup + usual care v. usual care alone (antibiotics + symptomatic treatments)</i>				
Fever	NA	NA	1 W	Hu HC 2010 (932)
Cough	NA	NA	1 W	Hu HC 2010 (1103)

CI, confidence interval; EST, effect size test; OTP, observation time point; MD, mean difference; RR, risk ratio; D, day; W, week; iv, injection of vein.

and Qin, 2019; Zhan, 2021; Zheng, 2017). There was no statistically significant difference between patients treated with antibiotics and those treated with a combination of antibiotics and Huatan Qingfei decoction.

The quality of the evidence was low or moderate because of non-standard randomisation, vague reporting, and no information on the registered protocol, allocation and concealment, or implemented blinding. The other major limitation is that, in all the studies on pneumonia, both the intervention and control groups were treated with intravenous antibiotics, followed by long courses of oral antibiotics. There was no attempt to shorten the course of antibiotics in the groups receiving herbal medicine; therefore, whether *Patrinia Herba* may reduce antibiotic consumption is unclear. In a study on influenza, the comparator group received monoxidine, which is not a standard treatment and has not been proven to work in any RCTs, unlike oseltamivir, which is currently the treatment of choice (National Institute for Health and Care Excellence, 2009). Furthermore, the outcomes were measured on day 2, which was very early. It would be useful to determine the impact on day 7.

Implications and Suggestions for Future Trials

In response to increasing antibiotic resistance, detailed reports should be made on the information of participants treated with

antibiotic agents, and the dosage, length, and name used. In this review, five studies used antibiotics as comparators. However, two trials failed to mention the type of antibiotics and how they were administered to how many participants (Hu, 2010; Liu, 2008). Three trials provided little information on participants to clarify the appropriate use of antibiotics (Li and Qin, 2019; Zhan, 2021; Zheng, 2017). Hence, the effects of Chinese herbs on antibiotics remain unclear. Further research is needed to determine whether *Patrinia Herba* could be used to shorten the course of antibiotics and thereby help reduce antibiotic resistance.

One suggestion is that there should be a more rigorous design and clearer reporting for future antibiotic-related trials. First, antibiotics should be used as recommended by current guidelines to ensure that the results are applicable and generalisable. Second, disease severity should be reported to ensure that antibiotic use is reasonable and necessary. Finally, when antibiotics are used as comparators, the type and course of the antibiotics should be reported in as much detail as possible to better judge the effectiveness of the interventions being tested.

There are various forms of preparations and dosages used for *Patrinia Herba* herbal products, such as decoctions, granules, injections, and syrups. Although this discourages data pooling, it provides a greater number of options to study the effect of *Patrinia Herba*. The 'Jiangxi KYZ study in 1981' assessed an intravenous injection with fast absorption (Yichun, 1981), whereas Hu (2010) used a syrup in the treatment of paediatric pneumonia.

The influence of the tongue coating can be added to the outcome measurements. The colour and nature of tongue coating are key elements guiding diagnosis, prognosis, and treatment in TCM theory (Liang et al., 2002, 2020). The information gathered on tongue changes may help in the selection of TCM syndrome differentiation and treatment options. Only one trial included in this review observed changes before and after treatment. As the *P*-value was not reported, a definite conclusion was not possible.

It is also suggested that specific species of *Patrinia Herba* should be reported. The five of six included trials were unclear of the distinction between *P scabiosaefolia* and *P villosa*, although their chemical compositions are very different (Liu et al., 2020). Only one of the six publications retrieved in this review reported the specific species used.

Despite the lack of evidence, our findings are consistent with a systematic review of the traditional uses and pharmacology of *Patrinia Herba* by Gong et al. (2021). In this review, *Patrinia Herba* was used for colds (Miao nationality) and inflammation (Korea) and has anti-inflammatory, antioxidant, antibiotic, sedative, and hypnotic effects. Based on the evidence we identified, the resolution of fever, cough, shortness of breath, chest pain, sore throat, headache, and aversion to cold may be related to the anti-inflammatory, antioxidant, and antibiotic actions of *Patrinia Herba*. The improvement in general malaise may be related to the sedative and hypnotic effects.

Limitations

This study provided a general and preliminary description of the effectiveness and safety of *Patrinia Herba*. A conclusive summary of the specific effects of *P scabiosaefolia* species or *P villosa* cannot be made, as the included trials seldom reported the exact species of *Patrinia Herba*. The composition of phytochemicals differs between herbal preparations (Liu et al., 2020), and the methods of preparation vary. These could not be considered equivalent and should be evaluated separately and reflected in the design of trials. We contacted the authors but failed to receive a response from them to retrieve more relevant information. Hence, in this review, only the results of different types of preparations are presented, and the effectiveness and safety of *Patrinia herba* are summarised. There was a potential risk of contamination as some included trials used antibiotics or other complementary approaches in addition to *Patrinia Herba* as part of the treatment plan. A real-world study in primary clinic practice analysing patients with fever (66, 983 patients) and cough (163, 514 patients) showed that the acupoint application group has a lower proportion of antibiotic use than the non-application group (Li et al., 2022). It was unclear which parts of the effects were due to the herb as the additional interventions may lead to an overestimation of the true association between the treatments and the outcomes.

Conclusion

Low- or moderate-quality evidence shows *Patrinia Herba* used as a single herb or within formulae may be effective for ARTIs in terms of symptom relief. Limited data are reported on AEs, and no major AEs are observed. More high-quality placebo-controlled RCTs are needed to assess the effectiveness of symptom relief and reduction in antibiotic use.

Funding statement

This review was funded by the National Key Research and Development Project (grant no. 2018YFE0102300) in China and by Innovate UK (grant no. 104287–610239).

Data availability

All data used in this review are available upon request from the corresponding authors.

Ethical approval

This review do not include human participants or animal experiments. The *Patrinia Herba* pictures used in the review were authorised by the plant photo bank of China (CC_BY_NC_ND).

Financial support statement

This review was funded by the National Key Research and Development Project (grant no. 2018YFE0102300) in China and by Innovate UK (grant no. 104287–610239).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hermed.2023.100791.

References

- De Sutter, A.I.M., van Driel, M.L., Kumar, A.A., Lesslar, O., Skrt, A., 2012. Oral anti-histamine-decongestant-analgesic combinations for the common cold. *Cochrane Database Syst. Rev.* 2, CD004976. <https://doi.org/10.1002/14651858.CD004976.pub3>
- Gao, X.M., 2007. *Chinese Medicine*. China Press of Traditional Chinese Medicine Co Ltd.
- GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018. Disease and Injury Incidence and Prevalence Collaborators., 2018. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 392, 1789–1858. [https://doi.org/10.1016/S0140-6736\(18\)32279-7](https://doi.org/10.1016/S0140-6736(18)32279-7)
- Gong, L.N., Zou, W., Zheng, K.Y., Shi, B.R., Liu, M.H., 2021. The Herba Patriniae (Caprifoliaceae): a review on traditional uses, phytochemistry, pharmacology and quality control. *J. Ethnopharmacol.* 265, 113264. <https://doi.org/10.1016/j.jep.2020.113264>
- Harris, A.M., Hicks, L.A., Qaseem, A., 2016. Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high-value care from the American College of Physicians and the Centers for Disease Control and Prevention. *Ann. Intern. Med.* 164, 425–434. <https://doi.org/10.7326/M15-1840>
- Higgins, J.P.T., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J., Welch, V.A. (Eds.), 2022. *Cochrane Handbook for Systematic Reviews of Interventions* Version 6.3 (updated February 2022). Available at: <www.training.cochrane.org/handbook>. Accessed July 14, 2022.
- Hu, H.C., 2010. 600 cases of Pneumonia syrup combined with antibiotics for child pneumonia. *Shanxi J. Tradit. Chin. Med.* 31, 293–294. <https://doi.org/10.3969/j.issn.1000-7369.2010.03.024>
- Huang, Z., Pan, X., Zhou, J., Leung, W.T., Li, C., Wang, L., 2019. Chinese herbal medicine for acute upper respiratory tract infections and reproductive safety: a systematic review. *Biosci. Trends* 13, 117–129. <https://doi.org/10.5582/bst.2018.01298>
- International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), 2016. Integrated Addendum to ICH E6(r1): Guideline for Good Clinical Practice E6(R2). Available at: <https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-clinical-practice-e6r2-4-step-2b_en.pdf>. Accessed July 14, 2022.
- Lee, E.J., Kim, C., Kim, J.Y., Kim, S.M., Nam, D., Jang, H.J., Kim, S.H., Shim, B.S., Ahn, K.S., Choi, S.H., Jung, S.H., 2012. Inhibition of LPS-induced inflammatory biomarkers by ethyl acetate fraction of *Patrinia scabiosaefolia* through suppression of NF- κ B activation in RAW 264.7 cells. *Immunopharmacol. Immunotoxicol.* 34, 282–291. <https://doi.org/10.3109/08923973.2011.602412>
- Li, R., Li, Q.N., Li, C.F., Lu, F., Zi, M.J., Gao, R., 2022. Influence of acupoint application on clinical use of antibiotics: a real world study of 1.23 million primary clinic patients. *Zhongguo Zhen jiu = Chin. Acupunct. Moxibustion* 42 (3), 241–249. <https://doi.org/10.13703/j.0255-2930.20210907-0002>
- Li, Y.C., Qin, L., 2019. 50 cases of Huatan Qingfei decoction combined with acupoint application and western medicine for community-acquired pneumonia. *Tradit. Chin. Med. Res.* 32, 16–18. <https://doi.org/10.3969/j.issn.1001-6910.2019.09.07>
- Liang, L., Wang, S.Z., Yang, D.X., Qu, N.N., 2020. A brief analysis on the pathogenesis outcome of novel coronavirus pneumonia according to tongue coating characteristics. *J. Liaoning Univ. Tradit. Chin. Med.* 22, 120–123. <https://doi.org/10.13194/j.issn.1673-842x.2020.03.031>
- Liang, R., Wang, Z.P., Hou, Y.F., Liu, W.L., Zhu, Y.C., Chen, J.X., et al., 2002. Correlative analysis on tongue manifestation and symptoms of acute respiratory infection diseases. *J. Basic Chin. Med.* 8, 9–13. <https://doi.org/10.3969/j.issn.1006-3250.2002.11.004>

- Lin, J., Cai, Q.Y., Xu, W., Lin, J.M., Peng, J., 2018. Chemical composition, anticancer, anti-neuroinflammatory, and antioxidant activities of the essential oil of *Patrinia scabiosaefolia*. *Chin J Integr Med.* 24, 207–212.
- Little, P., 2020. Non-steroidal anti-inflammatory drugs and covid-19. *BMJ* 368, m1185. <https://doi.org/10.1136/bmj.m1185>
- Liu, S.X., 2008. 41 cases of Qingre Huatan oral solution for pneumonia. *Shanxi Journal of Traditional Chinese Medicine* 29, 393–394. <https://doi.org/10.3969/j.issn.1000-7369.2008.04.007>
- Liu, Y., Liu, W., Wang, J., Liu, Y., Chen, C., Xiang, Z., 2020. Phytochemical and pharmacological review on two herbs of Baijiangcao: *Patrinia scabiosaefolia* Fisch. ex Trev. and *Patrinia villosa* (Thunb.) Juss. *Mini-Rev. Org. Chem.* 17, 496–517.
- National Institute for Health and Care Excellence, 2009. Amantadine, oseltamivir and zanamivir for the treatment of influenza Technology appraisal guidance [TA168]. Available at: <https://www.nice.org.uk/guidance/ta168/chapter/1-Guidance>. Accessed July 14, 2022.
- National Institute for Health and Care Excellence, 2018. Self-limiting respiratory tract and ear infections – antibiotic prescribing overview. Available at: <https://pathways.nice.org.uk/pathways/self-limiting-respiratory-tract-and-ear-infections-antibiotic-prescribing>. Accessed July 14, 2022.
- Ni, J.X., Gao, S.H., 2012. Understanding the viscera-related theory that the lung and large intestine are exterior-interiorly related. *J. Tradit. Chin. Med.* 32, 293–298. [https://doi.org/10.1016/s0254-6272\(13\)60028-x](https://doi.org/10.1016/s0254-6272(13)60028-x)
- Ottawa Hospital Research Institute, 2021. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non randomised studies in meta-analyses. Available at: www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed July 14, 2022.
- Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372, n71. <https://doi.org/10.1136/bmj.n71>
- Putri, W.C.W.S., Muscatello, D.J., Stockwell, M.S., Newall, A.T., 2018. Economic burden of seasonal influenza in the United States. *Vaccine* 36, 3960–3966. <https://doi.org/10.1016/j.vaccine.2018.05.057>
- Rashidi, K., Razi, B., Darand, M., Dehghani, A., Janmohammadi, P., Alizadeh, S., 2021. Effect of probiotic fermented dairy products on incidence of respiratory tract infections: a systematic review and meta-analysis of randomized clinical trials. *Nutr. J.* 20, 61. <https://doi.org/10.1186/s12937-021-00718-0>
- Renati, S., Linder, J.A., 2016. Necessity of office visits for acute respiratory infections in primary care. *Fam. Pract.* 33, 312–317. <https://doi.org/10.1093/fampra/cmw019>
- Research cooperation group of influenza prevention and control in Yichun region of Jiangxi Province, 1981. Effective of *Patrinia villosa* for flu: an observation on 401 cases. *Chin. J. Med.* 3, 39–41.
- Sterne, J.A., Hernán, M.A., Reeves, B.C., Savović, J., Berkman, N.D., Viswanathan, M., Henry, D., Altman, D.G., Ansari, M.T., Boutron, I., Carpenter, J.R., 2016. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 355, i4919. <https://doi.org/10.1136/bmj.i4919>
- Sun, X.C., Lei, L.Y., Huang, W.J., Shi, X.B., Song, Z.X., Tang, Z.S., 2018. Correlation between chemical components and antioxidant activity of *Patriniae Herba* extracts. *China Pharm.* 21, 2111–2113. <https://doi.org/10.3969/j.issn.1008-049X.2018.12.005>
- Tan, C., Sun, Z.L., Zhou, K.Y., Xu, J.P., 2003. Studies on chemical constituents and sedation and antibacterial effect of *Patrinia scabiosaefolia* Fisch. *J. Tradit. Chin. Vet. Med.* 22, 3–5. <https://doi.org/10.3969/j.issn.1000-6354.2003.04.001>
- Wang, Y., Su, X., 2021. Drug characteristics, regularity and application of Shennong's Classic of *Materia Medica* in the treatment of cough with dyspnea. *China Med. Her.* 18, 164–167.
- World Health Organization, 2020. The top 10 causes of death. Available at: <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death>. Accessed July 14, 2022.
- World Health Organization, 2021a. WHO coronavirus (COVID-19) dashboard. Available at: <https://covid19.who.int/>. Accessed July 14, 2022.
- World Health Organization, 2021b. Global shortage of innovative antibiotics fuels emergence and spread of drug-resistance. Available at: <https://www.who.int/news/item/15-04-2021-global-shortage-of-innovative-antibiotics-fuels-emergence-and-spread-of-drug-resistance>. Accessed July 14, 2022.
- Xia, R.Y., Hu, X.Y., Fei, Y.T., Willcox, M., Wen, L.Z., Yu, M.K., Zhang, L.S., Dai, M.Y., Fei, G.H., Thomas, M., Francis, N., 2020. Shufeng Jiedu capsules for treating acute exacerbations of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *BMC Complement. Med. Ther.* 20, 151. <https://doi.org/10.1186/s12906-020-02924-5>
- Xie, W., Liu, X.F., Xu, C.X., Zhou, P., Cao, H.B., 2018. A brief analysis of medicine for treating fever syndrome “Divine Farmer's Classic of *Materia Medica*”. *Lishizhen Med. Mater. Res.* 29, 1415–1418. <https://doi.org/10.3969/j.issn.1008-0805.2018.06.050>
- Xie, Y., Peng, J.Y., Fan, G.R., Wu, Y.T., 2008. Chemical composition and antioxidant activity of volatiles from *Patrinia villosa* Juss obtained by optimized supercritical fluid extraction. *J. Pharm. Biomed. Anal.* 48, 796–801. <https://doi.org/10.1016/j.jpba.2008.08.004>
- Xu, Z.M., Huang, Z.H., Zhu, B., Zhang, Y.H., 2007. Study on the sedative active parts of *Herba Patriniae*. *Zhejiang J. Integr. Tradit. Chin. West. Med.* 17, 347–348. <https://doi.org/10.3969/j.issn.1005-4561.2007.06.009>
- Yang, X.H., 2005. Varietal identification and application of *Patrinia herba*. *Shanxi J. Tradit. Chin. Med.* 21, 44. <https://doi.org/10.3969/j.issn.1000-7156.2005.06.030>
- Zhan, S.N., 2021. Effect of Huatan Qingfei decoction and acupoint application on community acquired pneumonia and its influence on inflammatory response and immune function. *J. Pract. Tradit. Chin. Intern. Med.* 35, 109–112. <https://doi.org/10.13729/j.issn.1671-7813.220190266>
- Zhang, A.R., Cao, J.H., 1996. Research and identification of *Radix physoclainae* and *Patrinia herba*. *Acta Chin. Med.* 11, 20–22. <https://doi.org/10.16368/j.issn.1674-8999.1996.03.010> <https://doi.org/10.1007/s11655-016-2459-4>
- Zhang, Y.Y., Xia, R.Y., Liang, S.B., Hu, X.Y., Dai, M.Y., Li, Y.L., et al., 2021. Chinese patent herbal medicine (Shufeng Jiedu capsule) for acute upper respiratory tract infections: a systematic review and meta-analysis. *Integr. Med. Res.* 10, 100726. <https://doi.org/10.1016/j.imr.2021.100726>
- Zheng, L.T., 2017. Curative effect of Huatan Qingfei decoction and acupoint application on community acquired pneumonia. *J. Sichuan Tradit. Chin. Med.* 35, 80–82.